NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

IN RE: QAPSULE TECHNOLOGIES, INC.,
Appellant

2018-1772

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 13/882,773.

Decided: March 11, 2019

DONALD GEORGE LEWIS, Lewis Kohn & Walker LLP, San Diego, CA, for appellant.

THOMAS W. KRAUSE, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, for appellee Andrei Iancu. Also represented by SARAH E. CRAVEN, FRANCES LYNCH.

Before NEWMAN, CHEN, and STOLL, *Circuit Judges.*

NEWMAN, *Circuit Judge.*

Qapsule Technologies, Inc. ("Qapsule") appeals from the Patent Trial and Appeal Board ("Board") determination that claims 1, 2, 5, 7, 13–15, 31, 33–35, and 38 of U.S. Patent Application No. 13/882,773 ("the '773 Application") are

anticipated by Perez[1] as evidenced by Mair,[2] Ye,[3] and Gonzales.[4] Because substantial evidence supports the Board's determination, and we discern no legal error in its analysis, we affirm.[5]

THE '773 APPLICATION

The '773 Application relates to "encapsulating recombinant enzymes and other cargo proteins within the interior space of protein nanoparticles." '773 Appl. at p. 2, ll. 32–34. The nanoparticles are assembled using shell proteins, such as viral coat proteins, in the presence of bifunctional polynucleotides and the desired cargo protein. *Id.* at p. 3, ll. 7–26. Claim 1 is representative:

> 1. A synthetic capsule construct for providing a protected chemical milieu, the construct comprising:
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> a shell having a plurality of shell proteins, said plurality of shell proteins being assembled with one another for forming said shell and defining an enclosure therein, each of said shell proteins, when

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[1] Perez et al., *Functional Analysis of PA Binding by Influenza A Virus PBJ: Effects on Polymerase Activity and Viral Infectivity*, 75 J. VIROLOGY 8127–36 (2001).

[2] Mair et al., *Receptor binding and pH stability- How influenza A virus hemagglutinin affects host-specific virus infection*, 1838 BIOCHIMICA ET BIOPHYSICA ACTA 1153–68 (2014).

[3] Ye et al., *Association of Influenza Virus Matrix Protein with Ribonucleoproteins*, 73 J. VIROLOGY 7467–73 (1999).

[4] Gonzalez et al., *Characterization of Influenza Virus PBJ Protein Binding to Viral RNA: Two Separate Regions of the Protein Contribute to the Interaction Domain*, 73 J. VIROLOGY 631–37 (1999).

[5] *Ex Parte* Finn et al., No. 2017-001118, 2017 WL 6055117 (P.T.A.B. Nov. 27, 2017) ("Bd. Op.").

> assembled for forming said shell, having an interior surface facing inwardly toward said enclosure and an exterior surface facing outwardly away from said enclosure, said shell serving to restrict permeability to and from said enclosure for providing the protected chemical milieu therein, said shell proteins being recombinant;
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> a cargo protein, said cargo protein being recombinant and optionally including a peptide tag; and
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> a bifunctional polynucleotide having both a first aptameric activity for binding said cargo protein and a second aptameric activity for retaining said bifunctional polynucleotide within said enclosure by assembly with the interior surface of said shell protein,
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> said bifunctional polynucleotide being non-naturally occurring; said bifunctional polynucleotide serving to link said cargo protein within said enclosure for providing the said cargo protein with the protected chemical milieu therein.

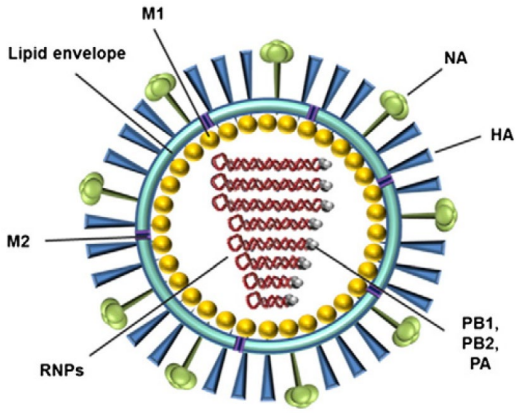
As relevant herein, the limitations of claim 1 include an enclosure made of recombinant "shell proteins," a recombinant "cargo protein," and a "bifunctional polynucleotide" having the function of linking the cargo protein within the enclosure. The '773 Application defines "shell protein" as "any protein or set of proteins capable of self-assembly or directed-assembly to form a 'shell,'" including viral and non-viral proteins. '773 Appl. at p. 40, ll. 26–30. The Application defines "cargo protein" as "any recombinant protein capable of being incorporated into a synthetic capsule construct." *Id.* at p. 42, ll. 1–3. And "bifunctional polynucleotide" is defined as a "polynucleotide having two or more aptameric activities," *id.* at p. 41, ll. 20–22, or "binding affinit[ies] . . . for a protein tag or protein binding site," *id.* at p. 39, ll. 23–25.

PROCEDURAL HISTORY

The '773 Application's claims were initially rejected as anticipated and/or obvious in view of a set of references not relevant to the present appeal. In view of the initial grounds of rejection, Qapsule appealed to the Board and obtained reversal of the examiner's rejections for want of reference disclosure of the claimed "aptameric activity for binding."

The Board, however, entered a new ground of rejection for claims 1, 2, 5, 7, 13–15, 31, 33–35, and 38 as anticipated by Perez as evidenced by Mair, Ye, and Gonzalez. Bd. Op. at *4.

The Board found that Perez discloses a recombinant influenza A virus and relied upon Mair as evidence of the inherent structural features of such a virus:



Bd. Op. at *5 (citing Mair at 1155, Figure 1). The Board found that the "M1" protein met the claim 1 limitation of "shell protein," that the mutated "PB1" protein of Perez met the limitation of a recombinant "cargo protein," and the mutated viral RNA of the "RNPs" constituted the "bifunctional polynucleotide" of claim 1, for it was non-naturally occurring and was capable of binding both the M1 shell protein and the PB1 protein. *See* Bd. Op. at *6–7.

The Board relied on Ye for teaching that the M1 protein binds to viral RNA. *See* Bd. Op. at *5 (citing Ye at p. 7467, col. 2 ("Two domains in M1 have been shown to affect the disposition of RNA. One domain residing in a palindromic stretch of basic amino acids (101RKLKR105) has been shown to bind vRNA . . . .")). And the Board relied on Gonzalez as teaching that the PB1 protein binds to the viral RNA. *See* Bd. Op. at *5 (citing Gonzalez at p. 636, col. 2 ("Since we show that PB1 protein on its own binds preferentially the 5′-terminal sequence of vRNA . . . .")). Accordingly, the Board concluded that "the influenza virus particles of Perez with mutated PB1 protein and vRNA inherently anticipate the requirements of claim 1." Bd. Op. at *7.

Faced with the new ground of rejection, Qapsule had the option of reopening prosecution before the examiner, or requesting rehearing. *See* 37 C.F.R. § 41.50(B)(2). Qapsule chose the rehearing route. Treating claim 1 as representative, Qapsule argued that "Claim 1 includes a limitation that the shell proteins are recombinant" whereas the shell proteins identified by the Board in Perez "are not recombinant." '773 Application, *Request for Rehearing*, filed Jan. 22, 2018, at 3 (J.A.64). Qapsule stated in its request for rehearing that Ye disclosed recombinant shell proteins, but not in combination with recombinant proteins as claimed. *See id*. But Qapsule acknowledged that the Board's new ground of rejection was for anticipation by Perez and not Ye. *See id*. Accordingly, Qapsule argued that Perez did not anticipate the rejected claims.

The Board determined that Qapsule's reliance on the term "recombinant" was an attempt to impose a method step into a claim for a product, that pursuant to *In re Dilnot*, 300 F.2d 945, 950 (CCPA 1962), "addition of a method step in a product claim, which product is not patentably distinguishable from the prior art, cannot impart

patentability to the old product."[6] The Board concluded that "whether the shell proteins were produced in a 'recombinant' eukaryotic expression system in MDCK cells or produced as taught by Perez by virus infection in the MDCK cells, the final constructs including the shell proteins would be expected to be structurally identical because they would share the same amino acid sequence, same glycosylation patterns (if any), as they were produced by the same cell." *Id.* And the Board remarked that Qapsule had failed to provide any evidence rebutting the inherency ruling. *See id.*

Qapsule appeals, arguing that the Board erred in its factual findings and application of the law of inherent anticipation.

DISCUSSION

As to the Board's factual findings, Qapsule argues that Perez does not inherently disclose the "bifunctional polynucleotide" claim limitation because Ye concluded that binding of the ribonucleoprotein to the viral shell proteins in influenza A requires the presence of nucleoproteins in addition to the viral RNA and the ribonucleoprotein. Qapsule asserts that the claimed synthetic capsule does not require ribonucleoprotein in order for binding to occur between M1 and the viral RNA. And without the presence of ribonucleoproteins, Qapsule argues that "the Board's proposed subset of elements drawn from Perez, *viz.* M1, vRNA, and PD1, would fail to assemble to form a virus particle." Appellant Reply Br. at 6. Accordingly, Qapsule contends that there are structural differences between the shell proteins and bifunctional polynucleotide as claimed, and those disclosed by Perez.

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[6] *Ex Parte* Finn et al., No. 2017-001118, 2018 WL 799026, at *1 (P.T.A.B. Feb. 1, 2018).

A reference anticipates a patent claim under 35 U.S.C. § 102(b) if every claim limitation is present in the reference. *See Verizon Servs. Corp. v. Cox Fibernet Va., Inc.*, 602 F.3d 1325, 1336–37 (Fed. Cir. 2010). A reference may anticipate inherently if a claim limitation that is not expressly described "is necessarily present, or inherent, in the single anticipating reference." *Id.* at 1337 (quoting *Schering Corp. v. Geneva Pharm.*, Inc., 339 F.3d 1373, 1377 (Fed. Cir. 2003)).

"[A]nticipation is a question of fact, including whether an element is inherent in the prior art." *In re Gleave*, 560 F.3d 1331, 1334–35 (Fed. Cir. 2009). Thus we review the Board's factual finding of inherent anticipation for support by substantial evidence. 5 U.S.C. § 706(2)(E); *Dickinson v. Zurko*, 527 U.S. 150, 152 (1999); *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). "Substantial evidence is something less than the weight of the evidence but more than a mere scintilla of evidence," *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000), and "means such relevant evidence as a reasonable mind might accept as adequate to support a conclusion," *Consol. Edison Co. of New York v. NLRB*, 305 U.S. 197, 229 (1938).

A. Waiver

The PTO solicitor argues that Qapsule waived its present arguments by failing to present them at the Board hearing and rehearing. By electing rehearing under 37 C.F.R. § 41.50(b)(2), Qapsule was required to "address any new ground of rejection and state with particularity the points believed to have been misapprehended or overlooked in entering the new ground of rejection and also state all other grounds upon which rehearing is sought." The PTO states that Qapsule in its rehearing request only argued that Perez failed to disclose a recombinant "shell protein," and that Qapsule's new arguments about the binding of the "bifunctional polynucleotide" and the application of inherent anticipation are waived.

The court "retains case-by-case discretion over whether to apply waiver." *Harris Corp. v. Ericsson Inc.*, 417 F.3d 1241, 1251 (Fed. Cir. 2005) (citing *Singleton v. Wulff*, 428 U.S. 106, 120 (1976)). Here the issues of Perez's disclosure of a shell protein binding to a bifunctional polynucleotide and the Board's application of inherent anticipation are arguments about claim scope that are sufficiently developed in the record before us. Because no party will be prejudiced by our resolution of these issues, we proceed to the merits without applying waiver.

B. Inherent Anticipation

The Board found that Ye discloses that the M1 protein (i.e., the recombinant "shell protein" as claimed) binds to viral RNA (the recombinant "bifunctional polynucleotide" as claimed). Bd. Op. at *5. The Board quoted Ye's disclosure that "[t]wo domains in M1 have been shown to affect the disposition of RNA. One domain residing in a palindromic stretch of basic amino acids (101RKLKR105) has been shown to bind vRNA . . . ." *Id.* (quoting Ye at p. 7467, col. 2). This is substantial evidence supporting the Board's conclusion that Perez inherently discloses "a bifunctional polynucleotide having . . . a second aptameric activity for retaining said bifunctional polynucleotide within said enclosure by assembly with the interior surface of said shell protein."

Qapsule acknowledges that the Board's understanding of Ye is correct. Appellant Reply Br. at 5 ("Although Ye teaches that vRNA binds to M1, Ye also teaches that ribonucleoproteins (RNP) also binds to M1 and that binding by both vRNA and ribonucleoproteins (RNP) are necessary for virus assembly . . . ."). Qapsule, however, attempts to differentiate the present claims by arguing that viral assembly in Ye occurs in the presence of ribonucleoprotein. However, the present claims use the open-ended term "comprising," and do not exclude capsule assembly in the presence of ribonucleoprotein as long as the claimed

"bifunctional polynucleotide" (here, the viral RNA) assembles with the interior surface of the "shell protein." *See Crystal Semiconductor Corp. v. TriTech Microelectronics Int'l, Inc.*, 246 F.3d 1336, 1348 (Fed. Cir. 2001):

> When a patent claim uses the word "comprising" as its transitional phrase, the use of "comprising" creates a presumption that the body of the claim is open. In the parlance of patent law, the transition "comprising" creates a presumption that the recited elements are only a part of the device, that the claim does not exclude additional, unrecited elements.

Similarly, the word "having," in the clause "a bifunctional polynucleotide having . . . a second aptameric activity for retaining said bifunctional polynucleotide within said enclosure by assembly with the interior surface of said shell protein" does not exclude additional, unrecited elements from participating in capsule assembly. *See id.:*

> The transition "having" can also make a claim open. However, the term "having" does not convey the open-ended meaning as strongly as "comprising." "Having," for instance, does not create a presumption that the body of the claim is open. Therefore, this court examines the claim in its full context to determine whether [Applicant's] use of "having" limits claim 1 to its recited elements.

(internal citation omitted).

Claim 1 does not require that the claim excludes capsule assembly in the presence of ribonucleoproteins, as Qapsule has argued. First, the whole of the claimed "synthetic capsule construct" is offset by the "comprising" transitional, signaling the intent to have an open-ended claim that would allow for additional, unrecited elements beyond the listed shell protein, cargo protein, and bifunctional polynucleotide. The specification defines "synthetic capsule

construct" broadly to mean "a non-naturally occurring capsule," '773 Appl. at p. 39, ll. 19–20, and defines the term "capsule" in equally broad language to mean "a nanoparticle sized structure having a well organized outer layer that defines an enclosure . . . ," *id*. at p. 39, ll. 14–16. Qapsule has not directed us to any language that would rebut the presumption that has arisen from its choice to use the "comprising" transitional.

Additionally, the use of the "having" transitional does not alter the construction, for it is specific to the recited "bifunctional polynucleotide" limitation and not the claimed "synthetic capsule construct" as a whole. The "having" transitional within this claim offsets two "aptameric activit[ies],"which the specification defines as "binding affinit[ies] . . . for a protein tag or protein binding site," '773 Appl. at p. 39, ll. 23–25. Although this usage, in conjunction with the "bifunctional" qualifier of nucleotide, could imply that the number of "aptameric affinities" of the polynucleotide should be limited, this does not restrict unrecited elements from participating in capsule assembly as long as the "bifunctional polynucleotide" possesses the two recited aptameric affinities.

In sum, it does not affect the Board's ground of rejection that Qapsule has purportedly created a capsule that will assemble in the presence of only a shell protein, cargo protein, and bifunctional polynucleotide, *see* Appellant Reply Br. at 6, for representative claim 1 is not so limited. Thus substantial evidence supports the Board's conclusion that the Perez recombinant viral RNA inherently meets the "bifunctional polynucleotide" limitation in claim 1.

Qapsule further argues that the Board misapplied the requirement of structural identity for inherent anticipation under *In re Best*. 562 F.2d 1252, 1256 (CCPA 1977) ("Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can

require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product."). We find that the Board properly applied the concept of inherency on an element-by-element basis in order to establish that the M1 protein, viral RNA, and PB1 protein would meet the claimed "shell protein," "bifunctional polynucleotide," and "cargo protein" limitations, respectively.

On appeal, Qapsule points to the presence of additional elements in Perez, such as a lipid envelope and other proteins, as evidencing a structural difference between Perez's influenza A disclosure and the recited limitations of representative claim 1. *See* Appellant Br. at 9–12. Qapsule contends that these structural differences negate anticipation. That is incorrect, as applied herein, for as discussed *supra*, Qapsule's claims are not limited to the three recited components. The Board correctly found that the Examiner met his burden of establishing structural identity of the claimed synthetic capsule construct in view of the scope of representative claim 1, and that this prima facie case has not been rebutted by the Applicant. *See In re Jung*, 637 F.3d 1356, 1362 (Fed. Cir. 2011) (explaining the burden-shifting framework during prosecution); *In re Mousa*, 479 F. App'x 348, 352 (applying the same specifically to inherency).

Qapsule also argues that unlike the influenza A of Perez, Qapsule's synthetic capsule is functionally different because it is non-infective and has utility in the chemical industry. Appellant Reply Br. at 8 ("Appellant's claimed synthetic capsule construct is a simple system with three components and is employable in industrial chemical processes; in contrast, Perez's virus particles are complex with many components and lack industrial applicability, but they might be employable for germ warfare."). However, unclaimed functional distinctions or uses are insufficient to overcome anticipation. It is not before us to decide

whether further specificity in the claims might distinguish these references.

"First, and most importantly, the language of the claim defines the scope of the protected invention." *Bell Commc'ns Research, Inc. v. Vitalink Commc'ns Corp.*, 55 F.3d 615, 619 (Fed. Cir. 1995); *see Yale Lock Mfg. Co. v. Greenleaf*, 117 U.S. 554, 559 (1886) ("The scope of letters-patent must be limited to the invention covered by the claim, and while the claim may be illustrated it cannot be enlarged by language used in other parts of the specification."). Unclaimed limitations cannot distinguish the claims. *Ventana Med. Sys., Inc. v. Biogenex Labs., Inc.*, 473 F.3d 1173, 1181 (Fed. Cir. 2006) ("[I]t is improper to limit the claim to other, unclaimed features.").

The structures of Perez anticipate representative claim 1. Unclaimed differences do not avoid anticipation, for claim 1 as written, in its breadth, reads on Perez. The Board correctly rejected claim 1 on this ground.

We have considered all of Qapsule's arguments, and affirm the judgment of the Board.

AFFIRMED

No costs.