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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COHERUS BIOSCIENCES INC.,
Petitioner,

v.

ABBVIE BIOTECHNOLOGY LTD.,
Patent Owner.

Case IPR2017-00823
Patent 9,085,619 B2

Before SUSAN L.C. MITCHELL, TINA E. HULSE, and MICHELLE N. ANKENBRAND, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Coherus Biosciences Inc. ("Petitioner") filed a Replacement Petition requesting an *inter partes* review of claims 16–19 and 24–30 of U.S. Patent No. 9,085,619 B2 (Ex. 1001, "the '619 patent"). Paper 10 ("Pet."). AbbVie Biotechnology Ltd. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 13 ("Prelim. Resp.").

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Upon considering the Petition, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of claims 16–19 and 24–30 of the '619 patent. Accordingly, we decline to institute an *inter partes* review of those claims.

A. Related Proceedings

Petitioner filed three additional petitions for *inter partes* review of the '619 patent on different grounds in IPR2017-00822, IPR2017-01008, and IPR2017-01009.[1] Pet. 4–5.

[1] Petitioner originally filed two petitions requesting an *inter partes* review of the '619 patent in IPR2017-00826 and IPR2017-00827. Paper 4, 1. The Board dismissed those petitions at Petitioner's request, so Petitioner could proceed with the petitions in IPR2017-01008 and IPR2017-01009, which Petitioner represents are "substantively the same as, and intended to replace," the petitions filed in IPR2017-00826 and IPR2017-00827. *See* IPR2017-00826, Paper 11; IPR2017-00827, Paper 11.

The parties state that U.S. Patent No. 8,420,081, a patent claiming a common priority application with the '619 patent, is the subject of U.S. Patent Interference No. 106,057, declared May 18, 2016. Pet. 6; Paper 4, 1.

The parties also identify U.S. Patent Application No. 15/096,043, which claims priority to the application that matured into the '619 patent and is pending. Pet. 5; Paper 4, 2.

B. The '619 Patent

The '619 patent, titled "Anti-TNF Antibody Formulations," issued on July 21, 2015. Ex. 1101, [45], [54]. The '619 patent relates to "methods and compositions for aqueous protein formulations" that "comprise water and a protein, where the protein is stable without the need for additional agents," such as a buffer system. *Id.* at 3:34–37, 3:66–4:2. The specification explains that certain physical and chemical instabilities (e.g., aggregation and deamidation) "must be overcome" to make an efficacious and commercially viable pharmaceutical protein formulation. *Id.* at 1:24–37. The specification details a number of factors that contribute to the challenges in developing protein formulations, including the high concentrations at which some proteins have to be formulated for therapeutic efficacy and the processes related to long-term storage and lyophilization, which involve thawing and freezing cycles. *Id.* at 2:20–66.

With those factors in mind, the specification describes the field of pharmaceutical protein formulation as requiring a careful balance of ingredients and concentrations to enhance protein stability and therapeutic requirements while, at the same time, limiting negative side-effects. *Id.* at 3:8–11; *see id.* at 3:11–14 ("Biologic formulations should include stable protein, even at high concentrations, with specific amounts of excipients reducing potential therapeutic complications, storage issues, and overall

cost.”). The specification explains that such a balance typically was achieved by including additives or excipients in the formulation that interact with the protein in solution to maintain the stability and solubility of the protein, as well as to keep the protein from aggregating. *Id.* at 1:38–44. The specification further states that the “[t]he near universal prevalence of additives in all liquid commercial protein formulations indicates that protein solutions without such compounds may encounter challenges with degradation due to instabilities.” *Id.* at 1:57–61.

Contrary to the specification’s statement regarding the challenges of developing a protein formulation having no additives, the ’619 patent discloses “an aqueous formulation comprising a protein and water” that provides “a number of advantages over conventional formulations in the art,” including stability “without the requirement for additional excipients, increased concentrations of protein without the need for additional excipients to maintain solubility of the protein, and low osmolality.” *Id.* at 28:43–49. According to the specification, the formulations do not rely on a buffering system and other excipients to keep the protein in the formulation “soluble and from aggregating.” *Id.* at 30:5–7.

The ’619 patent includes examples of aqueous pharmaceutical formulations comprising various concentrations of adalimumab and water without a buffering system. *See id.* at 51:48–54:54, 60:47–63:67.

C. Illustrative Claim

Petitioner challenges claims 16–19 and 24–30 of the '619 patent, of which claim 16 is the only independent claim. Claim 16 is representative and is reproduced below:

> 16. An aqueous pharmaceutical formulation comprising:
>
> (a) an anti-tumor necrosis factor alpha antibody comprising a light chain variable region (LCVR) having a CDR2 domain comprising the amino acid sequence of SEQ ID NO:3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, and a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, wherein the concentration of the antibody is 50-200 mg/ml; and
>
> (b) water;
>
> wherein the formulation does not comprise a buffering system.

Ex. 1101, 152:16–33.

Claims 17 and 18 depend from claim 16 and further recite an antibody comprising certain additional amino acid sequences that are present in adalimumab (claim 17) and adalimumab itself (claim 18). *Id.* at 152:33–39. Claim 19 requires the formulation of claim 16 to further comprise "a non-ionizable excipient." *Id.* at 152:40–41. Claims 24–26 limit the pH range of the formulation of claim 16, and

claims 27–30 limit the pH range of the formulation of claim 18. *Id.* at 152:52–65.

D. The Asserted Ground of Unpatentability

Petitioner asserts that claims 16–19 and 24–30 of the '619 patent are anticipated under 35 U.S.C. § 102(e) by Gokarn '011.[2] Petitioner also relies on the Declaration of Klaus-Peter Radtke, Ph.D. (Ex. 1102).

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner asserts that as of November 30, 2007, a person of ordinary skill in the art of pharmaceutical antibody formulation would have had an advanced degree in biology, biochemistry, or chemistry (or related discipline) with at least two years of experience preparing formulations of proteins suitable for therapeutic use. Pet. 20 (citing Ex. 1102 ¶¶ 61–62). At this stage of the proceeding, Patent Owner does not contest Petitioner's proposed level of ordinary skill in the art. Prelim. Resp. 10.

On this record, we adopt Petitioner's uncontested definition of the level of ordinary skill in the art. We further note that the prior art itself demonstrates the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown") (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985)).

[2] Gokarn et al., US 2016/0319011 A1, published Nov. 3, 2016 ("Gokarn '011," Ex. 1103).

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, and absent any special definitions, we generally give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

We determine that it is unnecessary to expressly construe any claim terms for purposes of this Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

C. Anticipation by Gokarn '011

Petitioner asserts that claims 16–19 and 24–30 of the '619 patent are anticipated by Gokarn '011. Pet. 32–50. Patent Owner disputes Petitioner's assertion. Prelim. Resp. 27–38. On this record, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing the challenged claims are anticipated by Gokarn '011.

1. Gokarn ’011 (Ex. 1103)

Although Petitioner challenges the ’619 patent claims based on Gokarn ’011, Petitioner relies primarily on the disclosure of Gokarn Provisional,[3] which Gokarn ’011 incorporates by reference in its entirety (Ex. 1103 ¶ 1). Pet. 35–50.[4] Accordingly, we refer to the disclosure of Gokarn Provisional in our overview of the asserted reference.

Gokarn Provisional, titled “Bufferless Protein Formulation,” states that “antibodies at sufficiently high concentrations possess adequate buffering capacity in the pH range of 4.0 to 6.0 to provide pH control for a liquid formulation.” Ex. 1104, 4:5–8.[5] Accordingly, Gokarn Provisional relates to “liquid formulations and methods of formulating protein pharmaceuticals wherein the active protein compound in the pharmaceutical formulation is the primary source of the pH control.” *Id.* at 4:9–13. Gokarn

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[3] Yatin Gokarn, U.S. Provisional App. No. 60/690,582, filed June 14, 2005 (“Gokarn Provisional,” Ex. 1104).

[4] Regarding Gokarn ’011, the Petition simply states that “Gokarn ’011 incorporates these same disclosures [as Gokarn Provisional] . . . and also reiterates them in its own words, as noted by Dr. Radtke.” *See, e.g.*, Pet. 40 (citing Ex. 1102 ¶¶ 92–96), 41 (citing Ex. 1102 ¶¶ 86, 100), 42 (citing Ex. 1102 ¶ 102). Petitioner, however, does not substantively address what Gokarn ’011 “reiterates” in the Petition. Moreover, Petitioner’s claim chart only includes citations to Gokarn Provisional. Pet. 46–50. Thus, to the extent Petitioner relies on any disclosure of Gokarn ’011 other than Gokarn Provisional, we do not consider that here, as our rules prohibit incorporating arguments by reference from the expert declaration into the Petition. *See* 37 C.F.R. § 42.6(a)(3).

[5] When citing Exhibit 1104, we cite the unique page numbers provided pursuant to 37 C.F.R. § 42.63(d)(2)(i) in the lower right corner of the exhibit.

Provisional states that "one or more types of polypeptides act as the buffering agent for the pharmaceutically active compound," and in the preferred embodiment, "the pharmaceutically active compound is the buffering agent." *Id.* at 4:13–17.

The pharmaceutical proteins that can be formulated according to Gokarn Provisional's method include large and small proteins, different antibodies, and naturally or non-naturally occurring peptides and proteins, such as peptibodies, maxibodies, and interbodies. *Id.* at 5:10–15. Gokarn Provisional explains that it is not the function or structure of the protein that determines whether or not it can be the primary source of pH control, but rather, it is the presence of enough charged amino acid residues "that in high enough levels can provide pH control and obviate the need for a separate buffering agent." *Id.* at 5:15–23. According to Petitioner, Gokarn Provisional discloses actual data measuring the buffering capacity of formulations containing the antibody epratuzumab ("EMAB") without a buffer.[6] Pet. 25 (citing Ex. 1104, 8–10).

2. Analysis

Anticipation requires that "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (citation omitted). "To establish inherency, the extrinsic evidence 'must make clear

[6] Patent Owner disagrees with Petitioner's characterization of the EMAB data, asserting that Gokarn Provisional does not show possession of bufferless EMAB solutions because the investigations were "on-going." Prelim. Resp. 21 (citing Ex. 1104, 13). We do not need to resolve this dispute here, as we determine Petitioner has failed to meet its burden even if we assume Gokarn Provisional discloses bufferless EMAB formulations.

that the missing descriptive matter is necessarily present in the thing described in the reference.'" *Id.*

As an initial matter, Patent Owner contends that Gokarn '011 is not prior art because Gokarn '011 is not entitled to the benefit of the earlier filing date of Gokarn Provisional. Prelim. Resp. 10–27. Even if Gokarn '011 is entitled to Gokarn Provisional's filing date, we find that Petitioner fails to show a reasonable likelihood of prevailing on its asserted ground, as explained below. Thus, for purposes of this Decision, we need not determine whether Gokarn '011 qualifies as prior art, and we assume that Gokarn '011 is entitled to the June 14, 2005, filing date of Gokarn Provisional.

Petitioner offers claim charts and arguments identifying where it contends Gokarn Provisional discloses each limitation of the challenged claims. Pet. 35–50. A dispositive question regarding Petitioner's challenge is whether Petitioner has sufficiently shown that a person of ordinary skill in the art would "at once envisage" 50 mg/ml adalimumab upon reading Gokarn Provisional. Pet. 36–40. On this record, we determine that Petitioner has not made this showing.

According to Petitioner, Gokarn Provisional is expressly directed to pharmaceutical antibodies and discloses that "antibodies at sufficiently high concentrations, possess adequate buffering capacity in the pH range of 4.0 to 6.0 to provide pH control for a liquid formulation." *Id.* (citing Ex. 1104, 1:5–8, 1:9–13, 1:31–2:4; Ex. 1102 ¶¶ 87–88) (emphasis omitted). Petitioner also notes that the only claim of Gokarn Provisional recites a method for "preparing a pharmaceutical protein formulation containing an *antibody*, *in an amount sufficient for maintaining pH control*." *Id.* at 37–38 (citing Ex. 1004, 14; Ex. 1102 ¶ 89). Moreover, Petitioner argues that Gokarn

Provisional provides data regarding the antibody epratuzumab (EMAB) and its buffering capacity at "higher [antibody] concentrations (> 30 mg/mL)," and that it explains other antibodies will have similar buffering capacity at the same concentrations. *Id.* at 38 (citing Ex. 1104, 2–3, 13; Ex. 1002 ¶ 75).

In light of these disclosures, Petitioner alleges that a person of ordinary skill in the art "would have understood that the Gokarn Provisional discloses the specific genus of liquid pharmaceutical antibodies formulated in high concentrations (*i.e.*, around 30 mg/mL or higher)." *Id.* (citing Ex. 1102 ¶¶ 87, 89). And Petitioner contends that because the genus of liquid pharmaceutical antibodies known to be formulated at concentrations of at least about 30 mg/mL was "extremely limited in November 2007," a person of ordinary skill in the art would have "at once envisage[d] each member of this limited class." *Id.* at 38–39 (citing Ex. 1102 ¶¶ 31, 32, 45, 87, 90). In particular, Petitioner asserts that because Humira (adalimumab at 50 mg/mL) was the most prominent example of a high-concentration liquid antibody formulation, a person of ordinary skill in the art reading Gokarn Provisional "would have immediately envisioned adalimumab at 50 mg/mL (as in Humira®) as providing sufficient buffering capacity in the 4.5 to 5.5 range for a 'bufferless' formulation." *Id.* at 39 (citing Ex. 1102 ¶¶ 46, 87–91).

Having considered the arguments and evidence, we are not persuaded. Petitioner relies heavily on *In re Petering*, 301 F.2d 676 (CCPA 1962) and similar cases to support its argument. We find Petitioner's reliance on those cases to be misplaced. In *Petering*, the prior art disclosed a broad genus encompassing a "vast" and "perhaps even an infinite number" of chemical compounds, including the claimed compound. *Petering*, 301 F.2d at 681. The court found that such a "broad generic disclosure by itself," however,

did not describe the claimed compound within the meaning of 35 U.S.C. § 102(b). *Id*. Nevertheless, the court found that disclosure of "specific preferences" for certain substituents of the generic formula identified a "definite and limited class" of only 20 compounds. *Id*. The court deemed this narrower preferred class sufficient to describe each individual species "as fully" as if each had been explicitly drawn or named in the prior art reference. *Id*. at 682. Thus, according to the court, a skilled artisan, upon reading the prior art reference, would "at once envisage each member of this limited class." *Id*. at 681; *see also Ineos USA LLC v. Berry Plastics Corp.*, 783 F.3d 865, 872 (Fed. Cir. 2015) (finding anticipation based on disclosure of a "narrower preferred genus" of saturated fatty acid amides having 12–35 carbons); *In re Schaumann*, 572 F.2d 312, 315 (CCPA 1978) (finding anticipation where explicit "pattern of preferences" for lower alkyl secondary amines narrowed the genus to seven possible compounds).

In contrast, we are not persuaded that Gokarn Provisional discloses a "definite and limited class" of pharmaceutical antibodies that would allow a person of ordinary skill in the art to "at once envisage *each member* of this *limited* class." *Petering*, 301 F.2d at 681 (emphasis added). Even assuming, as Petitioner asserts, that Gokarn Provisional discloses a genus of "high concentration, liquid pharmaceutical antibody formulations" (Pet. 37), Petitioner has not shown that that genus amounts to a "definite and limited class." Rather, Petitioner attempts to further limit the genus to "known," high-concentration liquid pharmaceutical antibody formulations, identifying several examples of commercially available high-concentration antibody formulations (including Humira). Pet. 38–39; Ex. 1102 ¶¶ 29–32. But Petitioner fails to explain why the genus should be so limited. For example, Petitioner points to nothing in Gokarn Provisional that suggests limiting the

class of antibodies to only those known and commercially available at the time of filing. Nor does Petitioner point us to any case law that supports its narrowed definition of the alleged genus.

Contrary to Petitioner's assertions, the class of possible antibody formulations appears to be very broad. We agree with Patent Owner that Gokarn Provisional's mention of "antibodies at sufficiently high concentrations" does not identify any particular antibody or any particular antibody concentration that would narrow the class to a more limited number of antibody formulations. Prelim. Resp. 32.

Petitioner asserts that because Gokarn Provisional discloses data regarding the buffering capacity of EMAB at higher concentrations, a person of ordinary skill in the art would understand that "other antibodies will have similar buffer capacity at the same concentrations." Pet. 38. But Gokarn Provisional and Dr. Radtke's testimony belie Petitioner's broad assertion. Gokarn Provisional states that buffering capacity depends on the number of charged amino acids ("n") and the total concentration of the protein. Ex. 1104, 5:31–6:1. Gokarn Provisional then explains that "n" is "relatively constant *for a given class of monoclonal antibodies*." *Id.* at 6:3–10 (emphasis added). Consistent with that disclosure, Dr. Radtke opines that a person of ordinary skill in the art would have understood that "antibodies *within* [] *a given class*" have similar amino acid sequences and similar buffering capacities. Ex. 1102 ¶ 88 (emphasis added). Thus, even assuming Dr. Radtke's testimony and Gokarn Provisional's disclosure are correct, any alleged similarities between the buffering capacities of antibodies are limited to a given class of antibodies. The alleged genus of "pharmaceutical antibodies," however, is not limited to a given class.

Neither Gokarn Provisional nor Gokarn '011 is limited to any particular class of antibodies. As Patent Owner notes, claim 1 of Gokarn Provisional is directed to *any* antibody, and is not limited to any particular class or type of antibodies. Prelim. Resp. 34. And according to Gokarn '011, antibodies (and antibody derivatives) are "[h]ighly preferred proteins of the invention" and include numerous possibilities:

> monoclonal antibodies, polyclonal antibodies, genetically engineered antibodies, hybrid antibodies, bispecific antibodies, single chain antibodies, genetically altered antibodies, including antibodies with one or more amino acid substitutions, additions, and/or deletions (antibody muteins), chimeric antibodies, antibody derivatives, antibody fragments, which may be from any of the foregoing and also may be similarly engineered or modified derivatives thereof, fusion proteins comprising an antibody or a moiety derived from an antibody or from an antibody fragment, which may be any of the foregoing or a modification or derivative thereof, conjugates comprising an antibody or a moiety derived from an antibody, including any of the foregoing, or modifications or derivatives thereof, and chemically modified antibodies, antibody fragments, antibody fusion proteins, and the like, including all of the foregoing.

Ex. 1103 ¶ 218. Indeed, Gokarn '011 characterizes this lengthy list as "nam[ing] *just a few* such entities." *Id.* (emphasis added). In light of the breadth of possible antibodies disclosed by Gokarn Provisional and Gokarn '011, we find Gokarn Provisional's disclosure of pharmaceutical antibodies is not a genus defining a "definite and limited class," but rather a "broad generic disclosure" that does not describe the claimed species. *See Petering*, 301 F.3d at 681.

Having considered the current record, we are not persuaded that Petitioner has shown sufficiently that a person of ordinary skill in the art reading Gokarn Provisional would immediately envisage 50 mg/mL

adalimumab. Accordingly, we determine that Petitioner has not established a reasonable likelihood that it would prevail in showing Gokarn Provisional (as incorporated into Gokarn '011) anticipates the challenged claims.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioner has not established a reasonable likelihood of prevailing on its assertion that claims 16–19 and 24–30 of the '619 patent are unpatentable.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied* as to all challenged claims of the '619 patent, and no trial is instituted.

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