

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SHANGHAI HONGENE BIOTECH CORP.,
Petitioner,

v.

CHEMGENES CORP.,
Patent Owner.

IPR2023-00875
Patent 8,309,707 B2

Before JOHN G. NEW, ZHENYU YANG, and CYNTHIA M. HARDMAN,
Administrative Patent Judges.

YANG, *Administrative Patent Judge.*

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Shanghai Hongene Biotech Corp. (“Petitioner”) filed a Petition (Paper 1, “Pet.”) seeking *inter partes* review of claims 1 and 2 of U.S. Patent No. 8,309,707 B2 (Ex. 1001, “the ’707 patent”). ChemGenes Corp. (“Patent Owner”) did not file a Preliminary Response.

We have authority 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) (2018).

For the reasons provided below, we determine Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). Accordingly, we institute *inter partes* review of all challenged claims based on all grounds raised in the Petition.

A. Related Matters

According to the parties, Patent Owner asserted the ’707 patent against Petitioner in Case No. 1-22-cv-10290 (D. Mass.) but later voluntarily dismissed the district court action. Pet. vii; Paper 4, 2.

Petitioner also filed IPR2023-00490 and IPR2023-00862, challenging two other patents asserted in the district court action. Pet. vii–viii; Paper 4, 2.

B. The ’707 Patent

The ’707 patent “relates to the synthesis of novel RNA monomer phosphoramidites, and corresponding solid supports that are suitable for a novel method of RNA oligonucleotide synthesis in reverse 5′→3′ direction.” Ex. 1001, 1:24–27.

The ’707 patent explains that, at the time of its alleged invention, defined sequence RNA synthesis in the 3′→5′ direction was well

established. *Id.* at 1:35–54. According to the '707 patent, however, “the synthesis of RNA in the reverse direction (5'-3' direction) ha[d] not been achieved.” *Id.* at 1:55–57.

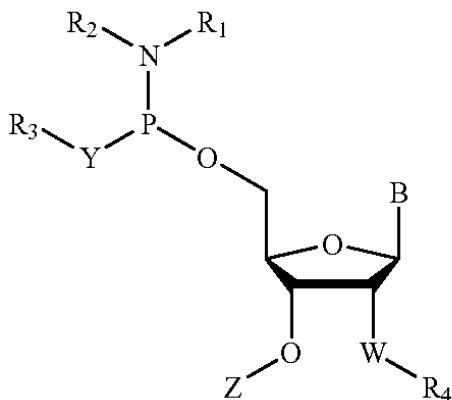
The '707 patent discloses reverse RNA monomer phosphoramidites for RNA synthesis in 5'→3' direction, which leads to “very clean oligo synthesis that allows for the introduction of various modifications at the 3'-end cleanly and efficiently.” *Id.* at 8:34–39.

C. Illustrative Claim

Claim 1 is illustrative of the claimed subject matter. We reproduce below those parts of claim 1 relevant to our present analysis.

1. A phosphoramidite having formula (1),

Formula (1)



where,

Y is an oxygen atom or a sulfur atom;

W is selected from the group consisting of an oxygen diradical, a N—H diradical and a fluorine radical, and R₄ is selected so that,

...

if W is a N—H diradical, then R₄ is of the form R₅^x where x is selected from the group consisting of fluorenylmethyloxycarbonyl (Fmoc), trifluoroacetyl, acetyl, alkanoyl, and aroyl; and

...

B is selected from the group of nucleoside base radicals consisting of . . . and 1-uracilyl-;

. . .

Z is a protecting group selected from the group consisting of dimethoxytriphenylmethyl (DMT), monomethoxytriphenylmethyl (MMT) and trimethoxytriphenylmethyl (TMT);

R₁ is an alkyl or aryl radical;

R₂ is an alkyl or aryl radical; and,

R₃ is a cyanoethyl radical, alkyl radical or aryl radical.

Ex. 1001, 33:48–35:17.

D. Asserted Challenges to Patentability

Petitioner asserts the following challenges to patentability:

Claim Challenged	35 U.S.C. §	Reference(s)/Basis
1	102(b)	The '696 patent ¹
2	102(b)	The '696 patent

Petitioner also relies on the declaration of Phil S. Baran, Ph.D., as support for its Petition. Ex. 1003.

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, we construe a claim term “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. [§] 282(b).” 37 C.F.R. § 42.100(b) (2020). Under that standard, the words of a claim “are generally given their ordinary and customary meaning,” which is “the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention,

¹ US Patent No. 5,869,696, issued Feb. 9, 1999 (Ex. 1014, “the '696 patent”).

i.e., as of the effective filing date of the patent application.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

Claim terms need only be construed to the extent necessary to resolve the controversy. *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011). On this record and for purposes of this Decision, we see no need to address the construction of any claim term.

B. Level of Ordinary Skill in the Art

Petitioner contends that, as of the earliest possible priority date of the ’707 patent, an ordinarily skilled artisan would have had a Ph.D. (or equivalent degree) in organic or medicinal chemistry, and two to three years of post-graduate work experience in medicinal chemistry, synthetic organic chemistry, and nucleic acid chemistry, including the development of oligonucleotide therapeutics, diagnostics, or building blocks. Pet. 16 (citing Ex. 1003 ¶ 20). Alternatively, Petitioner proposes that an individual holding a Bachelor’s or Master’s degree in organic chemistry or medicinal chemistry, who had extensive work experience in these fields, and who had gained a thorough understanding of the development of nucleic acid-based materials, would also have qualified as an ordinarily skilled artisan. *Id.*

For purposes of this Decision, we adopt Petitioner’s definition of the level of ordinary skill because it is consistent with the prior art’s demonstration of the level of ordinary skill at the relevant time. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (holding that “the prior art itself [may] reflect[] an appropriate level” as evidence of the ordinary level of skill in the art) (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985)).

C. Disclosures of the '696 Patent

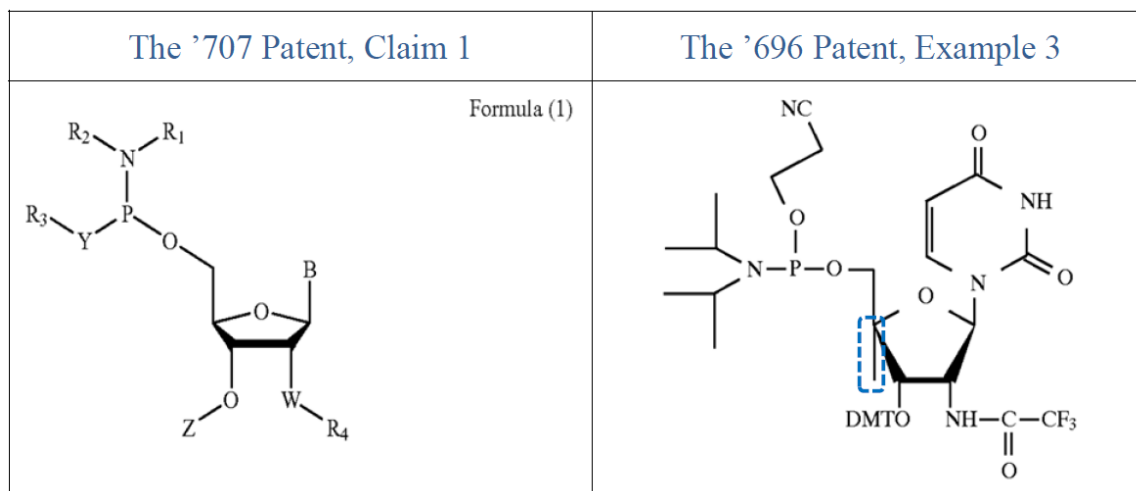
The '696 patent discloses “[u]niversal solid support oligonucleotide synthesis reagents, oligonucleotide synthesis processes, and reagents for cleaving oligonucleotides from solid supports.” Ex. 1014, Abstract. Specifically, it discloses the synthesis of 2'-trifluoroacetamido-3'-O-(4,4'-dimethoxytrityl)-2'-deoxyuridine-5'-succinate in Example 2 (*id.* at 12:1–13:20) and the synthesis of 2'-Trifluoroacetamido-3'-O-(4,4'-dimethoxytrityl)-2'-deoxyuridine-5'-O-(N,N'-diisopropyl)- β -cyanoethyl-phosphoramidite in Example 3 (*id.* at 13:23–67).

D. Alleged Anticipation of Claim 1

Petitioner asserts that the '696 patent anticipates claim 1. Pet. 21–29. Based on this record, and for at least the following reasons, we determine Petitioner has established a reasonable likelihood that it would prevail in this assertion.

For a claim directed to a genus, if a prior art reference discloses a species falling within the claimed genus, the species anticipates the genus. *In re Slayter*, 276 F.2d 408, 411 (CCPA 1960); *see also Fresenius USA, Inc. v. Baxter Int'l, Inc.*, 582 F.3d 1288, 1298 (Fed. Cir. 2009) (stating that when a claim element is written in Markush form, “the entire element is disclosed by the prior art if one alternative in the Markush group is in the prior art”).

Claim 1 is directed to a genus of compounds. Petitioner asserts that the '696 patent discloses a species of claim 1 in Example 3 as 2'-Trifluoroacetamido-3'-O-(4,4'-dimethoxytrityl)-2'-deoxyuridine-5'-O-(N,N'-diisopropyl)- β -cyanoethyl-phosphoramidite. Pet. 21–29 (citing Ex. 1003 ¶¶ 74–88). Petitioner provides the following comparison:



The figure above shows the side-by-side comparison of formula (1) of claim 1 with the compound of the '696 patent's Example 3. *Id.* at 23.

Petitioner argues that the compound of the '696 patent's Example 3 is a species of claim 1 where in formula (1), Y is an oxygen atom, W is a N-H diradical, R₄ is trifluoroacetyl, B is 1-uracilyl- nucleoside base radical, Z is a DMT protecting group, R₁ is an alkyl radical (specifically an isopropyl radical), R₂ is an alkyl radical (specifically an isopropyl radical), and R₃ is a cyanoethyl radical.² *Id.* at 21–28. On this record, we agree with Petitioner's analysis and adopt it as our own.

Thus, based on the current record, we determine Petitioner has established a reasonable likelihood that it would prevail in its assertion that

² Petitioner argues the vertical line (in the blue rectangle in the figure) extending downward from the 4' carbon of the compound of the '696 patent's Example 3 “does not denote a methyl group.” Pet. 24. Petitioner contends that the chemical name of Example 3's compound “does not reflect a methyl group (or any other substituent) on the 4' carbon.” *Id.* (citing Ex. 1003 ¶ 76, which in turn, cites Ex. 1014, 13:27–29). On this record, we find Petitioner's argument on this point persuasive.

the '696 patent, because of its disclosure of the compound of Example 3, anticipates claim 1. Therefore, we institute *inter partes* review.

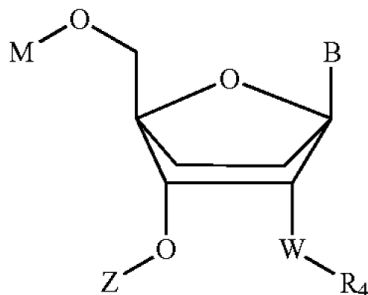
E. Alleged Anticipation of Claim 2

Petitioner asserts that the '696 patent anticipates claim 2. Pet. 29–37. Based on this record, and for at least the following reasons, we determine Petitioner has established a reasonable likelihood that it would prevail in this assertion too.

Claim 2, as relevant to our analysis, is reproduced below:

2. A derivatized nucleoside having a structure of formula 2,

Formula (2)



where,

M is a hydrogen radical or a linker;

if M is a linker, then it is represented by the formula Y—C(O) and, optionally, connected to a solid support suitable for oligonucleotide synthesis, wherein

Y is a chain of between 2 and 20 carbons, selected from the group consisting of alkyl, alkenyl, cycloalkyl, aryl, and aralkyl, in a hydrocarbyldiradical moiety, optionally comprising intervening —O—, —S—, —S(O)₂—, —C(O)—, and —NR₆—, where R₆ is a hydrogen radical, or a substituted C₁ to C₂₀ alkyl or a substituted aralkyl;

W is selected from the group consisting of an oxygen diradical, a N—H diradical and a fluorine radical, and R₄ is selected so that,

...

if W is a N—H diradical, then R₄ is of the form R₅^x where x is selected from the group consisting of fluorenylmethyloxycarbonyl (Fmoc), trifluoroacetyl, acetyl, alkanoyl, and aroyl;

...

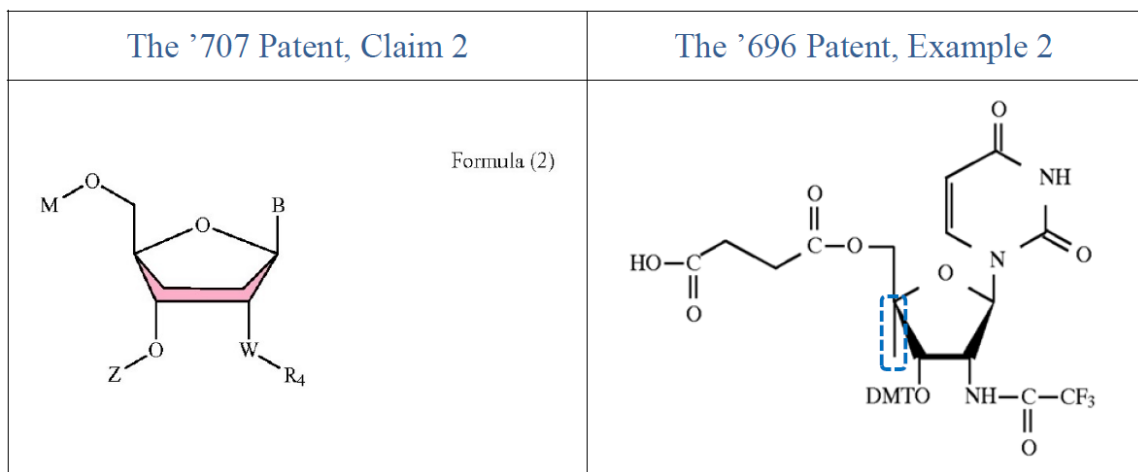
B is selected from the group of nucleoside base radicals consisting of ... and 1-uracilyl-;

...

Z is a protecting group selected from the group consisting of dimethoxytriphenylmethyl (DMT), monomethoxytriphenylmethyl (MMT) and trimethoxytriphenylmethyl (TMT).

Ex. 1001, 35:18–36:15.

Claim 2 is directed to a genus of compounds. Petitioner asserts that the '696 patent discloses a species of claim 1 in Example 2 as 2'-Trifluoroacetamido-3'-O-(4,4'-dimethoxy-trityl)-2'-deoxyuridine-5'-succinate. Pet. 29–37 (citing Ex. 1003 ¶¶ 89–105). Petitioner provides the following comparison:



The figure above shows the side-by-side comparison of formula (2) of claim 2 with the compound of the '696 patent's Example 2. *Id.* at 32.

Petitioner points out that “in Formula (2), the lower portion of the pentagon has normal lines without the space between them (shaded pink above) filled in to make thicker lines.” *Id.* “Despite this omission,” Petitioner asserts, a person of ordinary skill in the art “would have understood the pentagon in Formula (2) to represent ribose, not a bridged bicyclic molecule.” *Id.* (citing Ex. 1003 ¶ 92 n.13, which in turn, cites Ex. 1001, 13:1–13, Structure (15)). Based on the current record, we find Petitioner’s argument on this point persuasive.

Petitioner argues that the compound of the ’696 patent’s Example 2 is a species of claim 2 where in formula (2), M is a succinate linker “represented by the formula Y—C(O) in a hydrocarbyl diradical, wherein Y is an alkyl chain having 2 carbons, i.e., ethyl . . . and further comprises an intervening —C(O)—,” W is a N—H diradical, R₄ is trifluoroacetyl, B is 1-uracilyl- nucleoside base radical, and Z is a DMT protecting group.³ *Id.* at 21–28. On this record, we agree with Petitioner’s analysis and adopt it as our own.

³ Petitioner argues the vertical line (in the blue rectangle in the figure of Example 2) extending downward from the 4’ carbon of the compound of the ’696 patent’s Example 2 “does not denote a methyl group.” Pet. 32. Petitioner contends that the chemical name of Example 2 compound “does not reflect a methyl group (or any other substituent) on the 4’ carbon.” *Id.* at 32–33 (citing Ex. 1003 ¶ 93, which in turn, cites Ex. 1014, 12:3–5). On this record, we find Petitioner’s argument on this point persuasive. We note that the Petition misstates that paragraph 93 of Dr. Baran’s Declaration cites Exhibit 1014, 13:27–29. Paragraph 93, in fact, correctly cites Exhibit 1014, 12:3–5, for the chemical name of the compound in Example 2.

Thus, based on the current record, we determine Petitioner has established a reasonable likelihood that it would prevail in its assertion that the '696 patent, because of its disclosure of the compound of Example 2, anticipates claim 2.

III. CONCLUSION

Based on the current record, and for the reasons explained above, we find Petitioner has demonstrated a reasonable likelihood that it would prevail with respect to at least one claim challenged in the Petition. We therefore institute an *inter partes* review of all challenged claims on all asserted grounds.

At this stage of the proceeding, the Board has not made a final determination as to the construction of any claim term or the patentability of any challenged claim. We encourage the parties to further address all relevant issues of all challenges to fully develop the record during trial. Our view with regard to any finding or conclusion reached in the foregoing could change upon further development of the record during trial.

Any argument not raised in a timely Patent Owner Response to the Petition, or as permitted in another manner during trial, shall be deemed waived. In addition, nothing in this Decision authorizes Petitioner to supplement information advanced in the Petition in a manner not permitted by the Board's Rules.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review is hereby instituted on all challenged claims of the '707 patent based on all the asserted grounds set forth in the Petition; and

FURTHER ORDERED, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4(b), notice is hereby given of the institution of a trial commencing on the entry date of this decision.

IPR2023-00875
Patent 8,309,707 B2

FOR PETITIONER:

Jeremy Edwards
Raymond Chan
Xiaofan Yang
Jack Shaw
PROCOPIO, CORY, HARGREAVES & SAVITCH, LLP
Jeremy.edwards@procopio.com
Raymond.chan@procopio.com
Frank.yang@procopio.com
Jack.shaw@procopio.com

FOR PATENT OWNER:

Daniel Shores
Joseph Hynds
Aydin Harston
Melissa Santos
ROTHWELL, FIGG, ERNST & MANBECK, P.C.
dshores@rfem.com
jhynds@rfem.com
aharston@rfem.com
msantos@rfem.com