Trials@uspto.gov
571-272-7822

Paper 67
Date: May 21, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE PATENT TRIAL AND APPEAL BOARD

---

GILEAD SCIENCES, INC.,
Petitioner,

v.

REGENTS OF THE UNIVERSITY OF MINNESOTA,
Patent Owner.

---

IPR2017-01712
Patent 8,815,830 B2

---

Before ERICA A. FRANKLIN, ZHENYU YANG, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges.*

YANG, *Administrative Patent Judge*.

# JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
*35 U.S.C. § 318(a)*

## INTRODUCTION

Gilead Sciences, Inc. ("Petitioner") filed a Petition (Paper 1 ("Pet.")), seeking an *inter partes* review of claims 1–9, 11–21, and 23–28 of U.S. Patent No. 8,815,830 B2 (Ex. 1001, "the '830 patent"). We instituted trial to review the challenged claims. Paper 46 ("Dec."). Thereafter, Regents of the University of Minnesota ("Patent Owner") filed a Response to the Petition (Paper 54, "PO Resp."), Petitioner filed a Reply (Paper 57), and Patent Owner filed a Sur-Reply (Paper 58). An oral hearing for this proceeding was held on February 3, 2021, and a transcript of that hearing is of record. *See* Paper 66 ("Tr.").

The Board has jurisdiction under 35 U.S.C. § 6 and issues this final written decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons provided below, and based on the evidence and arguments presented in this proceeding, we conclude Petitioner has established by a preponderance of the evidence that claims 1–9, 11–21, and 23–28 of the '830 patent are unpatentable.

### *Related Matters*

According to the parties, Patent Owner asserted the '830 patent against Petitioner in *Regents of the University of Minnesota v. Gilead Sciences, Inc.*, No. 16-cv-02915 (D. Minn.). Pet. x; Paper 3, 1. The case was later transferred to the U.S. District Court for Northern District of California and was docketed as *Regents of the University of Minnesota v. Gilead Sciences, Inc.*, No. 3:17-cv-06056 (N.D. Cal.). Paper 22, 1; Paper 23, 1.

Petitioner also filed three other petitions (IPR2017-01753, IPR2017-02004, IPR2017-02005), all challenging the claims of the

'830 patent. Paper 23, 1. We previously denied institution in those proceedings. IPR2017-01753, Paper 42; IPR2017-02004, Paper 38; IPR2017-02005, Paper 40.

*Case History*

Petitioner filed the Petition on July 7, 2017. Paper 5. With our authorization, the parties briefed the issue of whether the doctrine of sovereign immunity applies in this proceeding such that we should grant Patent Owner's Motion to Dismiss the Petition. Papers 14, 15, 16.

While the Motion to Dismiss in this case was pending, the Board denied Patent Owner's motions to dismiss based on sovereign immunity in several other *inter partes* review proceedings. *LSI Corp. v. Regents of the Univ. of Minn.*, IPR2017-01068, Paper 19 (PTAB Dec. 19, 2017); *Ericsson Inc. v. Regents of the Univ. of Minn.*, IPR2017-01186, -01197, -01213, -01214, -01200, -01219 (PTAB Dec. 19, 2017). On February 12, 2018, Patent Owner filed a Notice of Appeal, seeking immediate appellate review of those decisions. *See, e.g.*, IPR2017-01186, Paper 22.

Under such circumstances, and at the request of Patent Owner, we suspended this proceeding in view of the appellate adjudication of the state-sovereign-immunity issue. Papers 17, 22, 25, 28. Petitioner then sought, and was granted, leave to intervene in those appeals. Paper 26, 2.

On June 14, 2019, the Federal Circuit affirmed the Board's decision denying Patent Owner's motion to dismiss in those proceedings. *Regents of the Univ. of Minn. v. LSI Corp.*, 926 F.3d 1327, 1330 (Fed. Cir. 2019) (holding state sovereign immunity does not apply to IPR proceedings). On January 13, 2020, the Supreme Court denied Patent Owner's petition for

writ of certiorari. *Regents of the Univ. of Minn. v. LSI Corp.*, 140 S. Ct. 908 (Jan. 13, 2020) (No. 19-337). The next day, we denied Patent Owner's Motion to Dismiss and lifted the stay order in this proceeding. Paper 32.

*The '830 Patent*

The '830 patent issued from application No. 14/229,292 ("the '292 application"), filed on March 28, 2014, which is a continuation of application No. 13/753,252 (hereinafter "NP4"), filed on January 29, 2013, which is a continuation of application No. 11/721,325 (hereinafter "NP3"), filed on June 8, 2007, which is a national stage application of PCT/US2005/044442 (hereinafter "NP2"), filed on December 8, 2005, which claims priority to provisional application No. 60/634,677 (hereinafter "P1"), filed on December 9, 2004. Ex. 1001, codes (21), (22), (60), (63), 1:7–15; Pet. 29.

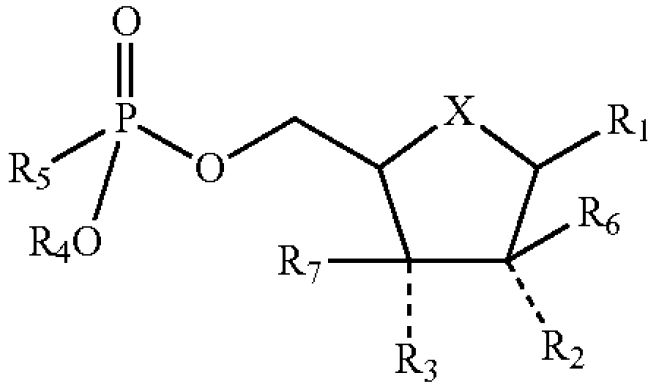
The '830 patent relates to nucleosides with antiviral and anticancer activity, specifically nucleotide phosphoramidate prodrugs that are potentially good substrates for human histidine triad nucleotide-binding protein 1 ("hHINT1"). Ex. 1001, 2:13–47. According to the '830 patent, "[i]nspection of the active site of hHINT1 has revealed that hydrogen bonding, ion pairing or polar interactions at the 2'- and 3'-positions preferentially interact with the active site residue Asp-43, which is consistent with the reduced ability of 2'-deoxy nucleoside phosphoramidates to serve as substrates." *Id.* at 2:36–42. In addition, the '830 patent discloses that compounds containing an electropositive group at the 2'-position "are especially good substrates for hHINT1." *Id.* at 2:44–48.

The ’830 patent acknowledges that “U.S. Pat. No. 6,475,985 reports certain specific nucleoside phosphoramidate analogs having anticancer and/or antiviral properties.” *Id.* at 1:61–63. It states that there were other, continued interests “in phosphoramidate nucleoside analogs due to their demonstrated utility as prodrugs of antiviral and anticancer nucleoside monophosphates, or pronucleotides.” *Id.* at 1:63–66. The ’830 patent states that despite the prior-art studies on this topic, there was still “a need for chemotherapeutic agents with antiviral and[/]or anticancer properties.” *Id.* at 2:6–8. According to the ’830 patent, its invention provides such “compounds that act as antiviral and[/]or anticancer agents.” *Id.* at 2:48–49.

*Illustrative Claim*

Claim 1 is independent and is reproduced below:

1. A compound of formula I:




wherein:

$R_1$ is guanine, cytosine, thymine, 3-deazaadenine, or uracil, optionally substituted by 1, 2, or 3 U; wherein each U is independently halo, hydroxy, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_6$)cycloalkyloxy, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkanoyloxy, trifluoromethyl, hydroxy($C_1$-$C_6$)alkyl, —$(CH_2)_{1\text{-}4}P(=O)(OR_w)_2$, aryl, aryl($C_1$-$C_6$)alkyl, or $NR_xR_y$;

$R_2$ is halo;

$R_6$ and $R_7$ are independently H or $(C_1$-$C_6)$alkyl;

$R_3$ is hydroxy;

$R_4$ is hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, aryl, aryl$(C_1$-$C_6)$alkyl, or 2-cyanoethyl;

$R_5$ is an amino acid;

X is oxy, thio, or methylene;

each $R_w$ is independently hydrogen or $(C_1$-$C_6)$alkyl;

$R_x$ and $R_y$ are each independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, phenyl, benzyl, phenethyl, or $(C_1$-$C_6)$alkanoyl; or $R_x$ and $R_y$ together with the nitrogen to which they are attached are pyrrolidino, piperidino or morpholino;

wherein any $(C_1$-$C_6)$alkyl of $R_1$, $R_4$-$R_7$, $R_w$, $R_x$, and $R_y$ is optionally substituted with one or more halo, hydroxy, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyloxy, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkanoyloxy, trifluoromethyl, azido, cyano, oxo (=O), $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S—$(C_1$-$C_6)$alkyl-, aryl, heteroaryl, alkyl$(C_1$-$C_6)$alkyl, or heteroaryl$(C_1$-$C_6)$alkyl, or $NR_{aj}R_{ak}$; wherein each $R_{aj}$ and $R_{ak}$ is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, phenyl, benzyl, or phenethyl;

and wherein any aryl or heteroaryl may optionally be substituted with one or more substituents selected from the group consisting of halo, hydroxy, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyloxy, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkanoyloxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, and amino;

or a pharmaceutically acceptable salt thereof.

*Instituted Ground of Unpatentability*

We instituted trial to determine whether claims 1–9, 11–21, and 23–28 of the '830 patent are unpatentable based on the following single ground:

| Claims Challenged | 35 U.S.C. § | References |
|---|---|---|
| 1–9, 11–21, 23–28 | 102 | Sofia[1] |

Petitioner relies on the Declarations of Gerardus Josephus Petrus Henricus Boons, Ph.D. Exs. 1011,[2] 1039. Patent Owner relies on the Declaration of Andrea Brancale, Ph.D. Ex. 2058.

ANALYSIS

*Legal Standards*

In an *inter partes* review, the burden of persuasion is on the petitioner to prove unpatentability by a preponderance of the evidence, and that burden never shifts to the patentee. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015).

A patent claim is entitled to the benefit of the filing date of an earlier filed, related application if it meets the requirements of 35 U.S.C. § 120. *Hollmer v. Harari*, 681 F.3d 1351, 1355 (Fed. Cir. 2012). "Section 120 places the burden on the patent owner to provide a clear, unbroken chain of

[1] Sofia et al., U.S. Patent Appl. Pub. No. 2010/0016251, published January 21, 2010 (Ex. 1004).

[2] Exhibit 1011 was originally executed by Victor E. Marquez, Ph.D. Later, we granted Petitioner's request to substitute the Marquez Declaration in support of the Petition (Ex. 1011), with the Boons Declaration. Paper 48. Dr. Boons states that he adopts as his own the substantive statements and opinions in the Marquez Declaration. Ex. 1036 ¶ 29.

priority." *Droplets, Inc. v. E*TRADE Bank*, 887 F.3d 1309, 1317 (Fed. Cir. 2018) (citing *Medtronic CoreValve, LLC v. Edwards Lifesciences Corp.*, 741 F.3d 1359, 1366 (Fed. Cir. 2014)).

To claim "the benefit of the filing date of an earlier application under 35 U.S.C. § 120, each application in the chain leading back to the earlier application must comply with the written description requirement of 35 U.S.C. § 112." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1571 (Fed. Cir. 1997); *see also Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1344 (Fed. Cir. 2013) ("[C]laims added during prosecution must find support sufficient to satisfy § 112 in the written description of the original priority application.").

"[T]o satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue." *Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000). It, however, must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. *Id.* "Put another way, one skilled in the art, reading the original disclosure, must immediately discern the limitation at issue in the claims." *Id.*

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003); *see also Droplets*, 887 F.3d at 1316 (emphasizing that § 120 embodies an important public policy and requires "strict adherence to its requirements"). Accordingly, "[e]ntitlement to a filing date

does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed." *Lockwood*, 107 F.3d at 1571–72; *see also Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2010) (en banc) ("[A] description that merely renders the invention obvious does not satisfy the requirement."). Likewise, a "mere wish or plan" for obtaining the claimed invention does not satisfy the written description requirement. *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997).

The test for written description support "requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Ariad*, 598 F.3d at 1351. A sufficient description of a genus "requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can visualize or recognize the members of the genus." *Id.* at 1350 (internal quotation marks omitted). "[A]n adequate written description requires a precise definition, such as by structure, formula, chemical name, physical properties, or other properties, of species falling within the genus sufficient to distinguish the genus from other materials." *Id.*

The primary consideration in written description analysis is factual and must be assessed on a case-by-case basis. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1562 (Fed. Cir. 1991); *see also Smith v. Horne*, 450 F.2d 1401, 1404 (CCPA 1971) ("The question as to whether an application forms a proper support for a claim to a composition which is not specifically disclosed, but which falls among compositions suggested by

general language in the application is one which must be determined largely by the particular circumstances of each case."). The Federal Circuit has warned that each case involving the issue of written description "must be decided on its own facts. Thus, the precedential value of cases in this area is extremely limited." *Vas-Cath*, 935 F.2d at 1562 (quoting *In re Driscoll*, 562 F.2d 1245, 1250 (CCPA 1977)).

*Claim Construction*

In an *inter partes* review based on a petition filed before November 13, 2018, the Board interprets a claim term in an unexpired patent according to its broadest reasonable construction in light of the specification of the patent in which it appears. 37 C.F.R. § 42.100(b) (2016);[3] *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under that standard, and absent any special definitions, we assign 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, in the context of the entire patent disclosure. *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. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

---

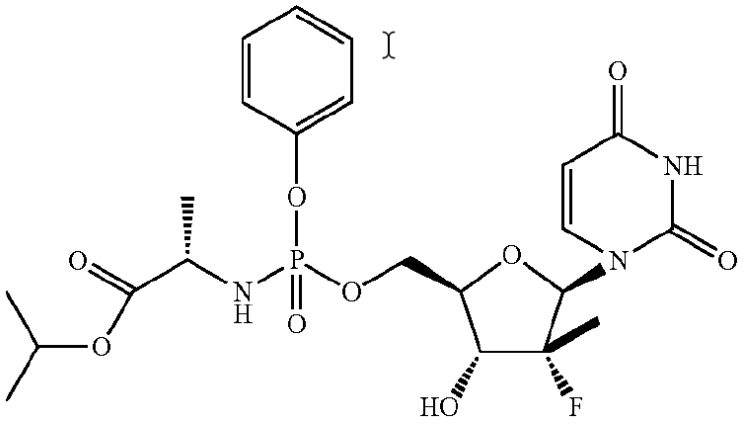
[3] The rule changing the Board's claim construction standard to the same standard used by district courts does not apply here, as the Petition was filed before the effective date of the final rule, November 13, 2018. *See* Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018) (amending 37 C.F.R. § 42.100(b) effective November 13, 2018).

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 construe any term expressly.

*Anticipation by Sofia*

Petitioner argues that Sofia anticipates claims 1–9, 11–21, and 23–28. Pet. 16–27.

Sofia discloses phosphoramidate prodrugs of nucleoside derivatives for the treatment of viral infections. Ex. 1004, Abstract. Example 25 of Sofia is (S)-2-{[(2R,3R,4R,5R)-5-(2,4-Dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-4-fluoro-3-hydroxy-4-methyl-tetrahydro-furan-2-ylmethoxy]-phosphorylamino}-propionic acid isopropyl ester. *Id.* at 58. It has the following structure:




The figure above shows the structure of example 25 of Sofia. *Id.* at 49. According to Petitioner, example 25 of Sofia contains, in the nomenclature of the '830 patent, oxy at X, uracil at $R_1$, fluoro at $R_2$, hydroxy at $R_3$, phenyl at $R_4$, the isopropyl ester of L-alanine, an amino acid at $R_5$, methyl at $R_6$, and hydrogen at $R_7$. Pet. 18 (citing Ex. 1011 ¶ 143). Thus, Petitioner asserts that

example 25 of Sofia meets every limitation of challenged claim 1. *Id.* at 18–19. Petitioner also points to evidence to support its argument that example 25 of Sofia meets every additional limitation of challenged claims 2–9, 11–21, and 23–28. *Id.* at 20–27.

Patent Owner does not dispute, and after reviewing the record, we agree with the parties, that Sofia discloses every limitation of each asserted claim.

This, however, does not end our inquiry, because the outcome of this case also turns on the priority date of the challenged claims, and thus, the prior-art status of Sofia. As explained below, we agree with Petitioner that the challenged claims are not entitled to a priority date earlier than March 28, 2014. Therefore, Sofia qualifies as prior art.

*Priority Date*

According to Petitioner, none of the priority applications (P1, NP2, NP3, and NP4) provides written description support for the challenged claims. Pet. 27–73. Thus, Petitioner contends that the priority date of the challenged claims is no earlier than March 28, 2014, the filing date of the application that issued as the '830 patent. *Id.* at 27. Patent Owner argues that Petitioner fails to establish NP2 lacks written description support for the challenged claims. PO Resp. 21–75. As explained below, based on the evidence of record, we find Petitioner's arguments more persuasive.

As a preliminary matter, we note that (1) NP2 incorporates P1 by reference, and contains additional disclosure (*see* Ex. 1007, 1:9–11, 26:22–27:7); (2) NP3 contains the same disclosure as NP2 (*compare* Ex. 1006, *with* Ex. 1007); and (3) NP4 was filed after the publication date of

Sofia (*see* Ex. 1001, code (63)). Thus, in this Decision, as Patent Owner does in its Response, we focus our analysis on NP2, and through the incorporation by reference, P1. We also focus, as the parties do, on substituents at $R_2$, $R_3$, $R_5$, $R_6$, and $R_7$. *See* Pet. 35–39; PO Resp. 26.

Petitioner's Arguments

NP2 discloses a genus of nucleoside phosphoramidates with a skeleton, specified by formula I, identical to challenged claim 1's skeleton. Ex. 1007, 3:18–19. Petitioner presents Table 3 in the Petition, reproduced below, to compare the substituents at each relevant position between P1/NP2 and challenged claim 1:

| | P1 | '830 patent claim 1 |
|---|---|---|
| **$R_2$** | H, halo, hydroxy, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_6$)cycloalkyloxy, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkanoyloxy, trifluoromethyl, azido, cyano, -$N(R_z)C(=O)N(R_{aa})(R_{ab})$, -$N(R_z)C(=O)OR_{ac}$, or $NR_{ad}R_{ae}$, provided that one of $R_2$ and $R_6$ is hydroxy halo, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_6$)cycloalkyloxy, trifluoromethyl, cyano, or $NR_{ad}R_{ae}$; $R_z$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 3:23-4:2]; $R_{aa}$ and $R_{ab}$ are each independently H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl; or $R_{aa}$ and $R_{ab}$ together with the nitrogen to which they are attached are pyrrolidino, piperidino or morpholino [Ex. 1008, at 4: 24-26]; $R_{ac}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, | halo |

| | P1 | '830 patent claim 1 |
|---|---|---|
| | or phenethyl [Ex. 1008, at 4: 27-28];<br>$R_{ad}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 4: 29-30];<br>$R_{ae}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 5: 1-2]. | |
| **$R_3$** | H, halo, hydroxy, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_6$)cycloalkyloxy, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkanoyloxy, trifluoromethyl, azido, cyano, -$N(R_z)C(=O)N(R_{aa})(R_{ab})$,<br>-$N(R_z)C(=O)OR_{ac}$, or $NR_{ad}R_{ae}$ [Ex. 1008, at 4: 3-6];<br>$R_z$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 3:23-4:2];<br>$R_{aa}$ and $R_{ab}$ are each independently H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl; or $R_{aa}$ and $R_{ab}$ together with the nitrogen to which they are attached are pyrrolidino, piperidino or morpholino [Ex. 1008, at 4: 24-26];<br>$R_{ac}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 4: 27-28];<br>$R_{ad}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 4: 29-30];<br>$R_{ae}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 5: 1-2]. | hydroxy |
| **$R_5$** | amino acid, peptide, or $NR_aR_b$ [Ex. 1008, at 3: 9]; | amino acid |

| | P1 | '830 patent claim 1 |
|---|---|---|
| | The term "peptide" describes a sequence of 2 to 25 amino acids or peptidyl residues. The sequence may be linear or cyclic. A peptide can be linked to the remainder of a compound of formula I through the carboxy terminus, the amino terminus, or through any other convenient point of attachment. Preferably, a peptide comprises 2 to 25, or 5-25 amino acids. [Ex. 1008, at 8: 18-22];<br>Each $R_a$ and $R_b$ is independently H, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, aryl, or aryl$(C_1$-$C_6)$alkyl; or $R_a$ and $R_b$ together with the nitrogen to which they are attached form a pyrrolidino, piperidino or morpholino [Ex. 1008, at 4: 15-17]. | |
| **$R_6$** | H, halo, hydroxy, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyloxy, $(C_1$-$C_6)$alkanoyl, $(C_1$-$C_6)$alkanoyloxy, trifluoromethyl, azido, cyano, -$N(R_z)C(=O)N(R_{aa})(R_{ab})$,<br>-$N(R_z)C(=O)OR_{ac}$, or $NR_{ad}R_{ae}$, provided that one of $R_2$ and $R_6$ is hydroxy halo, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyloxy, trifluoromethyl, cyano, or $NR_{ad}R_{ae}$ [Ex. 1008, at 3:23-4:2];<br>$R_z$ is H, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 3:23-4:2];<br>$R_{aa}$ and $R_{ab}$ are each independently H, $(C_1$-$C_6)$alkyl, $(C_3$- | H or $(C_1$-$C_6)$alkyl |

| | P1 | '830 patent claim 1 |
|---|---|---|
| | $C_6$)cycloalkyl, phenyl, benzyl, or phenethyl; or $R_{aa}$ and $R_{ab}$ together with the nitrogen to which they are attached are pyrrolidino, piperidino or morpholino [Ex. 1008, at 4: 24-26];<br>$R_{ac}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 4: 27-28];<br>$R_{ad}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 4: 29-30];<br>$R_{ae}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 5: 1-2]. | |
| **$R_7$** | H, halo, hydroxy, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_6$)cycloalkyloxy, ($C_1$-$C_6$)alkanoyl, ($C_1$-$C_6$)alkanoyloxy, trifluoromethyl, azido, cyano, -$N(R_z)C(=O)N(R_{aa})(R_{ab})$,<br>-$N(R_z)C(=O)OR_{ac}$, or $NR_{ad}R_{ae}$;<br>$R_z$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 3:23-4:2];<br>$R_{aa}$ and $R_{ab}$ are each independently H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl; or $R_{aa}$ and $R_{ab}$ together with the nitrogen to which they are attached are pyrrolidino, piperidino or morpholino [Ex. 1008, at 4: 24-26];<br>$R_{ac}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 4: 27-28]; | H or ($C_1$-$C_6$)alkyl |

| | P1 | '830 patent claim 1 |
|---|---|---|
| | $R_{ad}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 4: 29-30];<br>$R_{ae}$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_6$)cycloalkyl, phenyl, benzyl, or phenethyl [Ex. 1008, at 5: 1-2]. | |

Petitioner presents Table 3 to compare the substituents at each relevant position between P1/NP2 and challenged claim 1. Pet. 35–39; *see also* Ex. 1007, 3:16–4:33.

According to Petitioner, the table above shows the comparison of substituents between disclosures in P1/NP2 and the challenged claim 1. Pet. 35, 55 ("Differences between the disclosure in NP3/NP2 and '830 patent claim 1 is the same as shown above in Table 3.").

Petitioner argues that "a combinatorial calculation of the number of substituents encompassed by $R_2$, $R_3$, $R_5$, $R_6$, and $R_7$ in NP3/NP2 formula I (the R groups narrowed in '830 patent claim 1) results in 7,441,875 classes of R group substituents from which the later claimed '830 patent claim 1 subgenus is derived." *Id.* at 56 (citing Ex. 1011 ¶ 96, emphasis omitted), *see also id.* at 39–40 (citing Ex. 1011 ¶¶ 54–60, asserting the same regarding the substituents disclosed in P1). According to Petitioner:

> The '830 patent subgenus selects one substituent (halo) out of 15 possibilities for $R_2$, one substituent (hydroxy) out of 15 possibilities for $R_3$, one substituent (amino acid) out of three possibilities for $R_5$, two substituents [H or ($C_1$-$C_6$)alkyl] out of 15 possibilities for $R_6$, and two substituents [H or ($C_1$-$C_6$)alkyl] out of 15 possibilities for $R_7$. This is akin to selecting seven trees

> from a forest of 7,441,875 trees, with no guidance in P1 [or NP2] pointing the POSA to those seven particular trees.

Pet. 40 (citing Ex. 1011 ¶ 61, emphases omitted), 56–57 (citing Ex. 1011 ¶ 97).

Petitioner asserts that, although challenged claim 1 narrows the scope of substituents disclosed in P1 and NP2, there are no blaze marks in either P1 or NP2 "to guide a POSA to select those specific classes of R group substituents from the myriad possibilities in the broad genera disclosed" in P1 or NP2. *Id.* at 56 (citing Ex. 1011 ¶ 95), *see also id.* at 39 (citing Ex. 1011 ¶ 53). For example, Petitioner points out that neither application "disclose[s] preferred definitions for each R group substituent in Formula I," or "teach[es] any improved properties, such as improved antiviral or anticancer activity for compounds with the R groups selected in the '830 patent claim 1 subgenus." *Id.* at 40.

Instead, Petitioner argues that P1 and NP2 actually direct a POSA to select other classes of R group substituents because the only compounds "useful in the methods of the invention" have hydroxy—not halo, as in challenged claim 1—at $R_2$, and the only synthetic scheme for making the compounds in P1 and NP2 is one that results in hydroxy at $R_2$. *Id.* at 41, 43 (citing Ex. 1008, Figs. 1, 3), 57, 59 (citing Ex. 1007, Figs 1, 3); *see also* Ex. 1007, 7:9–14; Ex. 1008, 7:9–14.

In addition, P1 and NP2 disclose that compounds containing an electropositive group at the 2'-position "are especially good substrates for hHINT1." Ex. 1007, 3:11–14; Ex. 1008, 3:9–11. Petitioner argues that halogens, such as fluorine, are electronegative, not electropositive. Pet. 43–44, 59–60 (citing Ex. 1011 ¶ 103). According to Petitioner, "fluorine is the

most electronegative element in the periodic table." *Id.* at 44 (citing Ex. 1011 ¶¶ 66–67; Ex. 1021, emphasis omitted). Thus, Petitioner concludes the teachings in P1 and NP2 that "electropositive groups at the 2'-position are favored for phosphoramidate hydrolysis" would lead a POSA in a different direction from selecting halo at $R_2$. *Id.* (citing Ex. 1011 ¶ 68), 60 (citing Ex. 1011 ¶ 104).

Petitioner further contends that neither P1 nor NP2 discloses "any representative species or subgenus that falls within the scope of '830 patent claim 1." *Id.* at 42, 57. Nor do they contain any examples of compounds that fall within the scope of that subgenus. *Id.* at 42–43, 57. In P1, all "representative compounds" have hydroxy at $R_2$. *Id.* at 43 (citing Ex. 1008, Figs. 1, 3); *see also* Ex. 1008, 7:9–13 (stating compounds in Figures 1 and 3 are "representative compounds" and compounds "useful in the methods of the invention"). NP2 discloses 24 additional "[r]epresentative compounds." Ex. 1007, 26:22–27:7. According to Petitioner, all but one of these compounds have hydroxy at $R_2$. Pet. 59. The only one left contains hydrogen, again, not halo, at $R_2$. *Id.* It also has hydroxy, and not hydrogen or ($C_1$-$C_6$)alkyl, as required in challenged claim 1, at $R_6$. *Id.* Thus, Petitioner concludes all the representative compounds in P1 and NP2 are outside the scope of challenged claim 1. *Id.* at 43 (citing Ex. 1011 ¶¶ 63–65), 59 (citing Ex. 1011 ¶¶ 101–102).

Petitioner acknowledges that both P1 and NP2 contain numerous multiple dependent claims. *Id.* at 44, 60. According to Petitioner, however, there is nothing in P1 or NP2 singling out the claimed classes of R group substituents as preferred, and there are "no blaze marks directing a POSA to

select" the R group substituents falling within the scope of challenged claim 1 subgenus from the many R groups recited in other claims. *Id.* at 44–45 (citing Ex. 1008, 23–24; Ex. 1011 ¶¶ 69–73), 60–62 (citing Ex. 1007, 40–41; Ex. 1011 ¶¶ 105–109).

For P1, Petitioner points out the relevant claims "are all multiple dependent claims which themselves depend from large numbers of other multiple dependent claims." *Id.* at 45. For example, claim 47 recites "[t]he compound of any one of claims 1–46, wherein $R_7$ is hydrogen or ($C_1$-$C_6$)alkyl." *Id.* at 45–46 (citing Ex. 1008, 27, emphasis omitted). Petitioner argues "[t]here are no blaze marks in this claim or any of the claims of P1 specifically pointing to the substituents recited in '830 patent claim 1." *Id.* at 46 (citing Ex. 1011 ¶ 74). Thus, according to Petitioner:

> [E]ven if claim 47 were to be understood by a POSA as demonstrating a "preference" for $R_7$ as hydrogen or ($C_1$-$C_6$)alkyl, claim 47 still represents 70,875 classes of R group substituents for $R_2$, $R_3$, $R_5$, and $R_6$ with no blaze marks in P1 to direct the POSA to the classes of R group substituents later claimed in the '830 patent claim 1 subgenus.

*Id.* at 46 (citing Ex. 1011 ¶ 74).

To reach challenged claim 1, Petitioner argues, it would require hindsight to pick, among 46 claim possibilities in claim 47, four claims (claims 13, 21, 33, and 45), without any direction in P1's disclosure. *Id.* Given the multiple classes of substituents for each of $R_2$, $R_3$ and $R_5$, "and the lack of blaze marks in P1 to direct a POSA to select $R_2$ as halo, $R_3$ as hydroxy, and $R_5$ as amino acid (as specifically claimed in the '830 patent claim 1 subgenus) from the 7,441,875 other possible combinations,"

Petitioner concludes that the applicant "was not in possession of the '830 patent claim 1 subgenus as of the filing date of P1." *Id.* at 47.

For NP2, Petitioner points out that it differs from P1 in the organization of the multiple dependent claims. *Id.* at 61. This, according to Petitioner, "precludes combinations that would result in the classes of R group substituents later claimed in the '830 patent." *Id.* at 65 (emphasis omitted). Thus, Petitioner concludes "even in hindsight[,] a POSA would not be able to combine the classes of R group substituents later claimed in the '830 patent claim 1 subgenus from the disclosures and claims of . . . NP2." *Id.* (citing Ex. 1011 ¶ 119).

For similar reasons, Petitioner also contends that neither P1 nor NP2 provides written description support for the challenged dependent claims. *Id.* at 50–53 (citing Ex. 1011 ¶¶ 84–90), 66–69 (Ex. 1011 ¶¶ 122–131). According to Petitioner, "there are no 'preferences' or other teachings" in P1 or NP2 that "would provide direction to a POSA, with no foreknowledge of the later-claimed '830 patent subgenus, to select the narrowed $R_2$, $R_3$, $R_5$, $R_6$, and $R_7$ groups claimed in the '830 patent dependent claims." *Id.* at 50 (citing Ex. 1011 ¶ 84), 66 (citing Ex. 1011 ¶ 122).

In sum, Petitioner concludes

> Given the enormous size of the genera of compounds disclosed in [P1 and] NP2, the lack of blaze marks that would direct a POSA to the specifically narrowed R groups claimed in the '830 patent, combined with the teachings in [P1 and] NP2 that would direct a POSA to select something other than the later claimed R groups, a POSA would have understood that Applicant was not in possession of the subject matter of the '830 patent claims.

*Id.* at 69 (citing Ex. 1011 ¶ 132), *see also id.* at 53–54 (citing Ex. 1011 ¶ 91).

Patent Owner's Arguments

Patent Owner argues that Petitioner overstates the number of possible combinations in NP2's broadest genus because it ignores (1) the Polar Proviso,[4] and (2) "'hydrogen or ($C_1$-$C_6$)alkyl' was of special interest at $R_6$ and $R_7$." PO Resp. 4, 28–29 (citing Ex. 2058 ¶¶ 360–362, 376–385, 390–393). Patent Owner also challenges the factorial approach to counting the number of subgenera as "hopelessly exaggerated." Sur-Reply 8 (citing *Snitzer v. Etzel*, 465 F.2d 899, 903 (CCPA 1972), emphasis omitted). Instead, Patent Owner adopts a multiplication approach. PO Resp. 45–46 (citing Ex. 2058 ¶¶ 287–289).

Patent Owner also faults Petitioner for ignoring "P1's disclosure when analyzing NP2's, despite P1 being incorporated by reference in NP2." *Id.* at 4 (emphasis omitted), 55–56. According to Patent Owner, P1's dependent claims and NP2's specific values are reinforcing blaze marks, and must be considered together, and Petitioner's failure to do so is fatal. *Id.* at 55–56.

Patent Owner further contends that "[a] P1 dependent claim and corresponding NP2 'specific value' identif[y] the ***exact*** substituent(s) Challenged Claim 1 requires at ***every*** challenged R position." *Id.* at 5, 30. Thus, Patent Owner argues, "the only plausible basis for challenging written

[4] Patent Owner points out that, in NP2, "[w]hile Formula I recites fifteen possibilities for each of $R_2$ and $R_6$, the 2′-position selections are limited by the following: '***provided that*** one of $R_2$ and $R_6$ is hydroxy, halo, ($C_1$-$C_6$)alkoxy, ($C_3$-$C_6$)cycloalkyloxy, trifluoromethyl, cyano, or $NR_{ad}R_{ae}$.'" PO Resp. 3–4. Because "[a]ll seven classes following 'provided that' are polar," Patent Owner refers to this restriction on $R_2$/$R_6$ selections as "Polar Proviso." *Id.* at 4.

description would be to allege that NP2 does not demonstrate possession of a genus incorporating them together." *Id.* at 30. According to Patent Owner, "[t]here are at least four ways in which blaze marks demonstrate possession of Challenged Claim 1's combination." *Id.* at 31.

First, Patent Owner asserts that "P1's claim 47 recites Challenged Claim 1's combination of substituents." *Id.* at 33. According to Patent Owner:

> A P1 multiple dependent claim—which NP2 incorporates by reference—claims Challenged Claim 1's subgenus: claim 47 ("$R_7$ is hydrogen or ($C_1$-$C_6$)alkyl") depends from claim 45 ("$R_6$ is hydrogen or ($C_1$-$C_6$)alkyl") depends from claim 33 ("$R_5$ is an amino acid") depends from claim 21 ("$R_3$ is hydroxy") depends from claim 13 ("$R_2$ is halo") depends from claim 2 ($R_1$ meets Challenged Claim 1's list of options) depends from claim 1 ($R_4$ and X meet Challenged Claim 1's list of options).

*Id.* at 6, *see also id.* at 31–33 (the same).

Second, Patent Owner argues "Challenged Claim 1's subgenus was one of a limited number of options identified by NP2's specific values for narrowing NP2's genus at the challenged R positions." *Id.* at 31. Patent Owner emphasizes there is "a clear interrelationship between the $R_2$/$R_6$ selections at the 2'-position and between the $R_3$/$R_7$ selections at the 3'-position." *Id.* According to Patent Owner, "[t]hese inter-relationships limit the number of combinations identified as of special interest." *Id.*, *see also id.* at 7 (the same).

Patent Owner argues that "NP2's specific values and P1's corresponding dependent claims concerning the 2' and 3'-positions ($R_2$/$R_6$ and $R_3$/$R_7$) identify just ***fifty-six*** subgenera of special interest: seven 2'-position permutations multiplied by eight 3'-position permutations." *Id.* at 44

(citing Ex. 2058 ¶ 263), *see also id.* at 6–7, 35–43 (analyzing substituents at the 2′- and 3′-positions). Adding the "only three options at $R_5$" in Formula I, Patent Owner concludes "Challenged Claim 1's subgenus is among only 168 combinations of class selections at $R_2$-$R_3$ and $R_5$-$R_7$ (seven at $R_2$/$R_6$ times eight at $R_3$/$R_7$ times three at $R_5$) that NP2's specific values and P1's claims identify as of special interest," not 7,441,875, as Petitioner alleges.[5] *Id.* at 44–45.

Third, Patent Owner points out that "***[a]ll*** of NP2's compounds (NP2's example compounds 100–123 and the compound of P1's claim 49) have the same 3'-position selections (hydroxy at $R_3$ and hydrogen at $R_7$) satisfying Challenged Claim 1's requirements." *Id.* at 49 (citing Ex. 1007, 14:23–25, 26:22–27:10; Ex. 2058 ¶¶ 297–308). In Patent Owner's view,

> NP2's examples blaze an undeniable trail to this single combination of choices as of special interest at the 3′-position. When that single combination of $R_3$/$R_7$ selections is considered with the seven (or at most ten) choices NP2's specific values and P1's corresponding dependent claims specify at $R_2$/$R_6$ . . . and the three choices Formula I permits at $R_5$, NP2 provides blaze marks to twenty-one (or at most thirty) subgenera of special interest.

*Id.* (citing Ex. 2058 ¶ 315). Patent Owner asserts that "POSAs would have readily envisaged all these subgenera, including Challenged Claim 1's subgenus." *Id.* (citing Ex. 2058 ¶ 316).

---

[5] Alternatively, Patent Owner asserts "[e]ven if one counts options reciting species of classes in Formula I," the total is still only 300: "ten each at the 2' and 3'-positions," and three at $R_5$. PO Resp. 44–46 (citing Ex. 2058 ¶¶ 264, 288, emphasis omitted).

Fourth, according to Patent Owner, of NP2's 25 compounds (compounds 100–123 and one recited in P1's claim 49), seven (compounds 105–108, 119–120, and 122) "satisfy all Challenged Claim 1's requirements except the Polar Proviso is met at $R_2$ by hydroxy rather than halo," and six additional examples (compounds 100–103 and 110–111) satisfy all disputed elements except $R_2$. *Id.* at 50–51 (citing Ex. 1007, 26:26–27:5; Ex. 2058 ¶¶ 322–323, emphasis omitted). Thus, Patent Owner argues that "over half of NP2's examples would satisfy the contested $R_2/R_3/R_5/R_6/R_7$ genus but for having hydroxy rather than halo at $R_2$." *Id.* at 51 (citing Ex. 2058 ¶ 324, emphasis omitted). Because halo is one of the Polar Proviso's six alternatives to hydroxy (*id.* (citing Ex. 1007, 3:29–4:1)), Patent Owner contends that

> POSAs would have recognized [the inventor]'s special interest in six subgenera within Formula I, corresponding to the $R_3$ and $R_5$-$R_7$ selections in the majority of NP2's examples combined with each of the six Polar Proviso classes recited for $R_2$ in NP2's "specific value[s]" (and in P1's dependent claims). One of these six subgenera corresponds exactly to Challenged Claim 1.

*Id.* at 53 (citing Ex. 2058 ¶¶ 329–331, emphasis omitted).

According to Patent Owner, these four blaze marks "are consistent and reinforcing—collectively compelling the conclusion that NP2 supports the Challenged Claims." *Id.* at 5, 53.

Discussion

After reviewing the entire record and weighing evidence offered by both parties, we find NP2, which incorporates P1 by reference, does not provide sufficient written support for the challenged claims. We focus our analysis on claim 1.

As an initial matter, we find no *ipsis verbis* disclosure of the subgenus of challenged claim 1, even though Patent Owner contends that P1's claim 47 encompasses challenged claim 1's exact subgenus. *See* PO Resp. 5, 32–33. P1's claim 47 specifies that "$R_7$ is hydrogen or ($C_1$-$C_6$)alkyl." Ex. 1008, 27:1–2. Claim 47, however, is a multiple dependent claim that depends from "any one of claims 1–46." *Id.* To reach the combination of $R_2$, $R_3$, $R_5$, and $R_6$ recited in challenged claim 1, an ordinarily skilled artisan would have to select the substituents defined in claims 13 ("$R_2$ is halo"), claim 21 ("$R_3$ is hydroxyl"), claim 33 ("$R_5$ is an amino acid"), and claim 45 ("$R_6$ is hydrogen or ($C_1$-$C_6$)alkyl") from the 46 claims, most of which are themselves multiple dependent claims. *See* Pet. 45–47; PO Resp. 5, 32–33.

Such picking and choosing from a "laundry list" disclosure does not constitute an *ipsis verbis* disclosure of every subgenus, including the subgenus of challenged claim 1. *See Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996) ("[J]ust because a moiety is listed as one possible choice for one position does not mean there is *ipsis verbis* support for every species or sub-genus that chooses that moiety.").

*Ipsis verbis* disclosure, however, is not necessary to satisfy the written description requirement of section 112. *Id.* at 1570. Instead, when analyzing the written description support for a claimed species, or as here, a claimed subgenus, in description of a broader genus, we look for blaze marks that single out particular trees in a forest. *In re Ruschig*, 379 F.2d 990, 994–95 (CCPA 1967). These blaze marks must be clear because "it is easy to bypass a tree in the forest, even one that lies close to the trail." *Fujikawa*, 93 F.3d at 1571. In this case, we find the point at which one must leave the trail to find

the tree is not well marked in P1 and NP2. Thus, P1 and NP2 do not provide sufficient written description support for the subgenus of challenged claim 1.

Before delving into the facts of this case, we discuss the parties' dispute over the law on written description. Petitioner argues:

> A broad generic description of an invention does not provide written description support to that genus unless the description: (1) discloses a representative number of species falling within the scope of the genus or (2) includes ***preferences that narrow the genus to a sufficiently small disclosure*** so that a POSA can easily "visualize or recognize" the members of the genus.

Pet. 31 (citing *Ariad*, 598 F.3d at 1349–50, emphasis added).

In Patent Owner's view, the emphasized language above misstates the law on written description. PO Resp. 22. According to Patent Owner, *Ariad* neither limits blaze marks to preferences, nor suggest a "sufficiently small disclosure" test. *Id.* at 22–23 (emphasis omitted). Instead, Patent Owner argues "blaze marks evidencing a subgenus was of 'special interest'—even if not 'preferred'—demonstrates possession of that subgenus and provides written description support." *Id.* at 21 (citing *Fujikawa*, 93 F.3d at 1571).

Although we agree with Patent Owner that blaze marks do not require identifying the species- or subgenus-at-issue as preferred, such as in preferred embodiments, we do not discern material difference between "preferences," as stated by Petitioner, and "special interest," as emphasized by Patent Owner.

Indeed, *Smith v. Horne*, a binding authority that Patent Owner relies on (PO Resp. 51, 52, 59, 62 (citing *Smith*, 450 F.2d at 1404)), explains that "[t]he indication or lack of indication of a preference for the composition, in the application disclosure, is an important factor to be considered in making

the determination [of written description support], since anyone attempting to carry out the disclosure of an application would logically begin with the preferred examples given." 450 F.2d at 1404. The Federal Circuit later reiterated the same in *Heymes v. Takaya*, another binding authority in which the court affirmed a BPAI decision relied upon by Patent Owner.[6] 867 F.2d 616 (Fed. Cir. 1989).

At bottom, we agree with Petitioner that regardless of the label we apply, when analyzing written description support, "the task is to search for blaze marks that guide a skilled artisan to the claimed subgenera." Reply 3–4 (citing *Fujikawa*, 93 F.3d at 1571); *see also Smith*, 450 F.2d at 1404 ("The determining factor is whether the application would fairly suggest to the skilled worker in the art the particular composition claimed, or whether the desirability of that composition could be as[c]ertained only by extensive experimentation.").

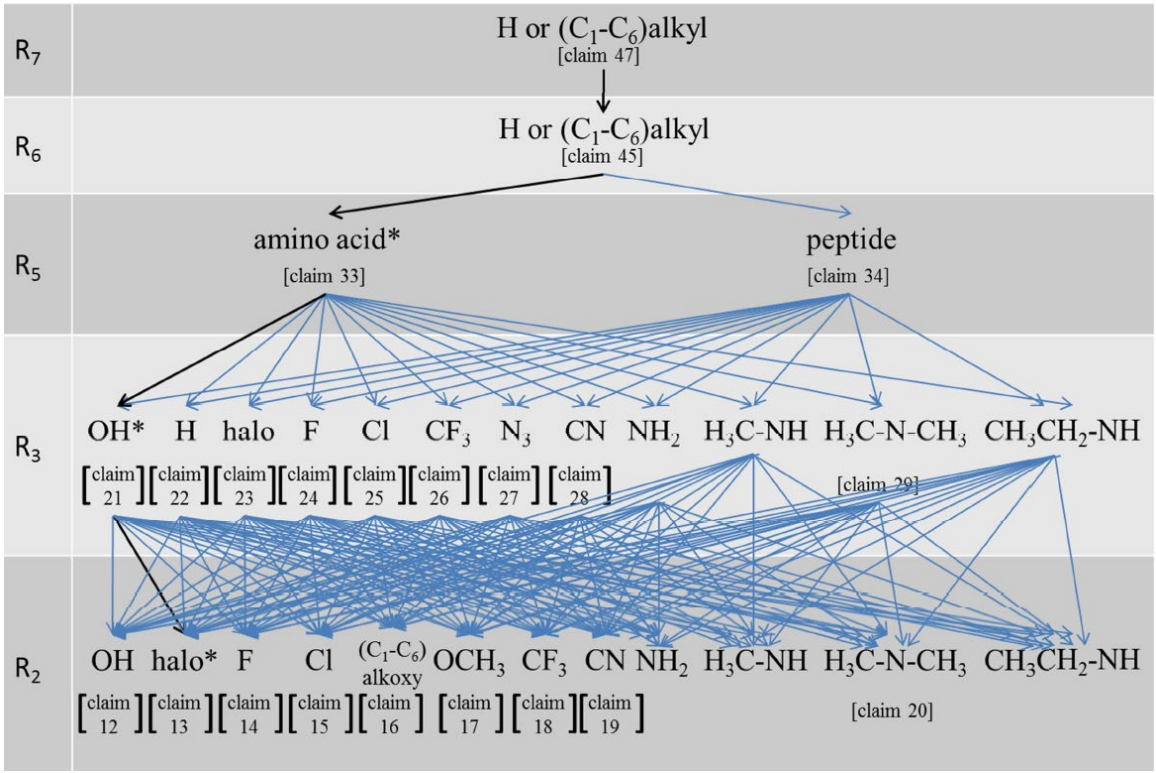
As for Patent Owner's argument that "there are at least four ways in which blaze marks demonstrate possession" of the subgenus of challenged claim 1 (PO Resp. 5–9, 31–53), we are not persuaded.

First, we are not persuaded that P1's claim 47, viewed as a part of NP2 because P1 is incorporated into NP2 by reference, constitutes an adequate blaze mark. As explained above, claim 47 is a multiple dependent claim that depends from "any one of claims 1–46." Ex. 1008, 27:1–2. To reach the subgenus of challenged claim 1, an ordinarily skilled artisan would

[6] Patent Owner cites *Heymes v. Takaya*, 6 U.S.P.Q.2d 1448 (BPAI Feb. 10, 1988) *passim*, and recognizes that the BPAI decision was affirmed in 867 F.2d 616 (Fed. Cir. 1989). *See* PO Resp. vi.

have to select claims 13, 21, 33, and 45 from the numerous multiple dependent claims. PO Resp. 5, 32–33. Petitioner presents the following figure to illustrate this point:

**Figure 1. Potential Combinations of Multiple Dependent Claims of P1**




The figure above is Petitioner's presentation of "an enormous number of possibilities" when "picking and choosing from P1's claims," "even starting with claim 47." Pet. 47. We agree with Petitioner regarding the magnitude of those possibilities.

P1 itself does not contain any disclosure to guide an ordinarily skilled artisan to choose a specific $R_2$, $R_3$, or $R_5$ at each position, let alone the claimed combination. NP2 incorporates P1 by reference, and also lists "specific values" for each R position. For example, for $R_2$, NP2 discloses:

A specific value for $R_2$ is hydroxy.
A specific value for $R_2$ is halo.
A specific value for $R_2$ is fluoro.
A specific value for $R_2$ is (C1-C6)alkoxy.
A specific value for $R_2$ is methoxy.
A specific value for $R_2$ is trifluoromethyl.
A specific value for $R_2$ is cyano.
A specific value for $R_2$ is amino, mthylamino, dimethylamino, ethylamino, or dimethylamino.

Ex. 1007, 12:8–17. These specific values for $R_2$ duplicate those recited in claims 12–20 in P1. *See* Ex. 1008, 23:6–24. Similarly, NP2 discloses specific values for $R_3$, $R_5$, $R_6$, and $R_7$ that duplicate those recited in claims 21–29 and 33–48 in P1. *Compare* Ex. 1008, 23:25–24:17, 24:25–27:7, *with* Ex. 1007, 12:18–27, 13:4–14:22.

Patent Owner argues "NP2's specific values and P1's dependent claims are mutually reinforcing." PO Resp. 34. Even if that is the case, NP2's specific values only reinforce P1's claims that there are multiple choices at each relevant R position. They do not guide an ordinarily skilled artisan to pick claims 13, 21, 33, and 45 of P1 to combine with claim 47 in order to narrow the substituents to the combination of challenged claim 1. As Petitioner correctly points out, "[a] POSA could just as likely combine claim 17 (where $R_2$ is methoxy), claim 27 (where $R_3$ is azido), and claim 35 (where $R_5$ is a peptide), in combination with claim 47, or any other combination of claims." Pet. 46 (citing Ex. 1011 ¶ 75). It would require hindsight to pick, among 46 claim possibilities—many of which are multiple dependent claims themselves—claims 13 ("$R_2$ is halo"), 21 ("$R_3$ is hydroxy"), 33 ("$R_5$ is an amino acid"), and 45 ("$R_6$ is hydrogen or ($C_1$-$C_6$)alkyl") to reach the subgenus of challenged claim 1.

That, of course, is assuming that an ordinarily skilled artisan would not have started with claim 48, another multiple dependent claim, which recites "$R_3$ is hydrogen or alkyl" and limits $R_7$ to a list of fourteen categories of substituents. Ex. 1008, 27:4–7. P1 and NP2 do not guide against starting with claim 48. In fact, NP2 discloses the same $R_3$ and $R_7$ substituents as in P1's claim 48, and labels it, in contrast to the "specific value(s)" when listing other substituents, a "specific compound," which suggests a special interest in this combination. *See* Ex. 1007, 14:19–22. In any event, were claim 48 the starting point, then no matter how it is combined with the claims it depends from, an ordinarily skilled artisan would not have reached the subgenus of challenged claim 1.

Second, we also are not persuaded that "Challenged Claim 1's subgenus is among only 168 combinations of class selections at $R_2$-$R_3$ and $R_5$-$R_7$ . . . that NP2's specific values and P1's claims identify as of special interest." *See* PO Resp. 45 (citing Ex. 2058 ¶¶ 287–289). For example, in counting the choices for $R_7$, Patent Owner treats the "fourteen classes" of substituents in P1's claim 48 and NP2's corresponding specific compound as a single option. *Id.* at 40. Similarly, for $R_6$, Patent Owner treats the "various classes"—in fact, also fourteen classes—of substituents in P1's claim 46 and the corresponding specific value in NP2 as a single option. *Id.* at 35, *see also id.* at 37 (treating "$R_2$ is amino, methylanino, dimethylamino, ethylamino, or dimethylamino" as a single option), 41 (treating "$R_3$ is amino, methylamino,

dimethylamino, ethylamino, or dimethylamino" as a single option). Thus, Patent Owner undercounts the combinations of substituents at $R_2/R_3/R_6/R_7$.[7]

Third, we further are not persuaded that a single combination of selections at the 3'-position is a sufficient blaze mark for written description support of the subgenus of challenged claim 1. Patent Owner emphasizes that "***[a]ll*** of NP2's compounds . . . have the same 3'-position selections (hydroxy at $R_3$ and hydrogen at $R_7$) satisfying Challenged Claim 1's requirements." *Id.* at 49 (citing Ex. 1007, 14:23–25, 26:22–27:10; Ex. 2058 ¶¶ 297–308). This, according to Patent Owner, should limit the selection of $R_3/R_7$ combination to only one. *Id.*

---

[7] Patent Owner also undercounts the number of substituents at $R_5$. *See* PO Resp. 44 ("Formula I includes only three options at $R_5$."). P1 and NP2 both disclose $R_5$ as "an amino acid, a peptide, or $NR_aR_b$." Ex. 1007, 4:9; Ex. 1008, 4:9. They both, however, define "each $R_a$ and $R_b$ is independently hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, aryl, or aryl$(C_1$-$C_6)$alkyl; or $R_a$ and $R_b$ together with the nitrogen to which they are attached form a pyrrolidino, piperidino or morpholino." Ex. 1007, 4:15–17; Ex. 1008, 4:15–17. P1 further includes claims, and NP2 further includes corresponding specific values, directed to $NR_aR_b$. Ex. 1007, 13:6–14:12; Ex. 1008, 24:29–26:18 (claims 35–44). In our view, thus, $NR_aR_b$ represents more than a single option at $R_5$. Nonetheless, the Petition, as well as the supporting expert declaration, fail to take this into consideration. *See* Pet. 47 (Figure 1 listing only amino acid and peptide as options for $R_5$); Ex. 1011 ¶ 58 (expert testifying $R_5$ "only has three classes of R group substituents"). It is not until the Reply that Petitioner recognizes "all possibilities for the variables $R_a$ and $R_b$." Reply 17. That is simply too late. Thus, for purpose of this Decision, we consider there are only three options for $R_5$. *See* Patent Trial and Appeal Board Consolidated Trial Practice Guide November 2019, 73 ("Petitioner may not submit new evidence or argument in reply that it could have presented earlier.").

Patent Owner, however, neglects to explain why an ordinarily skilled artisan would focus on this $R_3/R_7$ combination while ignoring the fact that P1 and NP2 exemplifies hydroxy, not halo, at $R_2$. Indeed, as Petitioner points out, all "representative compounds" and compounds "useful in the methods of the invention" in P1 and figures of NP2, as well as twenty-three out of twenty-four additional "[r]epresentative compounds" in NP2, have hydroxy at $R_2$.[8] Pet. 43 (citing Ex. 1008, Figs. 1, 3), 57–59 (citing Ex. 1007, 26–27, Figs. 1, 3); Ex. 1007, 7:9–13; Ex. 1008, 7:9–13. Thus, we agree with Petitioner that Patent Owner "inconsistently cherry-picks only a portion of R groups in NP2's compounds to create an imaginary example found nowhere in the written description." Reply 21.

Fourth, we are not persuaded that the fact that thirteen out of twenty example compounds in NP2 "satisfy Challenged Claim 1's requirements for all challenged R positions except $R_2$ and meet the Polar Proviso at $R_2$ but with hydroxy rather than halo" serves as an adequate blaze mark for challenged claim 1's subgenus, which requires halo at $R_2$. *See* PO Resp. 32 (emphasis omitted), *see also id.* at 9–10, 50–53 (the same). Indeed, written description analysis requires "[t]aking each claim . . . as an integrated whole rather than as a collection of independent limitations." *Novozymes*, 723 F.3d at 1349. On this point, we agree with Petitioner that

> [Patent Owner's] efforts to make NP2's examples into blaze marks is pure hindsight. On the one hand, [Patent Owner]

[8] The only one left contains hydrogen, again, not halo, at $R_2$. Pet. 59 (citing Ex. 1011 ¶ 101); *see also* Ex. 1038, 36:3–14 (Patent Owner's expert testifying that "[a]t the R2 position, there is variation between two groups, hydrogen or hydroxyl").

> suggests a skilled artisan would not look beyond the specific substituents contained in NP2's examples at every position other than $R_2$/$R_6$. POR, 51; Boons [Ex. 1039] ¶¶73-78. On the other hand, [Patent Owner] broadens $R_2$ and $R_6$ beyond the substituents reflected in each example (hydrogen and hydroxy) in order to manufacture imaginary possibilities where $R_2$ is halo. POR, 51. There is no reasonable justification for interpreting the examples as teaching the selections made at some positions ($R_3$ and $R_7$) but not at others ($R_2$ and $R_6$); either NP2's examples blaze a trail to selections actually made, or they blaze no trail at all. Whatever the case, NP2's examples do not lead a skilled artisan to the subgenera claimed in the '830 patent. Boons [Ex. 1039] ¶¶ 103-105.

Reply 22.

Patent Owner's other arguments, some of which have more merit than others, do not change the outcome of this case. For example, Patent Owner faults Petitioner for ignoring the Polar Proviso. PO Resp. 3–4. In response, Petitioner points out that the proviso itself does not mention polarity, despite the label Patent Owner coins, and that NP2 mentions polarity only once, despite the special interest Patent Owner alleges. Reply 10–11 (citing Ex. 1007, 3:5–9). According to Petitioner, regardless of what "polar" means, the proviso leaves out as many polarity substituents as it includes. *Id.* at 11–12 (citing Ex. 1039 ¶¶ 36–42).

Patent Owner does not dispute these arguments. Instead, Patent Owner accuses Petitioner of "Dwell[ing] on Labels While Neglecting Substance." Sur-Reply 22. Patent Owner explains that "all the Polar Proviso classes are capable of 'polar interactions,'" and "certain classes in Formula I excluded from the Polar Proviso" are not polar. *Id.* at 23. Patent Owner

further argues that "[i]t is immaterial that other classes excluded from the Polar Proviso may theoretically permit polar interactions." *Id.*

We do not need to resolve the parties' dispute on this issue, other than observing that NP2 discloses polar interactions at the 2'- and 3'-positions, together with hydrogen bonding and ion pairing at these positions, "preferentially interact with the active site residue Asp-43, which is consistent with the reduced ability of 2'-deoxy nucleoside phosphoramidates to serve as substrates." *See* Ex. 1007, 3:5–9.

We, however, agree with Patent Owner that, because the Polar Proviso is not considered, the Petition overstates the number of possible combinations in NP2's broadest genus. PO Resp. 4, 28–29. In fact, Petitioner recognizes this and has revised the number of possible combinations with different R substituents from 7,441,875 in the Petition to 4,266,675 in the Reply to account for the proviso. Reply 25–26 (citing Ex. 1039 ¶¶ 58–66).

We also question the propriety of Petitioner's factorial approach in calculating the number of subgenera in formula I. *See* Pet. 39–40 (citing Ex. 1011 ¶¶ 54–60); *see also* Ex. 1011 ¶¶ 56–57 (testifying that "for $R_2$ alone, there are 32,767 possible ways to combine the 15 classes of R group substituents," because "there is no teaching in P1 [or NP2] that discusses any preference for only choosing one of these classes, as opposed to choosing a combination of two classes, or three classes, etc."). Neither Petitioner nor its expert has provided sufficient evidence or argument to show P1 or NP2 teaches more than one class of substituent at each R position. Thus, we find Petitioner's number of subgenera higher than warranted.

At the same time, as explained above, we find the number of subgenera Patent Owner put forth, 168, to be significantly lower than the proper count. But, even if we were to accept that NP2 identifies 168 combinations of substituents at the relevant R positions, we still find insufficient blaze marks in NP2 to guide an ordinarily skilled artisan to the subgenus of challenged claim 1. We reach this conclusion in view of evidentiary record in this case, and guidance from the Federal Circuit and its predecessor court, including that found in *Ruschig*, *Fujikawa*, and *Novozymes*.

In *Ruschig*, the applicants challenged the decision by the Patent Office's Board of Appeals, finding chlorpropamide, the compound of the claim-at-issue, "is not named or identified by formula and it can find support only as choices made between the several variables involved." 379 F.2d at 991–92. The Board concluded "[t]his is not regarded as adequate support for a specific compound never named or otherwise exemplified in the specification as filed," and the Court of Customs and Patent Appeals affirmed. *Id.* at 992.

The court noted "the general disclosure of the application encompasses something like half a million possible compounds. It also discloses a number of specific compounds." *Id.* at 993. The appellants argued an original claim was "in effect one of the 'guides,'" because "there are 'approximately' 48 compounds within the scope of that claim[,] all of which are 'readily determinable by skilled chemists.'" *Id.* at 994.

Rejecting this argument, the court stated:

> Specific claims to single compounds require reasonably specific supporting disclosure and while . . . naming [the compounds] is not essential, something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required. Surely, given time, a chemist could name (especially with the aid of a computer) all of the half million compounds within the scope of the broadest claim, which claim is supported by the broad disclosure. This does not constitute support for each compound individually when separately claimed.

*Id.*

The appellants further contended that "[o]ther 'guides' allegedly lead[] to chlorpropamide." *Id.* According to the appellants, the specification disclosed eleven processes for making the many compounds of the invention, five of which employ an alkylamine at R(2) in the general formula. *Id.* The court observed in that formula, "there is also the variable R which may be hydrogen, chlorine, bromine, methyl, or methoxy and R(1) which may be either chlorine or bromine." *Id.* Together with some other variables, the court concluded "[t]his makes for more than a few unidentified possibilities not determined by the use of alkylamine alone." *Id.*

To lead to the claimed compound, "R must be hydrogen and R(1) must be chlorine and the alkylamine, R(2), must be propylamine." *Id.* The appellants argued that the "guide" became "more crystallized by the recitation of the alkylamines which can be employed in the four or five reactions described as using them." *Id.* at 995. The appellants emphasized n-propylamine as one of those amines recited. *Id.*

Rejecting this argument, the court first noted the specification listed nineteen primary amines that may be used. The court explained that listing propylamine with eighteen others does not add anything to "the initial

statement that one may use an alkyl amine containing from 2 to 6 carbon atoms," because "[p]ropylamine is such an amine but one is not led to it in ***preference*** to the others merely by listing them all and identifying it, with the others, by name." *Id.* (emphasis added).

In the instant proceeding, formula I in NP2 encompasses a large number of subgenera. In fact, Patent Owner acknowledges that even P1's claim 47 encompasses many subgenera. Tr. 29:1–3. Patent Owner argues P1 and NP2 identify 168 combinations of special interest. PO Resp. 45. But, to provide adequate written description support for challenged claim 1's single subgenus, "reasonably specific supporting disclosure," or, as the *Ruschig* court put it, "something more than the disclosure of a class of 1000, or 100, or even 48, [subgenera] is required." 379 F.2d at 994. A class of 168 subgenera, even if that were the correct number, is squarely within the *Rushig's* illustrative range and is insufficient to provide reasonably specific support for a single subgenus.

Patent Owner argues that halo is one of seven (or ten) alternatives at $R_2$, and hydroxy is one of eight (or ten) alternatives at $R_3$. PO Resp. 35–46. But merely listing them together with the others, without more, would not guide an ordinarily skilled artisan to each specific substituent, let alone the claimed combination.

In *Fujikawa*, the application disclosed compounds of a certain generic structure with four variable groups (R, $R_0$, $R_1$, and $R_2$), each of which could be independently chosen from a list of functional groups. 93 F.3d at 1570. The subgenus-at-issue "is directed to compounds of the above structure in

which R is cyclopropyl and $R_0$ is 4–fluorophenyl."[9] *Id.* The Board of Patent Appeals and Interferences found insufficient blaze marks for the subgenus. *Id.* at 1570–71. The Federal Circuit affirmed. *Id.* at 1571.

There, the appellant pointed out that "with respect to practically every position on the compound," the claimed subgenus recited at least one of the preferred choices. *Id.* With respect to position R, the appellant argued that one of ordinary skill would have "substitute[d] cyclopropyl for isopropyl because the two substituents are isosteric." *Id.* The court rejected this argument, noting that "[a]lthough, in hindsight, the substitution of cyclopropyl for isopropyl might seem simple and foreseeable, [the] disclosure provides no indication that position R would be a better candidate for substitution than any other." *Id.* Thus, the court concluded that the disclosure would not lead an ordinarily skilled artisan to the subgenus-at-issue. *Id.*

The facts in the instant proceeding are similar to those in *Fujikawa*. Here, all but one of the exemplary compounds in P1 and NP2 contain hydroxy, not halo, at $R_2$. Like in *Fujikawa*, although "in hindsight," the substitution of halo for hydroxy "might seem simple and foreseeable," neither P1 nor NP2 provides any suggestion that halo would be a better candidate than hydroxy, or any other substituents identified for $R_2$ in P1's claims and NP2's specific values.

[9] There was no dispute over the substituents at $R_1$ and $R_2$. *Fujikawa*, 93 F.3d at 1570.

Extending *Ruschig*'s metaphor, "it is easy to bypass a tree in the forest, even one that lies close to the trail, unless the point at which one must leave the trail to find the tree is well marked." *Fujikawa*, 93 F.3d at 1571. Here, although the specific values "do blaze a trail through the forest," the trail "runs close by" the tree, but "does not direct one to the . . . tree in particular, and does not teach the point at which one should leave the trail to find it." *Id.*

Similarly, in *Novozymes*, the claim-at-issue recited three limitations, each of which "is expressly stated in the disclosure" of a 2000 application. 723 F.3d at 1348. The Federal Circuit found "the supporting disclosure of the 2000 application provides only generalized guidance," but "contains no disclosure of any variant that actually satisfies" the claim. *Id.* at 1346, 1348. The court stated:

> Taking each claim—as we must—as an integrated whole rather than as a collection of independent limitations, one searches the 2000 application in vain for the disclosure of even a single species that falls within the claims or for any "blaze marks" that would lead an ordinarily skilled investigator toward such a species among a slew of competing possibilities.

*Id.* at 1349.

We have the same situation here. It is undisputed that P1 and NP2 expressly disclose the substituents at each R position as claimed; yet, they do not disclose challenged claim 1's subgenus, or provide sufficient blaze marks that would lead an ordinarily skilled artisan, among a myriad possibilities, to such a subgenus. Similar to the appellant in *Novozymes*, Patent Owner here works backward from a knowledge of challenged claim 1 by hindsight, and "seeks to derive written description support from an

amalgam of disclosures plucked selectively from" P1 and NP2. *See id.* "[V]iewing the matter from the proper vantage point 'of one with no foreknowledge of the specific [subgenus],'" and taking challenged claim 1 as a whole rather than as the sum of its individual limitations, we find the particular subgenus of challenged claim 1 lacks meaningful support in P1 and NP2. *See id.*

In sum, the disclosures of P1 and NP2 do not provide sufficient blaze marks to guide an ordinarily skilled artisan through the forest of disclosed possibilities toward the subgenus of challenged claim 1. Thus, NP2, with P1 incorporated by reference, does not provide adequate written description support for challenged claim 1.

Regarding the challenged dependent claims, Petitioner argues although they narrow the broad scope of the classes of R group substituents in independent claim 1, "similar to P1, there are no 'preferences' or other teachings in NP3/NP2 that would provide direction to a POSA, with no foreknowledge of the later-claimed '830 patent subgenus, to select the narrowed $R_2$, $R_3$, $R_5$, $R_6$, and $R_7$ groups" claimed therein. Pet. 66 (citing Ex. 1011 ¶ 122), *see also id.* at 50 (citing Ex. 1011 ¶ 50) (discussing P1). According to Petitioner, "[f]or similar reasons that '830 patent claim 1 does not have written description support in NP3/NP2, the dependent claims of the '830 patent also fail to have written description support in NP3/NP2." *Id.* at 66, *see also id.* at 50 (discussing P1).

Patent Owner contends that the additional limitations of the dependent claims use "language drawn verbatim from additional P1 dependent claims

and corresponding NP2 'specific values,'" or are supported by NP2's figures or examples. PO Resp. 74–75. We are not persuaded.

We reiterate that in analyzing written description support, we must take each claim "as an integrated whole rather than as a collection of independent limitations." *Novozymes*, 723 F.3d at 1349. The challenged dependent claims require picking and choosing multiple substituents, not just the one further limited in those claims. Thus, we agree with Petitioner, and determine, for similar reasons explained above, NP2, with P1 incorporated by reference, does not provide adequate written description support for challenged claims 2–9, 11–21, and 23–28.

In sum, because NP2, with P1 incorporated by reference, does not provide sufficient written description support for the challenged claims, the priority date of those claims is no earlier than March 28, 2014, the filing date of the application that issued as the '830 patent. Thus, Sofia qualifies as prior art and anticipates those claims.

## CONCLUSION[10]

After reviewing the entire record and weighing evidence offered by both parties, we determine that Petitioner has demonstrated by a

[10] Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding. See* 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent

preponderance of the evidence that Sofia anticipates claims 1–9, 11–21, and 23–28 of the '830 patent.

In summary:

| Claims | 35 U.S.C. § | Reference | Claims Shown Unpatentable | Claims Not Shown Unpatentable |
|---|---|---|---|---|
| 1–9, 11–21, 23–28 | 102 | Sofia | 1–9, 11–21, 23–28 | |
| **Overall Outcome** | | | 1–9, 11–21, 23–28 | |

ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1–9, 11–21, and 23–28 of the '830 patent are held unpatentable;

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

Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. *See* 37 C.F.R. § 42.8(a)(3), (b)(2).

FOR PETITIONER:

Alicia Russo
Frederick Millett
Robert S. Schwartz
Stephen K. Yam
VENABLE LLP
arusso@venable.com
Gilead830ipr@venable.com
RSchwartz@Venable.com

FOR PATENT OWNER:

Edward Gates
Richard Giunta
Gerald Hrycyszyn
WOLF, GREENFIELD & SACKS, P.C.
egates-ptab@wolfgreenfield.com
Rgiunta-ptab@wolfgreenfield.com
Ghrycyszyn-ptab@wolfgreenfield.com