Trials@uspto.gov
571-272-7822

Paper No. 73
Entered: December 18, 2017

[redacted]

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME CORP.
Petitioner,

v.

MAYNE PHARMA INTERNATIONAL PTY LTD.,
Patent Owner.

Case IPR2016-01186
Patent 6,881,745 B2

Before TONI R. SCHEINER, ERICA A. FRANKLIN, and JACQUELINE T. HARLOW, *Administrative Patent Judges.*

SCHEINER, *Administrative Patent Judge.*

FINAL WRITTEN DECISION
35 U.S.C. § 318(a); 37 C.F.R. § 42.73

I. INTRODUCTION

This is a Final Written Decision in an *inter partes* review challenging the patentability of claims 2, 6, and 9–14 of U.S. Patent No. 6,881,745 B2 (Ex. 1001, "the '745 patent"). 35 U.S.C. § 318(a); 37 C.F.R. § 42.73. We have jurisdiction under 35 U.S.C. § 6.

For the reasons that follow, we determine that Petitioner has demonstrated, by a preponderance of evidence, that claims 2, 6, and 9–14 are unpatentable.

A. Procedural History

Merck Sharp & Dohme Corp. ("Petitioner") filed a Petition (Paper 1, "Pet.") requesting an *inter partes* review of claims 1–3, 5–7, and 9–14 of the '745 patent.[1] Mayne Pharma International Pty Ltd. ("Patent Owner") filed a Preliminary Response (Paper 8, "Prelim. Resp.").[2] In our Decision on Institution (Paper 10, "Decision" or "Dec."), we determined that Petitioner had established a reasonable likelihood that it would prevail in its challenges to claims 1–3, 5–7, 9, 11, 12, and 14 as anticipated by Kai;[3] claims 1, 3, 5,

---

[1] Petitioner supported its Petition with documents titled "Declaration of David W. Grainger, Ph.D." (Ex. 1005), and "Declaration of Terrence F. Blaschke, M.D." (Ex. 1006). Those documents were not in compliance with 37 C.F.R. § 1.68, but were subsequently replaced, with our authorization, by sworn declarations in compliance with § 1.68, but otherwise identical to Exhibits 1005 and 1006. *See* Ex. 1066 ¶ 68; Ex. 1067 ¶ 29.

[2] Patent Owner supported its Preliminary Response with the Declaration of Robert A. Bellantone, Ph.D., dated September 19, 2016 (Ex. 2001, "Bellantone Declaration").

[3] Toshiya Kai et al, *Oral Absorption Improvement of Poorly Soluble Drug Using Solid Dispersion Technique*, 44 CHEM. PHARM. BULL. 568–571 (1996) ("Kai") (Ex. 1007).

and 7 as anticipated by Thorpe;[4] and claims 1–3, 5–7, and 9–14 as obvious over Kai, Sangekar,[5] and Babcock,[6] and instituted trial on those three grounds. Dec. 15–21, 23–25, 25–27. Subsequently, we granted Patent Owner's Motion to Amend (Paper Nos. 29, 61), canceling claims 1, 3, 5, and 7. Consequently, the claims and grounds remaining for consideration in this trial are:

References	**Basis**	**Claims Challenged**
Kai	§ 102	2, 6, 9, 11, 12, and 14
Kai, Sangekar, and Babcock	§ 103	2, 6, and 9–14

Following institution, Patent Owner filed a Response (Paper 30 (unredacted, confidential), "PO Resp."),[7] and Petitioner filed a Reply (Paper 40 (unredacted, confidential), "Reply").[8] Patent Owner supports its

[4] John E. Thorpe et al., *Effect of Oral Antacid Administration on the Pharmacokinetics of Oral Fluconazole*, 34 ANTIMICROBIAL AGENTS AND CHEMOTHERAPY 2032–2033 (1990) ("Thorpe") (Ex. 1020).
[5] WO 98/00113 A1, Surendra Sangekar et al., published January 8, 1998 ("Sangekar") (Ex. 1015).
[6] EP 1 027 886 A2, Walter Christian Babcock et al., published August 16, 2000 ("Babcock") (Ex. 1009).
[7] Patent Owner filed an unopposed Motion for Entry of Protective Order (Paper 17), and a Motion to Seal its Patent Owner Response, as well as certain confidential exhibits attached thereto. Paper 28. Patent Owner also filed a redacted version of the Preliminary Response. Paper 29. Citations herein apply to both redacted and unredacted versions of the Preliminary Response. Both Motions will be addressed in a separate order.
[8] Petitioner filed a Motion to Seal its Reply, as well as certain confidential exhibits attached thereto. Paper 38. Petitioner also filed a redacted version

Response with the Supplemental Declaration of Dr. Robert Bellantone (Ex. 2066). Petitioner supports its Reply with the Declarations of Mark G. Papich, D.V.M. (Ex. 1089) and Edmund J. Elder, Ph.D. (Ex. 1096).

Petitioner and Patent Owner each filed a Motion to Exclude certain exhibits and declaration testimony (Papers 48, 52, respectively); Petitioner and Patent Owner each filed an Opposition to the Motion of the other party (Papers 57, 56); and Petitioner and Patent Owner each filed a Reply to the other party's Opposition (Papers 63, 64). In addition, Patent Owner filed a Motion for Observation on Cross-Examination of Dr. Mark Papich (Paper 53), and a Motion for Observation on Cross-Examination of Dr. Edmund Elder (Paper 54). Petitioner filed Responses to each of Patent Owner's Motions for Observation (Papers 58, 59).

Oral argument was heard on September 13, 2017, and a transcript of the argument has been entered into the record (Paper 69, "Tr.").

B. Related Proceedings

The '745 patent has been asserted against Petitioner in *Mayne Pharma International Pty Ltd. v. Merck & Co., Inc. and Merck Sharp & Dohme Corp.*, Civil Action No. 15-438 (LPS) (CJB) (D. Del.), filed May 29, 2015. Pet. 56; Paper 5, 2; Prelim. Resp. 54. Petitioner was served with the complaint in that litigation on June 12, 2015. Pet. 56 (citing Ex. 1057, 1058).

---

of its Reply. Paper 41. Citations herein apply to both the redacted and unredacted versions of Petitioner's Reply. The Motion will be addressed in a separate paper.

C. The '745 Patent (Ex. 1001)

The '745 patent, titled "PHARMACEUTICAL COMPOSITIONS FOR POORLY SOLUBLE DRUGS," issued April 19, 2005 to David Hayes and Angelo Mario Morella. The specification describes "pharmaceutical compositions of drugs that are practically insoluble in aqueous media" (Ex. 1001, 1:17–19), e.g., azole antifungal drugs (*id.* at 4:66–5:15). According to the specification, "[b]y utilizing compositions in accordance with the present invention . . . drugs previously considered to present bioavailability problems may be presented in dosage forms with superior bioavailability." *Id.* at 7:22–25. Further according to the specification, "the specific benefits of the pharmaceutical composition . . . have been established by the inventors for azole antifungal drugs, such as itraconazole and saperconazole." *Id.* at 4:66–5:2.

The specification teaches that "the composition may be in the form of a solid dispersion of the practically insoluble drug and a polymer having acidic functional groups, and the composition may in vitro form a suspension." *Id.* at 2:52–55. "[T]he ratio of drug to polymer may be in the range of from 3:1 to 1:20 . . . [but] ratios in the narrower range of 3:1 to 1:5" or "1:1 to 1:3" or "1:1.5" are preferred. *Id.* at 5:46–50. Further, the polymers "may be one or more of the group comprising hydroxypropyl methylcellulose phthalate, polyvinyl acetate phthalate, (PVAP), hydroxypropylmethylcellulose acetate succinate (HPMCAS)" (*id.* at 5:25–28), and a particularly preferred polymer is "a polycarboxylic acid such as a hydroxypropyl methylcellulose phthalate such as . . . HP-50, HP-55 or HP-55S" (*id.* at 5:36–40).

Preferably, the "solid dispersion is formed by dispersing or dissolving the drug and the polymer in a suitable solvent, and subsequently spray drying to form the solid dispersion in the form of a powder" (*id.* at 5:58–61) "suitable for use in dosage forms such as tablets or capsules" (*id.* at 5:66).

According to the specification, "where the drug is itraconazole the inventive compositions have produced formulations that . . . have at least twice the bioavailability of, a commercially available itraconazole product (Sporanox™)." *Id.* at 7:27–30. For instance, in a randomized two-way crossover study, eight male volunteers were alternately dosed with a solid dispersion comprising 98 to 102 mg itraconazole and HP-50, and with "100 mg itraconazole as a marketed capsule (Sporanox™)," after an intervening washout period. *Id.* at 9:17–45. The pharmacokinetic performance of the two formulations is shown in the table below:

Parameter	Example capsule	Sporanox ™ capsule (Lot 98P0800E)	Ratio
C_{max} (ng/ml)	182.6	56.0	326%
T_{max} (h)	2.94	3.44	85.5%
AUC (ng.h/ml)	1776	622	285%
AUC_{inf} (ng.h/ml)	1875	664	282%

Id. at 9:50–57. According to the specification, "it can be seen from these results that significantly higher plasma itraconazole levels are obtained from the [test] formulation described in the example than the marketed capsule form under these conditions." *Id.* at 9:59–62.

D. Illustrative Claims

Petitioner challenges claims 2, 6, and 9–14 of the '745 patent, of which claims 9 and 12 are independent claims. Claims 9 and 12 are illustrative.

> 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 C_{MAX} of at least 100 ng/ml, after administration in the fasted state.

Id. at 11:15–28.

Claim 12 is identical to claim 9, except that the final clause reads "wherein in vivo the composition provides a mean AUC of at least 800 ng.hr/ml, after administration in the fasted state." *Id.* at 11: 33–45.

Claim 2 depends from canceled claim 1, and is of the same scope as claim 9, except that it lacks a recitation of the optional "one or more additional ingredients." Similarly, claim 6 depends from canceled claim 5, and is the same as claim 12, except that it lacks a recitation of the optional "one or more additional ingredients."

Claims 11 and 14 depend from claims 9 and 12, respectively, and specify that the pharmaceutical composition is in the form of a powder. Claims 11 and 13 depend from claims 9 and 12, respectively, and specify that the pharmaceutical composition is present in a capsule.

II. DISCUSSION

Petitioner bears the burden of proving unpatentability of the challenged claims, and the burden of persuasion never shifts to the patent owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). To prevail, petitioner must establish the facts

supporting its challenge by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d).

A. Level of Ordinary Skill in the Art

We begin by addressing the level of ordinary skill in the art. Patent Owner, supported by the testimony of Dr. Bellantone, contends that one of ordinary skill in the relevant art is "someone with a doctorate in Pharmaceutical Sciences, Chemistry, or Chemical Engineering, or similar or related field, and who has two or more years of experience in one or more aspects of pharmaceutics, such as drug preformulation or drug formulation." PO Resp. (citing Ex. 2066 ¶¶ 35–37). "Alternatively, the [person of ordinary skill in the art] may hold a Master's degree or undergraduate degree in a similar field and have at least five to seven years of additional experience." *Id.*

Petitioner, supported by the testimony of Dr. Grainger, describes one of ordinary skill in the art as a pharmaceutical chemist with "(1) an advanced scientific degree such as a Ph.D., M.D., Pharm D., or a Master's degree in chemistry, biochemistry, pharmacology, pharmaceutics, or a related field," or "(2) equivalent experience in chemistry, biochemistry, pharmacology, pharmaceutics, or a related field with experience in developing pharmaceutical formulations, optionally with a focus on formulations of poorly soluble drugs." Pet. 12–13 (citing Ex. 1005 ¶¶ 28–29). Petitioner further asserts that:

> These qualifications are not rigid. Greater education or a specific skill may make up for less experience, and vice-versa. Moreover, one individual need not have every qualification. A multidisciplinary with the necessary expertise in its ranks would suffice. Such a team could include—and a physical chemist

> would draw upon the skills of—a clinician having experience in treating antifungal infections.

Id. at 13 (citing Ex. 1005 ¶ 29).

There is considerable overlap between Patent Owner's and Petitioner's descriptions, as they are couched in overlapping, inclusive terms, such as "related field," "similar field," and "equivalent experience." We adopt Patent Owner's description, but determine that our disposition of this case would be the same under either description.

B. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under that standard, claim terms generally are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). *See also Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016) ("Under a broadest reasonable interpretation, words of the claim must be given their plain meaning, unless such meaning is inconsistent with the specification and prosecution history."). The Specification "is always highly relevant to the claim construction analysis. Usually it is dispositive, it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Any special definition for a claim term must be set forth in the specification with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994). Finally, only terms which

are in controversy need to be construed and only to the extent necessary to resolve the controversy. *See Nidec Motor Corporation v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017).

We determine that the following claim terms, recited directly or indirectly in all the challenged claims, require construction for resolution of the controversy in this case:

"*wherein in vivo the composition provides a [certain C_{MAX} or AUC level], after administration in the fasted state*" (the "wherein" clauses);

"*pharmaceutical composition*;" and

"*azole antifungal drug*."

The first of these claim terms is addressed immediately below. The meanings of the remaining terms are interrelated and are discussed below in Section II.C.2, in the context in which they arise.

"wherein in vivo the composition provides a [certain C_{MAX} or AUC level], after administration in the fasted state"

In the Petition, Petitioner contended that "the wherein clauses are not limiting (Pet. 16), but that Kai nevertheless discloses "C_{MAX} or AUC parameters for 100 mg azole doses *in vivo*" (*id.* at 23). In the Decision on Institution, based on the then existing record, we determined "as a necessary property of the claimed composition, the C_{MAX} and AUC parameters recited in the claims give meaning and purpose to the claims," and therefore, "meaningfully limit the claims, and are entitled to patentable weight." Pet. 10. Patent Owner concurs with this aspect of our construction (PO Resp. 17), and Petitioner does not dispute it. Having reconsidered the matter in light of the record developed at trial, we maintain this aspect of our construction.

The parties, however, disagree on the scope of the wherein clauses. In our provisional claim construction in the Decision on Institution, we noted that the specification explicitly states that "in vivo," the exact term used in the wherein clauses, "in general means in the living body of a plant or animal." Dec. 11 (citing Ex. 1001, 3:36–37). We further noted that although the specification discloses the results of a specific clinical trial involving administration of a particular azole, itraconazole, to humans, the challenged claims do not recite expressly that the pharmacokinetic parameters are in humans, nor, for that matter, do the challenged claims require any particular azole, much less the azole used in the clinical trial. *Id.* As it is generally improper to import limitations into a claim from an embodiment appearing in the written description when the claim language is broader than the embodiment, and we did not perceive that the patentees of the '745 patent had demonstrated a clear intention to so limit the claims, we determined that the broadest reasonable interpretation of the wherein clauses includes pharmacokinetic parameters in other animals, in addition to humans.[9]

[9] *See, e.g.*, *Superguide Corp. v. DirecTV Enterprises, Inc.,* 358 F.3d 870, 875 (Fed. Cir. 2004); *see also Liebel-Flarsheim Co. v. Medrad Inc.,* 358 F.3d 898, 906 (Fed. Cir. 2004) (discussing recent cases where the court expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1327 (Fed. Cir. 2002) (Even when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using "words or expressions of manifest exclusion or restriction.").

In its Petition, Petitioner contended that Kai discloses "C_{MAX} or AUC parameters for 100 mg azole doses *in vivo*" (Pet. 23), implicitly contending that Kai's parameters, measured in dogs, are measured in vivo. In its Reply, Petitioner contends, consistent with our provisional determination in the Decision on Institution (Dec. 12), that the broadest reasonable interpretation of the wherein clauses encompasses providing the requisite pharmacokinetic parameters in humans, but does not "limit[] the claims to pharmacokinetic parameters in humans" (Reply 13).

Patent Owner argues, as it did in its Preliminary Response, that "the clauses are properly construed to be limited to ***human*** C_{MAX} and AUC" parameters only. PO Resp. 17; *see also* Prelim. Resp. 21. According to Patent Owner, "it would be unreasonable to interpret the scope of the 'wherein' clauses in view of the general description of 'in vivo'" (PO Resp. 21), and a person of ordinary skill in the art "would understand that the statement was not intended to be definitional but meant merely to contrast 'in vivo' with 'in vitro'" (*id.*). In other words, Patent Owner argues essentially that one of ordinary skill in the art would understand "in vivo" to mean "in humans," in the context of the specification and claims. Patent Owner argues that a *Markman* decision in the co-pending district court litigation (issued subsequent to our Decision on Institution) held that "a person of ordinary skill in the art, in the context of this patent, would understand the claims to be limited to humans." PO Resp. 17 (citing Ex. 2065, 13). According to Patent Owner, "the parties' experts agree—that there is significant interspecies variability in the pharmacokinetics of a drug and that human pharmacokinetics are different from all non-human animals" (PO Resp. 18 (citing *inter alia*, Ex. 2001 ¶ 89; Ex. 2081 (Dr. Blaschke's

Deposition), 57–83)), and that this variability, at least in part, formed the basis of the district court's holding in the *Markman* hearing (*id.* (citing Ex. 2065, 13; Ex. 2066 ¶¶ 60–75)). In particular, the district court explained "because it is 'well-known and documented that azoles produce a variation in pharmacokinetic values between species,' a person of ordinary skill 'would immediately understand'—given the results reported from administration of an about 100 mg dose [to humans]—'that the claims of the '745 patent are directed to humans only.'" Ex. 2065, 13.

In a similar vein, Patent Owner contends that "the specification provides data from an *in vitro* dissolution assay performed at pH environments of 6.0 and 1.2 . . . typical parameters used to mimic the pH environments in the human small intestine and stomach," respectively. PO Resp. 20 (citing Ex. 1001:8:33–9:15). According to Dr. Bellantone, one of ordinary skill in the art "would understand that these are typical parameters used to mimic the pH environments in the human small intestine and stomach." Ex. 2001 ¶ 71.

In response, Petitioner argues that the '745 patent's "human testing examples do not limit" the wherein clauses to pharmacokinetic parameters in humans. Reply 12. Specifically, Petitioner argues that "if the examples were to be imported, they could not be imported piecemeal—they would have to be imported in their entirety" and "[t]hat would limit the claims not to just humans but also to itraconazole, which already has its own separate claims in the Patent."[10] *Id.* at 17–18. Moreover, Petitioner notes that the '745 patent indicates that "its formula 'preferably' should provide

[10] All of the non-challenged claims remaining in the '745 patent (i.e., claims 4, 8, 15, and 16) are limited to compositions containing itraconazole.

'acceptable absorption in the intestines' at pH ranges of '4.0 to 8.0.'" Reply 14; *see* Ex. 1001, 7:41–44 ("Preferably, the composition upon administration forms a suspension at a pH in the range of 4.0 to 8.0, but more preferably in the range 5.5 to 7.5, and may provide acceptable absorption in the intestines.").

Patent Owner further argues that "construing the 'wherein' clauses as directed to all animals would lead to absurd results" because "[t]here are numerous species of animals representing enormous physical and physiological variation," ranging from, e.g., "the 1.8 gram Etruscan shrew to the 7 ton bush elephant." PO Resp. 18. Patent Owner argues that "the minuscule shrew would likely perish if administered the '100 mg of an azole antifungal drug' recited in claim [9]" and "the elephant would be unlikely to achieve ***any*** appreciable C_{MAX}, let alone the recited 100 ng/ml, because of its enormous body mass." *Id.* at 19. According to Patent Owner, "interpreting the claims to encompass all animals would render meaningless the primary inventive aspect of the invention claimed in the '745 patent—the improved bioavailability of an azole antifungal drug in the fasted state" because "such improved absorption would make no difference in small animals like the shrew or large animals like the elephant for the claimed 100 mg dose because of their size in relation to the dose." *Id.*

Petitioner contends that "[t]his argument subtly smuggles a non-existent word into the Patent." Reply 17. Petitioner argues that the '745 patent "never says the thresholds must be met in 'all' *in vivo* models," rather, the '745 patent teaches that the thresholds must be met in an in vivo system, not every conceivable in vivo system. *Id.* Petitioner contends that this interpretation is consistent with the specification's use of "the unrestricted

term 'or' to define '*in vivo*' as in 'plants or animals.'" *Id.* "In other words," Petitioner argues, "so long as the composition produces the C_{MAX} and AUC minimums in *any* living system, that suffices." *Id.*

Finally, Patent Owner contends that "the prosecution history further demonstrates that the claims are limited to humans." PO Resp. According to Patent Owner:

> During prosecution, the Examiner rejected claims 1–11 as being anticipated by [Gilis].[11] (Reply Under 37 C.F.R. §1.111 (Feb. 17, 2004), Ex. 1004 at 0079, 0082.) The Examiner argued that [Gilis] inherently disclosed "a mean C_{MAX} of at least 100 ng/ml and an AUC of at least 800 ng.h/ml and a reduced food effect compared to the drug after administration in the fasted state." (Ex. 1004 at 0084.) Applicant argued that human tests in the patent examples with Sporanox, the commercial embodiment of [Gilis], did not produce the claimed C_{MAX} or AUC. (Id. at 0087; '745 patent at Ex. 2.) Thus, a POSA would understand that the Applicant relied on the human pharmacokinetic parameters reported in the '745 patent to distinguish [Gilis]. (Ex. 1004 at 0084; Ex. 2066 at ¶¶ 71–75.) At no time did the Examiner or the Applicant discuss the need for animal data to distinguish [Gilis]. As Petitioner told [the district court], and as a POSA would have understood, "[k]nowing the species of the subject taking the composition is critical in assessing C_{MAX} and AUC." (Ex. 2010 at 13 (Merck's Opening Claim Construction Brief).) Thus, a POSA would understand that the wherein clauses are limited to humans.

PO Resp. 22.

Petitioner disputes Patent Owner's characterization that "it used human testing data to distinguish the prior art Gilis reference in prosecution, allegedly thereby limiting the claims to humans." Reply 18. Petitioner

---

[11] U.S. Patent No. 5,633,015, issued May 27, 1997 to Paul M.V. Gilis, et al. (not submitted as an exhibit in this proceeding, but listed on the first page of the '745 patent).

contends that "Gilis is a patent on the formula for Sporanox®, an itraconazole product for humans and animals." *Id.* (citing Ex. 2069, 7, 27). Petitioner contends that "[a]fter rejection, [Applicants] argued that Gilis did not inherently—or "necessarily"—anticipate Mayne's claimed C_{MAX} and AUC levels because the compositions were made differently and had different forms." Reply 18 (citing Ex. 1004, at 86–89). Petitioner contends that the testing data was cited "only to show its formula improved upon Sporanox's bioavailability." *Id*. Petitioner contends that the arguments presented to the Examiner "had nothing to do with distinguishing Gilis based on human use." *Id.*

Having considered Petitioner's and Patent Owner's arguments developed at trial, and the evidence discussed above, including the prosecution history relied on, we are not persuaded that the broadest reasonable interpretation of the wherein clauses in light of the specification limits the pharmacokinetic parameters to humans.

First, we recognize that we must consider whether the district court's construction of the wherein clauses is consistent with the broadest reasonable construction of the term,[12] but are "not generally bound by a prior judicial construction of a claim term." *Power Integrations, Inc. v. Lee*, 797 F.3d 1318, 1326 (Fed. Cir. 2015). We further recognize that the broadest reasonable interpretation of disputed claim terms is "a different claim

[12] When a claim term has previously been construed by a district court, the Board must "assess whether [the court's] interpretation [is] consistent with the broadest reasonable construction of the term." *Power Integrations, Inc. v. Lee*, 797 F.3d 1318, 1324-27 (Fed. Cir. 2015).

construction standard than that applied by a district court" (*id.*), and may sometimes produce a different result.

Second, the specification of the '745 patent, following the stipulation that "[v]arious terms that will be used throughout this specification have meanings that will be well understood by a skilled addressee . . . will now be defined" (Ex. 1001, 3:7–10), states that "[t]he 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" (*id.* at 3:36–38). This definition is consistent with the plain meaning of the term "in vivo" as it would have been understood by one of ordinary skill in the art at the time of the invention of the '745 patent. *See, e.g.*, Ex. 1089 ¶ 6. Furthermore, there is nothing in the claims of the '745 patent to support deviation from the well accepted "general" definition of "in vivo" set forth in the specification.

Third, the only in vivo examples in the '745 patent involve administering a particular azole antifungal drug, itraconazole, to humans. Ex. 1001, 9:34–10:49. While we agree that the evidence of record supports Patent Owner's contention that significant interspecies variability exists in the pharmacokinetics of a drug, it is equally true that significant variability exists in the pharmacokinetics of different drugs or even different formulations of the same drug. *See, e.g.*, Ex. 1001, 7:27–30. Yet Patent Owner does not contend that the challenged claims are limited to any particular azole, nor would such an assertion bear scrutiny. We are not persuaded that one of ordinary skill in the art would understand "in vivo" in the claims to be limited to "in humans" based on the '745 patent's examples, given that the claims are not limited to the specific azole used in the

examples. Moreover, to the extent Patent Owner argues that the pH 6.0 recited in the dissolution assay mimics the pH of the human small intestine (PO Resp. 20), we note that the specification discloses a broader range: the composition preferably "upon administration forms a suspension at a pH in the range of 4.0 to 8.0, but more preferably in the range 5.5 to 7.5, and may provide acceptable absorption in the intestines" (Ex. 1001, 7:41–44). Again, we are not persuaded that one of ordinary skill in the art would understand "in vivo" in the claims to be limited to "in humans" based on the narrower pH used in the dissolution assays.

Fourth, Patent Owner's argument that "the minuscule shrew would likely perish if administered the '100 mg of an azole antifungal drug'" and "the elephant would be unlikely to achieve ***any*** appreciable C_{MAX}, let alone the recited 100 ng/ml, because of its enormous body mass" (PO Resp. 19) amounts to a binary choice between requiring that the composition provide the requisite minimum threshold pharmacokinetic parameters in humans and requiring that the composition provide those parameters in "all animals." This is a false choice. The claims are directed to the scenario where 100 mg of the composition is administered to a living animal produces at least a minimum C_{MAX} value. It is irrelevant that some animals will not satisfy both requirements. We agree with Petitioner that it is sufficient that the recited dose of the claimed composition produces the C_{MAX} and AUC minimums in a living system, irrespective of whether it does so in every living system.

Finally, we have reviewed the prosecution history of the '745 patent relied on by Patent Owner, and determine that it supports Petitioner's, rather than Patent Owner's contentions. That is, the arguments presented to the Examiner in response to an anticipation rejection based on inherency

focused on the differences between itraconazole formulations prepared according to the application that ultimately matured into the '745 patent, and "Sporanox™," the commercial embodiment of an itraconazole formulation prepared as disclosed in Gilis. Ex.1004, 86–89. We agree with Petitioner that the arguments presented therein "had nothing to do with distinguishing Gilis based on human use." Reply 18.

Having considered Petitioner's and Patent Owner's arguments developed at trial, and the evidence addressed above, we maintain our determination that the broadest reasonable interpretation of the wherein clauses encompasses C_{MAX} and AUC parameters in humans, but does not limit the wherein clauses to humans.

C. Anticipation of Claims 2, 6, 9, 11, 12, and 14 by Kai

Petitioner contends that Kai discloses administering to dogs a pharmaceutical composition consisting essentially of 100 mg of an azole antifungal drug and a polymer with acidic functional groups (Pet. 20, 24 (citing Ex. 1007, 568; Ex. 1005 ¶ 38)),[13] and achieves the requisite pharmacokinetic properties (*id.* (citing Ex. 1007, 570; Ex. 1005 ¶ 40)). Patent Owner counters that Kai fails to anticipate the challenged claims because Kai "does not disclose pharmacokinetic parameters in humans" (PO Resp. 24), and also fails to disclose a "pharmaceutical composition" or azole antifungal "drug" because Kai's compound is "toxic and thus not suited for pharmaceutical use" (*id.* at 26).

[13] Exhibit 1005 was superseded by Exhibit 1066, which is identical to Exhibit 1005, except for the addition of a final paragraph in Exhibit 1066. Thus, citations to Exhibit 1005 in the Petition are equivalent to citations to Exhibit 1066 in subsequent papers.

1. Kai (Ex. 1007)

Kai discloses a solid dispersion technique for improving the oral absorption of the "triazol[e] antifungal agent," MFB-1041. Ex. 1007, 568. According to Kai, MFB-1041 "is an orally active triazol[e] antifungal agent which may have therapeutic benefits in aspergillus treatment" (*id.*), but "has low solubility and potentially poor oral absorption characteristics" (*id.*). Kai prepared a "solid dispersion" of MFB-1041 by dissolving it in a mixed solvent; adding a polymer to the solution (e.g., HP-55, a preferred polymer of the '745 patent) at a "drug-to-polymer" ratio of 1:1–1:5; and spray-drying the mixture to obtain a "solid dispersion powder." *Id.* The solid dispersion powder was administered to beagle dogs (10–12 kg each) "*per os* with 20 ml of water under a fasted condition at a dose of 10 mg/kg body weight." *Id.* The pharmacokinetic properties of several different formulations of MFB-1041 are shown in Table 1 below.

Table 1. Pharmacokinetic Parameters of MFB-1041 after Oral Administration to Beagle Dogs

Dosage forms	C_{max} (μg/ml)	T_{max} (h)	AUC (μg/ml h)
Crystal (MC suspension)	—	0.5	1.0
Metolose solid dispersion (1:5)	0.95	4	6.0
CMEC solid dispersion (1:5)	1.73	3	11.8
HP-55 solid dispersion (1:3)	1.90	2	11.8
HP-55 solid dispersion (1:5)	2.59	4	16.9

Ex. 1007, 570.

2. Analysis

Petitioner contends that Kai discloses a composition consisting essentially of a solid dispersion of a triazole compound, MFB-1041, and a polymer with acidic functional groups, which, when administered orally to living beagle dogs (10–12 kg each) in the fasted state, at a dose of 10 mg/kg

of body weight, provides a mean C_{MAX} above 100 ng/ml and a mean AUC above 800 ng.h/ml. Pet. 20, 24; Reply 4. Specifically, Petitioner contends that Kai's triazole, MFB-1041, is an "azole antifungal drug;" that Kai's solid dispersion powder containing MFP-1041 is a "pharmaceutical composition;" and that Kai's composition provides the requisite pharmacokinetic parameters in vivo. Pet. 20, 24 (citing Ex. 1007, 568, 570; Ex. 1005 ¶¶ 38, 40); Reply 5, 12.

Patent Owner contends that Kai "does not disclose pharmacokinetic parameters in humans," as required by the claims when properly construed (PO Resp. 24), and also fails to disclose a "pharmaceutical composition" or azole antifungal "drug" because Kai's MFB-1041 compound is "toxic and thus not suited for pharmaceutical use" (*id.* at 26).

Kai discloses Pharmacokinetic Parameters In Vivo

Patent Owner contends that Kai does not anticipate the challenged claims because the resultant C_{MAX} and AUC levels reported were not obtained in humans. Nevertheless, as discussed above in Section II.B.1, we determine that the broadest reasonable interpretation of the wherein clauses encompasses pharmacokinetic parameters in humans, but is not limited to humans.

Accordingly, having considered the record developed at trial, we agree with Petitioner that Kai discloses a composition consisting essentially of 100 mgs of an azole and a polymer with acidic functional groups, which,

in vivo, provides a mean C_{MAX} of at least 100 ng/ml and a mean AUC of at least 800 ng.h/ml, after administration in the fasted state.[14]

That determination, however, does not end the matter, and we turn to the question of whether Kai discloses a "pharmaceutical composition" containing an "azole antifungal drug" within the meaning of the claims—with particular emphasis on the meaning of the term "drug."

Kai Discloses a Pharmaceutical Composition Consisting Essentially of an Azole Antifungal Drug

Patent Owner contends that "Kai also does not anticipate because it does not disclose the 'pharmaceutical composition' or 'drug' recited in the claims." PO Resp. 26.

Patent Owner contends that "the patent examples demonstrate the improved properties of the inventive pharmaceutical composition by way of human clinical trials," and one of ordinary skill in the art "would have known that human testing is not permissible absent some evidence that the ingredients are suitable for administration to human subjects." *Id.* at 11 (citing Ex. 1001, 9:18–10:49; Ex, 2066 ¶¶ 41–43). Similarly, Patent Owner contends that the claim term "azole antifungal drug" should be construed as "a compound with an azole moiety having beneficial prophylactic and/or therapeutic antifungal properties when administered." PO Resp. 15. Patent Owner further contends "[a]s properly construed, therefore, a 'drug' must have some clinical relevance as determined by an assessment of its

[14] We note Patent Owner's argument that Kai's "dog pharmacokinetic data cannot be extrapolated to humans" (PO Resp. 25), but the argument is irrelevant. As discussed in Section II.B, we have determined that achieving the required minimum pharmacokinetic parameters in humans is not a requirement of the claims.

therapeutic or prophylactic benefits, as well as its adverse effects." *Id.* at 15–16.

Patent Owner contends that "Kai states without citation that MFB-1041 is an 'orally active' antifungal agent and speculates that it '***may***' have therapeutic benefit in aspergillus treatment." PO Resp. 28. Moreover, Patent Owner contends that Kai's MFB-1041 compound was known to be "toxic and thus [not a drug, and] not suited for pharmaceutical use." *Id.* at 26. Patent Owner notes that "Miyoshi reported that MFB-1041 caused clonic convulsions in mice when administered as an intravenous dose of 10 mg/kg—the same dose disclosed in Kai." *Id.* (citing Ex. 2009, 1; Ex. 2066 ¶¶ 80–88). According to Patent Owner, "[c]lonic convulsions involve repeated violent muscle contractions, which is a serious toxicity effect" (*id.* at 27 (citing Ex. 2066 ¶ 83), and "[f]or this reason alone, Kai cannot anticipate the Challenged Claims" (*id.* (citing *Mitsubishi Chem. Corp. v. Barr Labs, Inc.*, 435 F. App'x 927, 935 (Fed. Cir. 2011)).

Finally, Patent Owner cites Dr. Bellantone's testimony that he "confirmed with Dr. Kai . . . that MFB-1041 was never commercialized because it posed insurmountable toxicity problems" and "was never even tested in humans due to its unacceptable hepatic toxicity problems, which was evident even in animal studies." PO Resp. 29 (citing Ex. 2066 ¶¶ 89–93).

In response, Petitioner contends that Patent Owner "consistently described Kai's azole as a 'drug' mixed in a 'pharmaceutical composition'" prior to the present challenge. Reply 5. For example, Petitioner contends that the specification of the '745 patent repeatedly "call[s] the compound a

'drug' five times in only a few lines of text." *Id.* at 6 (citing Ex. 1001, 1:63–2:11). Similarly, Petitioner contends that:

> The Petition describes (at 7) how the parent application claimed a "pharmaceutical composition" of a "drug" based on the same specification, albeit a narrower composition than in the Patent. In prosecuting those parent claims, [Patent owner] spent years trying, and failing, to overcome Kai. [Patent Owner] never once argued in that time that Kai's azole was not a "drug" in a "pharmaceutical composition." Just the opposite: [Patent Owner] certified that Kai's azole is a "drug" in a "pharmaceutical composition."

Reply 6 (citing Ex. 1089 ¶¶ 29–35; Ex. 1003, 467–471, 475–487, 523-529).

Petitioner contends that nothing in the specification "excludes azoles with potentially negative as well as therapeutic properties" (*id.* at 7), and moreover, the '745 patent "expressly covers another known azole unsuited for human medicine, saperconazole" (*id.*). Petitioner points to a passage in the specification stating that "the specific benefits of the pharmaceutical composition . . . have been established by the inventors for azole antifungal drugs, such as . . . saperconazole." *Id.* (citing Ex. 1001, 4:66–5:3). Petitioner contends that "[s]aperconazole had been a promising antifungal, but its development had been discontinued in the 1990s—years before [Patent Owner] filed for the Patent—due to adverse side effects" (*id.*), and "Dr. Bellantone himself submitted a 1996 reference describing that history" (*id.* (citing Ex. 2001 ¶ 97 (citing, in turn, Ex. 2019, 3))). According to Petitioner, when asked about the passage explicitly identifying saperconazole as an azole antifungal drug, "Dr. Bellantone acknowledged on cross that this passage is 'inconsisten[t]' with the idea that the Patent does not cover azoles unsafe for humans." Reply 8 (citing Ex. 1088, 159:12–21).

Finally, Petitioner contends that Patent Owner's reliance on *Mitsubishi* for the broad premise that toxicity precludes a composition from being a pharmaceutical composition is inapposite here. Petitioner notes that the court in that case found that a highly acidic prior art mixture was not a "pharmaceutical composition for injection," but nevertheless "refused to limit the term to 'those compositions that are 'safe, effective, and reliable for use in humans.'" Reply 11 (citing *Mitsubishi*, 435 F. App'x at 934).

In order to determine whether Kai's MFB-1041 qualifies as an "azole antifungal drug" in a "pharmaceutical composition" within the broadest reasonable interpretation of those terms, we turn again to the specification and prosecution history of the '745 patent.

The specification states that "[t]he term 'drug' will be widely understood and denotes a compound having beneficial prophylactic and/or therapeutic properties when administered to, for example, humans." Ex. 1001, 3:20–22. With respect to the term "azole antifungal drug," the specification states that "the specific benefits of the pharmaceutical composition . . . have been established by the inventors for azole antifungal drugs, such as itraconazole and saperconazole, [but] similar benefits will be available for other classes of drugs." *Id.* at 4:66–5:3. Thus, itraconazole (to which the unchallenged claims are limited) and saperconazole are expressly identified as "azole antifungal drugs" suitable for "pharmaceutical composition[s]." Finally, the term "pharmaceutical composition" is not explicitly defined, but is described throughout the specification as containing a practically insoluble drug, e.g., itraconazole or saperconazole. *See, e.g.*, *id.* at 2:64–65, 4:66–5:37:45–48. There is no mention in the specification of

adverse effects—potential or otherwise—in connection with any of these terms.

We attach no significance to the specification's use of the term "drug" in discussing the Kai reference, as much of the language in the specification concerning Kai appears to be reproduced from the Kai reference itself. Ex. 10011:63–2:11. As for the prosecution history of the '745 patent, for similar reasons, we attach little significance to the Applicants' repeated references to Kai's MFB-1041 as a "drug," and to Kai's formulation of MFB-1041 as a "pharmaceutical composition" during prosecution of the '745 patent before the Examiner. Ex. 1003, 467–471, 475–487, 523-529.

However, Patent Owner's position that Kai's MFB-1041 cannot be a "drug," and therefore, a composition containing MFB-1041 cannot be a "pharmaceutical composition," is undercut by the explicit identification of saperconazole as an "azole antifungal drug" suitable for use in the "pharmaceutical compositions" of the '745 patent. Ex. 1001, 4:66–5:2 ("[T]he specific benefits of the pharmaceutical composition of the present invention have been established by the inventors for azole antifungal drugs, such as itraconazole and saperconazole."). As noted by Petitioner, Patent Owner's witness, Dr. Bellantone, cited Graybill (Ex. 2019) as evidence that another azole antifungal drug, genaconazole, was highly effective in clinical studies of certain fungal infections, but was withdrawn from those studies because hepatocellular carcinomas developed in laboratory animals that received it. Ex. 2001 ¶ 97 (citing Ex. 2019, 3). As Petitioner points out (Reply 7–8), Graybill further discloses that saperconazole also "appeared promising during early clinical development," but "was also withdrawn from

clinical trial because tumors appeared in laboratory animals that received it." Ex. 2019, 3.

As for Petitioner's characterization of Dr. Bellantone's testimony on cross examination, it is a mischaracterization to say that Dr. Bellantone acknowledged that the specification's identification of saperconazole as an azole antifungal agent is 'inconsisten[t]' with the idea that the Patent does not cover azoles unsafe for humans." Reply 8 (citing Ex. 1088, 159:12–21). What Dr. Bellantone actually acknowledged was an inconsistency between the identification of saperconazole and "the definition of the term 'drug' in column 3" of the '745 patent. That is, Dr. Bellantone testified that the identification of saperconazole as an azole antifungal drug is inconsistent with the definition of "drug" in column 3 because "they are talking about something that has beneficial prophylactic and/or therapeutic properties when administered, say, to humans." Ex. 1088, 159:12–160:19. Even so, it amounts to the essentially same thing, as the specification clearly and explicitly identifies saperconazole as an "azole antifungal drug," and the specification's definition of "drug" discusses beneficial properties, but says nothing about adverse effects.

Having considered the arguments and evidence developed at trial, we agree with Petitioner that Kai discloses a "pharmaceutical composition" containing an "azole antifungal drug" within the meaning of the claims.

3. Conclusion as to Anticipation

For the reasons discussed above, we determine that Petitioner has shown by a preponderance of the evidence that Kai discloses a 100 mg pharmaceutical composition consisting essentially of an azole antifungal drug and a polymer with acidic functional groups, wherein the composition

provides the requisite pharmacokinetic parameters in vivo when administered in the fasted state. Accordingly, we determine that Petitioner has demonstrated, by a preponderance of the evidence that claims 2, 6, 9, 11, 12, and 14 are anticipated by Kai.

D. Obviousness of claims 2, 6, and 9–14 over Kai, Sangekar, and Babcock

In the Petition, Petitioner contended essentially that the "[t]he differences between the prior art and the '745 patent are non-existent, or at most so small as to be an obvious step for a skilled pharmaceutical chemist to take." Pet. 45. Petitioner noted, however, that "various claims in the ['745] patent have miscellaneous features, including requiring the composition to be in . . . a 'capsule' (claims 10 and 13)" (*id.* at 49), but these "miscellaneous features" are taught by several of the references, and "would have been obvious to a skilled pharmaceutical chemist" (*id.* at 49–50).

Patent Owner reiterates that "Kai does not disclose (1) 'a pharmaceutical composition,' or (2) 'an azole antifungal drug.'" PO Resp. 32. Patent Owner contends that neither Sangekar nor Babcock cure these deficiencies. *Id.* Patent Owner further contends that "[t]he Petition fails to articulate a specific motivation for a [person of ordinary skill in the art] to combine Kai, Sangekar and Babcock in December 1999 to achieve the claimed invention." *Id.* at 34.

1. Analysis

As discussed above in Section II.C., we determine that Petitioner has demonstrated, by a preponderance of the evidence that claims 2, 6, 9, 11, 12,

and 14 are anticipated by Kai,[15] but it still remains determine whether the subject matter of claims 10 and 13 would have been obvious over the prior art.

Kai does not disclose that its pharmaceutical composition "is present in a capsule," as required by claims 10 and 13. We agree with Petitioner, however, that one of ordinary skill in the art would have had a reason to place Kai's solid dispersion powder into a capsule, with a reasonable expectation of successfully doing so, as Petitioner notes that Sangekar, for example, teaches that a comparable composition comprising a solid solution of a tetrahydrofuran azole antifungal in a polymer matrix "can be manufactured in a tablet or capsule form." Pet. 23–24, 27 (citing Ex. 1015, 2:13–18, 2:24–3:10). *See KSR Int'l Co. v. Teleflex Inc.,* 550 U.S. 398, 416 (2007). "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." *Id.* at 417.

That does not end the matter, because secondary considerations, when present, must "be considered en route to a determination of obviousness." *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1349 (Fed. Cir. 2012) (citation omitted). Evidence of failure of others, copying, praise by others, unexpected results, commercial success, and long-felt need may be "powerful, real-world indicators" that the claimed invention would have been non-obvious to one of ordinary skill in the art. *See WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1328 (Fed. Cir. 2016).

"For objective evidence of secondary considerations to be accorded substantial weight, its proponent must establish a nexus between the

[15] It is well settled that "anticipation is the epitome of obviousness" (*In re McDaniel*, 293 F.3d 1379, 1385 (Fed. Cir. 2002))

evidence and the merits of the *claimed invention.*" *In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011) (quoting *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1246 (Fed. Cir. 2010)). We apply "a presumption of nexus for objective considerations when the patentee shows that the asserted objective evidence is tied to a specific product and that product 'is the invention disclosed and claimed in the patent.'" *WBIP*, 829 F.3d at 1329 (citations omitted). Where the secondary considerations offered actually result from something other than what is both claimed and novel in the claim, there is no nexus to the merits of the claimed invention. *Tokai Corp. v. Easton Enters., Inc.*, 632 F.3d 1358, 1369 (Fed. Cir. 2011) (If commercial success is due to an element in the prior art, no nexus exists."); *see also Ormco Corp. v. AlignTechnology, Inc.*, 463 F.3d 1299, 1312, 1313 (Fed. Cir. 2006) ("If the feature that creates the commercial success was known in the prior art, the success is not pertinent." Reasoning that success is due "'partially' to claimed features" and to unclaimed features and/or other features already in the art lacks the requisite nexus to show unobviousness.) (citations omitted). In the absence of an established nexus with the claimed invention, secondary consideration factors are entitled to little weight, and generally have no bearing on the legal issue of obviousness. *See In re Vamco Machine & Tool, Inc.*, 752 F.2d 1564, 1577 (Fed. Cir. 1985).

Patent Owner argues that Petitioner "tried and failed to create a solid dosage oral dosage form that could overcome the poor solubility of azoles and thereby provide improved bioavailability in the fasted state." PO Resp. 46. [redacted]

[redacted] Petitioner commercialized this formulation under the name Noxafil® ("the Noxafil Tablets"), which embodies at least claim 9 of the '745 patent" (*id.* at 47–48). Patent Owner contends that Petitioner's "copying of the invention claimed in the '745 patent, after trying and failing for years to develop a posaconazole formulation having improved bioavailability . . . is compelling evidence of non-obviousness." *Id.* at 50.

As evidence that "Petitioner has repeatedly praised the claimed invention as novel and innovative," Patent Owner contends that "Petitioner nominated the Noxafil Tablet development team for awards in innovative and scientific achievement," as well as the "Pharmaceutical Sciences and Drug Metabolism Excellence Award." PO Resp. 51. In addition, Patent Owner contends that Petitioner repeatedly praised and "extolled the remarkable and unexpected results of combining posaconazole with a polymer having acidic functional groups in a solid dispersion." *Id.* at 53. Patent Owner contends that "the success and praise enjoyed by the Noxafil Tablets is directly attributable to its improved pharmacokinetics obtained using the invention of the '745 patent." PO Resp. 50.

In addition, Patent Owner has provided evidence purporting to show that Petitioner's "Noxafil Tablets product is a resounding commercial success." *Id.* at 55 (citing Ex. 2077 ¶¶ 6–14, 25–32, 34–38, 40–48). Finally, Patent Owner contends that "Petitioner itself has recognized that a need for an oral dosage form that could enhance the bioavailability of poorly soluble azoles in the fasted state existed since at least 1992." *Id.* at 59.

Petitioner contends "as a matter of law, there is no nexus when the claimed ideas are already public" (Reply 24), and "the prior art already disclosed the claimed invention" (*id.*).

As discussed above, where the secondary considerations offered result from something other than what is both claimed and *novel* in the claim, there is no nexus to the merits of the claimed invention. Patent Owner contends that "the invention [of the '745 patent] is precisely directed to a pharmaceutical composition of an azole antifungal drug and a polymer having acidic functional groups that provides improved bioavailability in the fasted state as compared to existing treatments." PO Resp. 60. According to Patent Owner's own representations, then, the objective evidence as to failure of others, copying, praise, commercial success, long-felt need, etc., all relates to and/or is attributable to the combination of an azole antifungal drug with a polymer having acidic functional groups. This is precisely what Kai discloses—indeed, as discussed above, of the claims challenged under this ground, the sole feature that Kai does not disclose is the requirement, recited only in claims 10 and 13, of placing the solid dispersion powder in a capsule. Thus, the secondary considerations offered are not attributable to anything novel in the claims. Accordingly, we agree with Petitioner that "[t]here is no nexus here." Reply 24.

2. Conclusion as to Obviousness

Having considered the respective arguments of the parties, and the record developed at trial, including evidence of secondary considerations, we determine that Petitioner has demonstrated by a preponderance of the evidence that the subject matter of claims 2, 6, and 9–14 is obvious over the prior art cited.

E. Real Party in Interest

Patent Owner contends that the Petition was incomplete because it failed to identify Petitioner's parent company, Merck & Co., Inc. ("MCI") as a real party in interest; that Petitioner's failure to name MCI violates a core function of the requirement to name all real parties in interest; and that there is no precedent that would permit retroactive identification of MCI as a real party in interest. PO Resp. 60–63.

Patent Owner previously raised this issue in its Request for Rehearing (Paper 13), but we did not issue our Decision on Rehearing (Paper 70) until after the Patent Owner's Response was filed. For the reasons discussed in the Decision on Rehearing, we determined that permitting Petitioner to update its mandatory notices to include its parent company, MCI, as a real party in interest in this matter—without affecting the Petition's filing date—promotes the core functions described in the Trial Practice Guide with respect to RPIs, and serves the interests of justice. Paper 70 (Decision Denying Patent Owner's Request for Rehearing), 3–6.

Petitioner has updated its Mandatory Notices to reflect that Merck & Co., Inc. and Merck Sharp & Dohme are the real parties in interest. Paper 72. Accordingly, the issue is now moot.

F. Petitioner's Motion to Exclude

Petitioner filed a Motion to Exclude Evidence (Paper 48) seeking to exclude: (1) portions of the declarations of Patent Owner's witness, Dr. Bellantone, pertaining to allometric scaling (Exhibits 2001 and 2066); Exhibits 2098–2134 and 2131–2135 as irrelevant, containing hearsay, and/or unauthenticated; Exhibit 2138 as unauthenticated; Exhibit 2089 as inadmissible hearsay; and Exhibits 2068–2069, 2158, and 2162–2164 as none was cited in the Patent Owner Response or the accompanying expert exhibits.

Under the particular circumstances of this case, we need not assess the merits of Petitioner's Motion to Exclude Evidence as we did not rely on any of these items in reaching our decision. Accordingly, Petitioner's Motion to Exclude Evidence is dismissed as moot.

G. Patent Owner's Motion to Exclude

Patent Owner filed a Motion to Exclude Evidence (Paper 52) seeking to exclude (1) the Declarations of Petitioner's witnesses, Dr. Grainger (Exhibits 1005, 1061, 1066), Dr. Blaschke (Exhibits 1006, 1062, 1067), and Dr. Elder (Exhibit 1096); (2) Exhibits 1009, 1034, 1035, 1049, 1050, and 1053 as non-prior art; (3) and Exhibits 1024–1048 and 1050–1056 as not cited in the Petition. Paper 52, 2–9, 11, 13.

These exhibits did not factor into this Decision, or were regarded in a way not detrimental to Patent Owner.

Patent Owner further moves to exclude the Declaration of Petitioner's witness Dr. Papich (Exhibit 1089), as exceeding the scope of a Reply, as well as Exhibits 1101 and 1104, relied on by Dr. Papich. Paper 52, 9–10.

The Board repeatedly has denied, as improper, motions to exclude evidence that merely argue that evidence is outside the proper scope of a reply. Nevertheless, we have considered Patent Owner's argument with respect to those portions of Petitioner's Reply that are relied upon, and determine they do not belatedly raise new issues or present evidence that should have been presented in the Petition. Exhibits 1101 and 1104 did not factor into this Decision.

Finally, Patent Owner seeks to exclude Exhibit 2081. Paper 52, 14–15. Nevertheless, we relied on Exhibit 2081 only to the extent it was cited by Patent Owner, and not in a manner detrimental to Patent Owner.

Accordingly, Patent Owner's Motion to Exclude Evidence is dismissed with respect to Exhibits 1005, 1061, 1066, 1006, 1062, 1067, 1009, 1034, 1035, 1049, 1050, 1053, 1024–1028, 1050–1056, 1101, 1104, and denied with respect to Exhibits 1089 and 2081.

III. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 2, 6, and 9–14 of the U.S. Patent 6,881,745 B2 are held unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude is dismissed as moot;

FURTHER ORDERED that Patent Owner's Motion to Exclude is dismissed-in-part and denied-in-part; and

FURTHER ORDERED that this is a Final Written Decision; therefore, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

FOR PETITIONER:

Jane M. Love
GIBSON, DUNN & CRUTCHER LLP
jlove@gibsondunn.com

FOR PATENT OWNER:

Jeremy Lowe
Jonathan A. Harris
AXINN, VELTROP & HARKRIDER LLP
jlowe@axinn.com
jharris@axinn.com

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 4.26, the undersigned hereby certifies that a true and correct copy of JOINT MOTION TO SEAL FINAL WRITTEN DECISION was served upon Patent Owner's counsel of record:

Jeremy Lowe (Reg. No. 48,085)
jlowe@axinn.com

Jonathan A. Harris (Reg. No. 47,744)
jharris@axinn.com

AXINN, VELTROP & HARKRIDER, LLP
90 State House Square
Hartford, CT 06002
Phone: (860) 275-8100
Fax: (860) 275-8101

via electronic mail pursuant to agreement of the parties, on the date hereof.

Dated: Feb. 26, 2018

/Jane M. Love, Ph.D./
Jane M. Love, Ph.D.
Reg. No. 42,812
Lead Counsel for Petitioner
jlove@gibsondunn.com