

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARRAY BIOPHARMA INC.,
Petitioner,

v.

TAKEDA PHARMACEUTICAL COMPANY LIMITED,
Patent Owner.

Case IPR2015-00754
Patent 8,592,454 B2

Before ERICA A. FRANKLIN, BRIAN P. MURPHY, and
TINA E. HULSE, *Administrative Patent Judges*.

FRANKLIN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.108

I. INTRODUCTION

Array BioPharma Inc. (“Petitioner”) filed a Corrected Petition requesting an *inter partes* review of claims 1–7 and 12–17 of U.S. Patent No. 8,592,454 B2 (Ex. 1001, “the ’454 patent”). Paper 5 (“Petition” or “Pet.”). Takeda Pharmaceutical Company Limited (“Patent Owner”) filed a Preliminary Response to the Petition. Paper 9 (“Prelim. Resp.”).

On August 19, 2015, we instituted an *inter partes* review of claims 1–7 and 12–16 of the ’454 patent. Paper 10 (“Dec. Inst.”). Patent Owner filed a Patent Owner Response to the Petition. Paper 23 (“PO Resp.”). Petitioner filed a Reply to the Patent Owner Response. Paper 27 (“Pet. Reply”).

Additionally, Patent Owner filed a Contingent Motion to Amend seeking to replace any of original claims 1–7 and 12–16 found to be unpatentable with substitute claims 18–29 and proposed new claims 30–31. Paper 22 (“Amend Mot.”). Petitioner filed an Opposition to the Contingent Motion to Amend. Paper 28 (sealed); Paper 29 (redacted) (“Amend Opp.”). Patent Owner filed a Reply to Petitioner’s Opposition. Paper 39 (redacted); Paper 40 (sealed) (“Amend Reply”). Patent Owner also filed a Motion to Exclude with respect to eleven of Petitioner’s exhibits. Paper 42 (“Exclude Mot.”). Petitioner filed an Opposition to the Motion to Exclude. Paper 48 (“Exclude Opp.”). Patent Owner responded to that Opposition in a Reply in Support of the Motion to Exclude. Paper 50 (“Exclude Reply”).

On April 11, 2016, the parties presented arguments at an oral hearing. Paper 60 (“Tr.”).

The Board has jurisdiction under 35 U.S.C. § 6(c). In this Final Written Decision, issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–7 and 12–16 are unpatentable. Additionally, we *deny* the Motion to Exclude with respect to Exhibits 1011, 1012, and 1032, and *dismiss* the motion with respect to Exhibits 1020–1026 and 1033. Also, we *deny* the Motion to Amend.

A. Related Proceedings

Petitioner and Patent Owner identify no related proceedings. Pet. 3; Paper 7, 2.

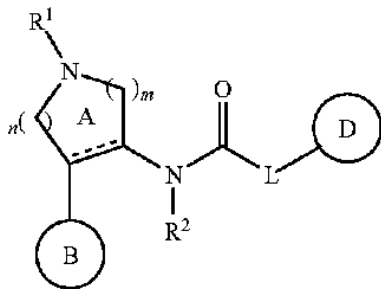
B. The '454 Patent

The '454 patent relates to a nitrogen-containing heterocyclic compound and its use as an agent for the treatment of various diseases. Ex. 1001, Abstract. The Specification explains that, based on the specific chemical structure, the compound has “a strong tachykinin receptor antagonistic action,” particularly with respect to NK-1, NK-2, and NK-3 receptors. *Id.* at 9:58–65. This antagonistic activity makes the compound useful as an agent for the prophylaxis and treatment of diseases associated with those receptors, including central nervous system diseases. *Id.* at 9:36–38; 75:22–27. The compound “may be used alone, or in admixture with a suitable, pharmaceutically acceptable carrier, for example, excipients.” *Id.* at 77:14–15. The Specification explains that “[t]he dose in terms of the compound of the present invention is not particularly limited if it causes no problems of side effects.” *Id.* at 81:9–11.

C. Illustrative Claims

Claims 1, 12, and 13 of the '454 patent are illustrative and are reproduced below:

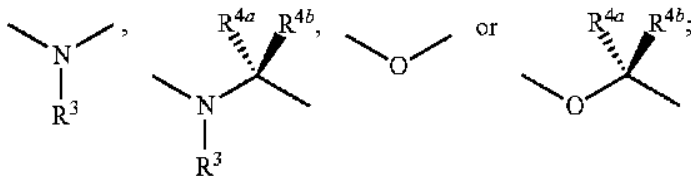
1. A compound represented by the formula



wherein:

ring A is a piperidine ring or a pyrrolidine ring and each straight line is a single bond and ----- is a single bond; ring B is an aromatic ring optionally having substituent(s); ring D is an aromatic ring optionally having substituent(s), wherein 6-quinolyl is excluded;

L is a group represented by the formula



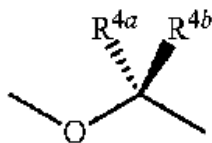
R², R³, R^{4a} and R^{4b} are each independently a hydrogen atom, an optionally halogenated C₁₋₆ alkyl group or an optionally halogenated C₃₋₆ cycloalkyl group, or R² and R³ are optionally bonded via an alkylene chain or an alkenylene chain, or R^{4a} and R^{4b} are optionally bonded via an alkylene chain or an alkenylene chain;

R¹ is a hydrogen atom or a substituent;

m and n are each independently an integer of 0 to 3; and

$m+n$ is an integer of 2 to 3;

provided that when L is a group represented by the formula



wherein each of R^{4a} and R^{4b} is as defined above, then ring

D is an aromatic ring having substituent(s);
excluding: N-[4-(biphenyl-4-yl)piperidin-3-yl]-N'-(naphthalen-2-yl)urea;
or a salt thereof.

12. A pharmaceutical composition comprising the compound or salt according to claim 1 and a pharmaceutically acceptable carrier.

13. A method of antagonizing an NK1 receptor in a mammal, comprising administering the pharmaceutical composition according to claim 12 to the mammal.

D. The Cited References and Declarations

Petitioner relies upon the following prior art references:

Shibayama	EP Patent Application No. 1623721 A1, published Feb. 8, 2006.	Ex. 1003
Rhim	KR Patent No. 10-0838645, issued June 10, 2008.	Ex. 1005

Petitioner also relies upon the Declarations of Michael Crimmins, Ph.D. (Ex. 1002 and Ex. 1011) and Peter Bernstein, Ph.D. (Ex. 1012).

Patent Owner relies upon the Declaration of David Hunt, Ph.D. (Ex. 2033).

E. The Instituted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–7 and 12–16 of the '454 patent on the following grounds (Pet. 6):

Claims Challenged	Basis	Reference
1–7 and 12–16	§ 102	Shibayama
1–7 and 12–16	§ 102	Rhim

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *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).

1. The Preambles and Wherein Clauses of Claims 13–16

Claim 13 recites the following preamble: “A method of antagonizing an NK1 receptor in a mammal.” Claim 14 recites the following clause: “wherein the method further antagonizes an NK2 receptor and/or an NK3

receptor.” Claim 15 recites the following preamble: “A method of antagonizing an NK2 receptor in a mammal.” Claim 16 recites the following clause: “wherein the method further antagonizes an NK1 receptor and/or an NK3 receptor.” In the Petition, Petitioner asserted that “[u]nder the broadest reasonable construction standard, the preamble[s] of claims 13 and 15 and the wherein clauses of claims 14 and 16 should not be considered a limitation on the claimed method.” Pet. 11. Patent Owner disagreed with Petitioner. Prelim. Resp. 17–25.

In the Institution Decision, we determined that the language of the preamble and wherein clause did not merely state the purpose or intended use of an invention. Rather, we determined that, when read in the context of the claims, the patent Specification, and the prosecution history, the preambles and wherein clauses of method claims 13–16 are necessary “to give life, meaning, and vitality” to the claims. *See Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1345 (Fed. Cir. 2003) (preamble language limits claim when it recites “the essence of the invention without which performance of the recited steps is nothing but an academic exercise”). The preambles of claims 13 and 15, moreover, provide antecedent basis for the term “the mammal” in the body of the respective claims, and the preambles of claims 14 and 16 provide antecedent basis for the term “further antagonizes” in the body of the respective claims. Where the preamble provides such antecedent basis, “it indicates a reliance on both the preamble and the claim body to define the invention.” *Catalina Mktg. Int’l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002) (citing *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257 (Fed. Cir. 1989)).

We agreed with Patent Owner that the Specification places importance not only on the compounds of the invention, but also on their “excellent antagonistic action for a tachykinin receptor and use thereof.” Ex. 1001, 1:12–13. More specifically, the Specification places importance on the fact that the chemical structure of the disclosed compounds enables strong NK-1, NK-2, and NK-3 receptor antagonistic action. *Id.* at 9:58–65. Indeed, during prosecution, in response to a non-final rejection based on anticipation of product claims directed to “medicaments” characterized as antagonists, the product claims were amended to recite methods of antagonizing a particular receptor, comprising an administering step. Ex. 1006,¹ 23–24; Ex. 2002,² 5. Moreover, but for the informing preambles or wherein clauses of these method claims, the utility of the administration step would not be appreciated.

Thus, we determined that the preambles of claims 13 and 15 and the wherein clauses of claims 14 and 16 recite claim limitations entitled to patentable weight. Neither party has challenged that determination in the Patent Owner’s Response or the Petitioner’s Reply. Nor do we see any reason to alter our earlier determination.

2. *Remaining Claim Terms*

Based on our analysis, we determine that no express claim construction is necessary for any of the remaining claim terms. *See Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)

¹ Non-Final Office Action, mailed Aug. 1, 2012.

² Amendment, filed Dec. 3, 2012.

(only terms which are in controversy need to be construed, and only to the extent necessary to resolve the controversy).

B. Level of Ordinary Skill in the Art

The level of skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1324 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966) and *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Petitioner asserted in the Petition that one of ordinary skill in the art at the time of the filing of the '454 patent “would likely [have] at least a graduate degree such as a Ph.D. in medicinal chemistry or organic chemistry and would include experience in an industrial or academic laboratory.” Pet. 16–17 (citing Ex. 1002 ¶ 21).

Patent Owner asserted that one of ordinary skill in the art “is an individual with an undergraduate degree in organic chemistry or similar discipline, with the specific kind of experience set forth in the Declaration of Dr. David Hunt.” PO Resp. 10–11 (citing Ex. 2033 ¶¶ 18–23).

In the Institution Decision, we explained that the evidence as a whole supports Petitioner’s broader description of the level of ordinary skill in the art. Accordingly, we adopted Petitioner’s statement of the level of ordinary skill in the art. Patent Owner has not challenged that finding in the Patent Owner’s Response. Nor do we see any reason to alter our earlier finding.

C. Anticipation by Shibayama

Petitioner asserts that claims 1–7 and 12–16 of the '454 patent are anticipated by Shibayama. Pet. 21–33. In the Patent Owner’s Response, Patent Owner challenges Petitioner’s contentions by asserting that

Shibayama does not enable one of skill in the art to prepare the claimed compounds and compositions. PO Resp. 1.

1. *Shibayama*

Shibayama is directed to an effector cell function inhibitor comprising a CCR5 antagonist. Ex. 1003 ¶ 1. Shibayama describes the object of its invention is “to provide a drug which specifically inhibits [the] function of effector cell[s]” and is “useful for the prevention and/or treatment of a disease in which [the] effector cell is concerned in the formation, advance and/or continuation of the disease, such as a transplant rejection, an autoimmune disease, an ischemic disease, an allergic disease, a cancer or a metastasis.” *Id.* ¶ 14. To that end, Shibayama describes discovering that an antagonist of a CCR5 chemokine receptor inhibits the function of effector cells. *Id.* ¶ 15. The CCR5 antagonist includes compounds represented by formula (I) and formula (II), each reproduced below:



Id. ¶ 16 (formula (I)), ¶ 37 (formula (II)). Notably, one of the preferred compounds represented by formula (II) and useful as a CCR5 antagonist is N-[4-(4-{[3-[(anilinocarbonyl)(butyl)amino]-4-(3-fluorophenyl)pyrrolidin-1-yl]methyl}phenoxy)phenyl]methanesulfonamide (“Compound 3”). *Id.* ¶ 67. Shibayama teaches that the disclosed CCR5 antagonists may be administered safely to mammals and describes an exemplary oral dosage of 30 mg/kg, administered twice daily. *Id.* ¶ 71. Shibayama describes

preparing pharmaceutical compositions comprising mixing the CCR5 antagonist with an excipient. *Id.* ¶ 19.

2. Claims 1–7 and 12

Petitioner asserts that Shibayama's Compound 3 anticipates expressly claims 1–7 and 12. Pet. 21–26. In support of the contention that the compounds recited in claims 1–7 are anticipated by Shibayama, Petitioner provides a detailed claim chart demonstrating how Shibayama's Compound 3 discloses each element of the compound of independent claim 1, followed by a discussion of how Shibayama discloses each element of the compounds recited in dependent claims 2–7. *Id.* at 21–23. As additional support, Petitioner refers to the Declaration of Dr. Crimmins, who provides a detailed discussion of how the structure of Shibayama's Compound 3 discloses each element of claims 1–7. Pet. 23–25 (citing Ex. 1002 ¶¶ 36–53).

Regarding claim 12, directed to a pharmaceutical composition comprising the compound or salt according to claim 1 and a pharmaceutically acceptable carrier, Petitioner relies upon Shibayama's disclosure that the compounds of the invention may be formulated into pharmaceutical compositions including one or more pharmaceutically acceptable carriers. Pet. 26 (citing Ex. 1003, 26–28) (describing preparing pharmaceutical compositions by mixing the CCR5 antagonist with excipients, water, solvents, etc.).

In the Patent Owner Response, Patent Owner asserts that claims 1–7 and 12 are not anticipated by Shibayama because Shibayama does not enable a skilled artisan to synthesize its Compound 3. PO Resp. 7, 12. In support of that contention, Patent Owner asserts that Shibayama does not disclose an example of how to make Compound 3. In addition, Patent Owner refers to

the declaration testimony of Dr. Hunt explaining that he conducted a database search for Compound 3 and found that it has been identified with a CAS registry number, but that no additional information was available for the compound. *Id.* at 8 (citing Ex. 2033 ¶¶ 46, 48).

Patent Owner refers also to the deposition testimony of Petitioner's declarant, Dr. Crimmins, who explained that "a person of ordinary skill in the art would be readily able to prepare [Compound 3] given other information in the art." *Id.* at 9 (quoting Ex. 2032, 16:6–11). Patent Owner relies on that statement to assert that a skilled artisan "would have to refer to a second reference, at least, to practice the invention of the challenged claims," and thus, Shibayama "is not enabling alone, and therefore not anticipatory." *Id.* Patent Owner asserts that during Dr. Crimmins' deposition he was asked to sketch a synthesis route for Compound 3, but responded that it would take him "'multiple days' with 'access to scientific literature' to come up with a 'reasonable approach to the synthesis of Compound 3.'" *Id.* at 11 (quoting Ex. 2032, 24:3–6). Based on that testimony, Patent Owner's position is, apparently, that undue experimentation would be required to synthesize Shibayama's Compound 3, asserting that "[a]t some point, a task becomes more than routine—it becomes something more than a task for one of ordinary skill in the art." *Id.*

In the Reply, Petitioner asserts that Patent Owner has not overcome the presumption that the prior art is enabled. Pet. Reply 3. In particular, Petitioner asserts that Patent Owner failed to analyze the relevant *Wands* factors to determine whether the experimentation that would be required of a person of ordinary skill in the art to synthesize Shibayama's Compound 3 would be undue. *Id.* at 6–8. According to Petitioner, merely relying upon

Dr. Hunt's database search does not "replace an analysis of the knowledge generally available to those of ordinary skill in the art." *Id.* at 9.

Further, Petitioner provides its own *Wands* analysis, supported by a second declaration from Dr. Crimmins that included his exemplary synthesis route for Shibayama's Compound 3 and testimony that such synthesis required no more than routine optimization for a person of ordinary skill in the art at the time of the invention. *Id.* at 18 (citing Ex. 1011, Crimmins' Opp. Decl. ¶¶ 52–54, App'x B).

To anticipate a claimed invention, a prior art reference must enable one of ordinary skill in the art to make the prior invention without undue experimentation. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003). Petitioner and Patent Owner have properly recognized that the cited prior art has a presumption of enablement. PO Resp. 4; Pet. Reply 2; *Amgen Inc.*, 314 F.3d at 1355. Both parties also recognize correctly that, due to the presumption, the burden of proving non-enablement of a prior art reference rests on the Patent Owner. PO Resp. 4; Pet. Reply 3; *Impax Labs., Inc. v. Aventis Pharms., Inc.*, 545 F.3d 1312, 1316 (Fed. Cir. 2008) (patentee may overcome the presumption of enablement by establishing with persuasive evidence that the prior art does not enable the claimed invention).

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)).

Factors to be considered in determining whether a disclosure would require undue experimentation . . . include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

Patent Owner has not performed a complete analysis of the *Wands* factors and, yet, has concluded that undue experimentation would be required to make the compounds of the invention. Specifically, Patent Owner offers no meaningful assessment of the quantity of experimentation necessary to synthesize Shibayama's Compound 3. Rather, Patent Owner criticizes Dr. Crimmins for being unable to sketch a synthesis route on the spot during his deposition and for suggesting that to do so, he would require multiple days and access to scientific literature. PO Resp. 11.

Regarding that testimony, Patent Owner relies upon the opinion of its declarant, Dr. Hunt, who states in his declaration that he agrees with Dr. Crimmins and further believes that developing a synthesis route for Compound 3 would be "beyond the ordinary artisan's level of skills exercised in a day-to-day fashion." Ex. 2033 ¶ 49. Dr. Hunt, however, does not provide an explanation for that belief. From his deposition testimony, it appears that he based that statement on the fact that Compound 3 "had never been made." Ex. 1010, 55:13–56:3 ("My concern with compound 3 was the fact that it had never been made. I could find no record of its synthesis."). In any event, Dr. Hunt clarifies in his deposition testimony that he believed that Compound 3 could have been made by one of ordinary skill at the time

of the '454 patent invention and that he *does not* “have an opinion” as to whether the synthesis of Compound 3 would have been routine. *Id.* at 56:8–24. In other words, Patent Owner has not provided persuasive testimony that synthesis of Compound 3 would have required more than routine experimentation.

With respect to the amount of direction or guidance presented and the presence or absence of working examples, we note that Patent Owner asserts that Shibayama provides the chemical name for Compound 3, but does not describe its synthesis or provide an example how to make or use it. PO Resp. 7. Based upon our review of Patent Owner’s Response, we do not find that Patent Owner or Dr. Hunt considered the nature of the invention, the state of the prior art, the predictability or unpredictability of the art, or the breadth of the claims prior to concluding that undue experimentation would be required to make Compound 3.

Finally, regarding the relative skill of those in the art, Patent Owner states, “[t]o fully investigate the knowledge those of skill in the art would have with respect to Compound 3, Dr. David Hunt . . . conducted a database search for that specific compound.” *Id.* at 8. That search provides, at most, evidence toward what was known about Compound 3. What is missing here is consideration of the *relative skill* in the chemical and pharmaceutical art, i.e., the skill of a person having a Ph.D. in medicinal or organic chemistry having industrial or academic laboratory experience, regarding *how to synthesize an identified compound* based upon the disclosure of Shibayama, including the chemical name of the compound.

Patent Owner’s inadequate analysis fails to support its conclusion that undue experimentation would be required to make Shibayama’s Compound

3 and, thus, is insufficient to rebut the presumption that the prior art is enabled. Because Patent Owner's initial evidence and argument failed to rebut that presumption, the burden of production regarding whether the prior art is enabled has not shifted to Petitioner.

Even if the burden had shifted to Petitioner to produce evidence and argument supporting enablement of Shibayama, we conclude that burden would have been met. In particular, we find that Petitioner persuasively addressed the quantity of experimentation necessary to synthesize Shibayama's Compound 3 by referring to the declaration of its declarant, Dr. Crimmins, who demonstrated that it would require only a few hours and routine techniques typically employed by persons of ordinary skill in the art at the time of the invention to develop a synthesis route for Compound 3. Pet. Reply 18 (citing Ex. 1011 ¶¶ 52–54, App'x B).

We find also that Petitioner established that the amount of direction or guidance presented in Shibayama included the chemical name for Compound 3 without explicitly setting forth a method of making the compound. *Id.* Regarding the presence or absence of working examples, Petitioner acknowledged that Shibayama did not provide an example of synthesizing Compound 3, but that it had been “at least constructively reduced to practice.” *Id.* at 19.

We find that Petitioner accurately characterized the nature of the invention as relating to chemical compounds, particularly those useful as CCR5 antagonists. *Id.* (citing 1003, Abstract). Dr. Crimmins explained that developing a synthesis route for organic molecules such as Compound 3, given the compound's chemical name, “is just a matter of routine laboratory work for a person of skill in the art.” *Id.* (citing Ex. 1011 ¶ 49). Petitioner

and Dr. Crimmins described the state of the prior art as well-developed with respect to the body of knowledge regarding organic chemistry synthesis and processes necessary for providing pharmaceutical compositions. *Id.* at 20 (citing Ex. 1011 ¶ 59). Patent Owner has not argued or established otherwise with persuasive evidence.

We agree with Petitioner and Dr. Crimmins that the relative skill of those in the art is “quite high.” *Id.* Dr. Crimmins also explained, reasonably, that persons of ordinary skill in the art do not typically design syntheses in settings such as a deposition wherein they have access only to paper and pencil, as was requested of him. Ex. 1011 ¶ 50. Rather, it is more customary that such artisans would employ “computational tools and industrial techniques for synthesizing and preparing pharmaceutical compounds.” Pet. Reply 20–21. In fact, Dr. Crimmins did precisely that when preparing the synthesis route for Compound 3 set forth in Appendix B.

Further, Petitioner and Dr. Crimmins persuasively described the predictability in the art relating to the organic chemical reactions used to synthesize Shibayama Compound 3 as “quite predictable.” *Id.* at 21 (citing Ex. 1011 ¶¶ 38, 61). Finally, regarding the breadth of the subject matter that must be enabled, we agree with Petitioner’s assertion that such breadth is “very narrow,” as it involves only enabling making Shibayama’s Compound 3. *Id.*

Based on the findings above, we agree with Petitioner that, on balance, the *Wands* factors tend to show that the level of any experimentation required to make Compound 3 would not have been undue for one skilled in the art.

Accordingly, we determine that Shibayama is enabling prior art properly considered as an anticipatory reference. Further, we find that Shibayama's Compound 3 satisfies each required claim element of the compounds recited in claims 1–7 for the reasons set forth in the Petition and the Declaration of Dr. Crimmins. *See* Pet. 21–26; Ex. 1002 ¶¶ 36–53. Additionally, we find that Shibayama discloses a pharmaceutical composition comprising such a compound and a pharmaceutically acceptable carrier, as required by claim 12. Ex. 1003, 26–28; Ex. 1002 ¶¶ 55–56. As Shibayama discloses each limitation of claims 1–7 and 12, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–7 and 12 are anticipated by Shibayama.

3. Claims 13–16

Claims 13–16 are directed to method claims for antagonizing NK receptors. As previously discussed, we have determined that the preambles of claims 13 and 15, along with the wherein clauses of claims 14 and 16, are claim limitations. Thus, we turn to Petitioner's arguments addressing those claim phrases as limitations. According to Petitioner, Shibayama anticipates inherently antagonizing the NK receptor(s) set forth in claims 13–16 by teaching the administration of a pharmaceutical composition comprising Shibayama's Compound 3. Pet. 27–28. Petitioner asserts that, although claims 13–16 vary with respect to which NK receptors are antagonized, "the operative step remains the same: administration of a pharmaceutical composition of claim 12 to a mammal." *Id.* at 27. Petitioner contends that the antagonism of NK receptors disclosed by the '454 patent is merely an inherent property of the compound of claim 1, such that administration to a mammal of a pharmaceutical composition comprising that compound would

necessarily result in each receptor antagonism recited by claims 13–16. *Id.* at 28 (citing Ex. 1002 ¶ 59). Therefore, Petitioner asserts that Shibayama’s teaching to administer a pharmaceutical composition that includes the same elements as the pharmaceutical composition of claim 12, meets each limitation of claims 13–16, wherein the “antagonizing” limitations are met inherently. *Id.* at 29.

In the Patent Owner’s Response, Patent Owner asserts only that claims 13–16 are not anticipated for the same reasons discussed regarding compound and composition claims 1–7, as claims 13–16 require the administration of such compounds and compositions. PO Resp. 12. We are not persuaded by Patent Owner’s non-enablement argument for the same reasons discussed regarding the compound and composition claims.

Moreover, we agree with Petitioner that the phrases in claims 13–16, requiring antagonizing NK receptor(s), merely recite the inherent effect of administering the claimed compounds to a mammal. *See* Pet. 28 (citing Ex. 1002 ¶ 59). In other words, upon performing the method step of administering the pharmaceutical composition of claim 12 to a mammal, the active compound necessarily antagonizes the NK1, NK2, and NK3 receptors, as recited in claims 13–16. Ex. 1002 ¶ 59. The claims do not recite any other step for this mechanism of action to occur. Indeed, the claims do not even require a specific dose for this function.

Shibayama teaches *administering to a mammal* a pharmaceutical composition that reads on claim 12. Ex. 1003, 26–28. Therefore, administration of the active compound in Shibayama’s pharmaceutical composition necessarily achieves the same effect as the administration of the compound claimed in the ’454 patent. Ex. 1002 ¶ 59; *see also* Ex. 1001,

9:58–65 (explaining that the chemical structure of the disclosed compounds enables strong NK1, NK2, and NK3 receptor antagonistic action). It is not significant that the inherent property of the compound to antagonize NK1, NK2, and NK3 receptors upon administration to a mammal may not have been appreciated by the inventors of the prior art. *See MEHL/Biophile Int’l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999) (“Where, as here, the result is a necessary consequence of what was deliberately intended, [i.e., administering the pharmaceutical composition,] it is of no import that the [prior art inventors] did not appreciate the results.”). Further, Shibayama necessarily discloses a method of antagonizing the recited NK receptors by disclosing a method of administering a composition that reads on claim 12.

Therefore, we find that Shibayama discloses each required element of claims 13–16 for the reasons set forth above and in the Petition. *See* Pet. 27–30; Ex. 1002 ¶ 59. As Shibayama discloses each limitation of claims 13–16, we determine that Petitioner has shown by a preponderance of the evidence that each of those claims are anticipated by Shibayama.

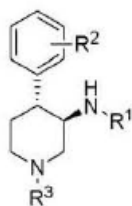
D. Anticipation by Rhim

Petitioner asserts that claims 1–7 and 12–16 are anticipated by Rhim. Pet. 33–45. In the Patent Owner’s Response, Patent Owner challenges Petitioner’s contentions by asserting that Rhim does not enable one of skill in the art to prepare the claimed compounds and compositions. PO Resp. 1.

1. Rhim

Rhim describes (3R)-Amino-(4R)-aryl piperidine compounds of formula 1, set forth below, or pharmaceutically acceptable salts thereof, and the compositions comprising these compounds or pharmaceutically acceptable salts. Ex. 1005, Abstract.

[Formula 1]



Id. Rhim teaches that the compounds of the invention are beta-secretase inhibitors. Pharmaceutical compositions comprising the compounds can be formulated by adding pharmaceutically acceptable carriers, adjuvants, and excipients. *Id.* at 11. Such compositions are useful for the treatment of Alzheimer's disease or Down syndrome by "preventing the formation of beta-amyloid protein which damages nerve neurons." *Id.* at Abstract. The dosage of the compounds varies by age, weight, sex, dosage forms, physical condition and severity of the disease. *Id.* at 10–11. For example, an adult weighing 70 kg, in general, may be prescribed 0.01–1000 mg/day. *Id.* at 11.

Rhim discloses several exemplary compounds of the invention, including Compounds 20 and 22, set forth below:

No.	Compound (Exemplary Embodiment)	R ¹	R ²	R ³
(20)	4-11(2-11)			H
(22)	4-21(3-10)			

Ex. 1005, 25. In addition to providing the chemical structure for Compounds 20 and 22, Rhim also provides guidance regarding how to synthesize those compounds. *Id.* at 12–20.

2. Claims 1–7 and 12

Petitioner asserts that at least Rhim's Compounds 20 and 22 anticipate expressly claims 1–7 and 12.³ Pet. 34. In support of the contention that claims 1–7 are anticipated by Rhim, Petitioner provides a detailed claim chart demonstrating how each of Rhim's Compounds 20 and 22 discloses every element of the compound of independent claim 1, followed by a discussion of how Rhim discloses each element of the compounds recited in dependent claims 2–7. Pet. 35–40. As additional support, Petitioner refers to the Declaration of Dr. Crimmins, who provides a detailed discussion of how the structures of Rhim's Compounds 20 and 22 each disclose every element of claims 1–7. *Id.* (citing Ex. 1002 ¶¶ 64–84).

Regarding claim 12, directed to a pharmaceutical composition comprising the compound or salt according to claim 1 and a pharmaceutically acceptable carrier, Petitioner refers to Rhim's disclosure that the compounds of the invention may be formulated into pharmaceutical compositions including one or more pharmaceutically acceptable carriers. Pet. 40 (citing Ex. 1005, 10–11, 26 (Examples 2–4) (describing preparing various pharmaceutical compositions by mixing the piperidine compounds of the invention with pharmaceutically acceptable carriers, adjuvants and excipients)).

In the Patent Owner Response, Patent Owner asserts that claims 1–7 and 12 are not anticipated by Rhim because Rhim makes clear that its

³ Petitioner asserts that at least six compounds disclosed by Rhim fall within the scope of the challenged claims of the '454 patent, but chose to analyze only Compounds 20 and 22. Pet. 34. Accordingly, we have limited our review to those same two compounds.

compounds and compositions are intended to be administered to humans, but Rhim does not enable a skilled artisan to synthesize its Compounds 20 and 22, “free of contaminants that rendered them unsuitable for administration to humans.” PO Resp. 12–13. In particular, Patent Owner asserts that Rhim does not enable making those compounds free of organic metal catalysts. *Id.* at 13. While acknowledging that Rhim teaches that “‘any known organic chemical reaction’ can be used,” *id.* at 14 (quoting Ex. 1005, 10:10–11), Patent Owner asserts that “the methods of synthesis set forth in [Rhim] all call for use of an organic metal catalyst in the last or near-to-last step,” *id.* According to Patent Owner and its declarant, Dr. Hunt, that step renders Rhim’s synthesis method for Compounds 20 and 22 unsuitable. *Id.* (citing Ex. 2033 ¶¶ 52–55).

In the Reply, Petitioner asserts that Patent Owner has not overcome the presumption that the prior art is enabled. Pet. Reply 3. In particular, Petitioner asserts that Patent Owner failed to analyze the relevant *Wands* factors to determine whether the experimentation that would be required of a person of ordinary skill in the art to synthesize Rhim’s Compounds 20 and 22 would be undue. *Id.* at 6–8. According to Petitioner, Patent Owner disregards the clear guidance provided in Rhim for making those compounds, as well as the guidance for refining compounds with chromatography and testing them for toxicity. *Id.* at 8. Additionally, Petitioner asserts that neither Patent Owner nor Dr. Hunt addresses “whether the explicit teachings found in [Rhim], when combined with knowledge generally available in the prior art—including standard purification tools and industry guidelines for metal residues—would make practicing the invention a matter of routine experimentation or optimization.” *Id.*

Further, Petitioner provides its own *Wands* analysis, supported by a second declaration from Dr. Crimmins that included his exemplary synthesis route for Rhim's Compounds 20 and 22, and testimony that Rhim enables a person of ordinary skill in the art to make and use those compounds. *Id.* at 13–17 (citing Ex. 1011 ¶¶ 34–43, App'x A).

As explained regarding our discussion of the challenge based upon Shibayama, to anticipate a claimed invention, a prior art reference must enable one of ordinary skill in the art to make the prior invention without undue experimentation. 35 U.S.C. § 112. The cited prior art has a presumption of enablement. *Amgen Inc.*, 314 F.3d at 1355. The burden of proving non-enablement of a prior art reference rests on the Patent Owner. *Impax Labs., Inc.*, 545 F.3d at 1316.

“[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *Genentech, Inc.*, 108 F.3d at 1365 (quoting *Wright*, 999 F.2d at 1561).

Factors to be considered in determining whether a disclosure would require undue experimentation . . . include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Wands, 858 F.2d at 737.

To begin, we note that claims 1–7 of the '454 patent recite compounds without requiring those compounds to be comprised in a pharmaceutical composition or administered to a mammal. Similarly, while Rhim discloses

pharmaceutical compositions comprising its compounds, the disclosed invention is also directed to those compounds alone. *See, e.g.*, Ex. 1005, Abstract (“The present invention relates to the (3R)-Amino-(4R)-aryl piperidine *compounds of formula 1* below or pharmaceutically acceptable salts thereof, *and* the compositions comprising these (3R)-Amino-(4R)-aryl piperidine compounds or pharmaceutically acceptable salts thereof” (emphasis added)). Thus, we agree with Petitioner that Patent Owner’s argument that Rhim is not enabled because Rhim discloses a method that results in compounds containing toxins unsuitable for administration to humans is misdirected with respect to Rhim’s compound claims, which Petitioner relies upon as anticipating compound claims 1–7 of the ’454 patent. As that was Patent Owner’s only argument advanced to support its contention that Rhim is not enabling with respect to making Compounds 20 and 22, we determine that Patent Owner has not overcome the presumption that Rhim is enabling with respect to those compounds.

Claim 12 of the ’454 patent is directed to a pharmaceutical composition comprising the compound of claim 1. Thus, we consider whether Patent Owner has rebutted the presumption that Rhim is enabling with respect to its disclosure of making a pharmaceutical composition comprising either Compound 20 or 22. We agree with Petitioner that Patent Owner has failed to do so. Patent Owner has concluded that Rhim’s disclosure would require undue experimentation without a complete analysis of the *Wands* factors. Indeed, based upon our review of Patent Owner’s Response, we do not find that Patent Owner or Dr. Hunt considered the quantity of experimentation necessary to make Rhim’s pharmaceutical composition comprising either Compound 20 or 22; the nature of the

invention; the state of the prior art; the predictability or unpredictability of the art; or the breadth of the claims prior to concluding that undue experimentation would be required to make Rhim's pharmaceutical composition comprising Compound 20 or 22.

Rather, Patent Owner addresses, in a cursory manner, only the amount of direction or guidance presented in Rhim, Rhim's working examples, and the relative skill of those in the art. For example, Patent Owner asserts that Rhim's disclosure requires the use of "a metallic organic catalyst in the last or near-to-last synthesis step" and that "[t]hose of skill in the art would recognize that such a method would provide compounds unsuitable for pharmaceutical administration, and regard those methods as a text book illustration only." PO Resp. 2. What is missing critically from that discussion is consideration of whether one skilled in the art, with Rhim's guidance, would have been able to make Rhim's pharmaceutical composition comprising either Compound 20 or 22, uncontaminated with toxic metal.

Thus, we determine that Patent Owner's incomplete analysis fails to support its conclusion that undue experimentation would be required to make Rhim's pharmaceutical composition comprising Compound 20 or 22 and is, therefore, insufficient to rebut the presumption that the prior art is enabled. Because Patent Owner's initial evidence and argument failed to rebut that presumption, the burden of production regarding whether the prior art is enabled has not shifted to Petitioner.

Even if that burden had shifted to Petitioner to produce evidence and argument supporting enablement of Rhim, we conclude that burden would have been met. In particular, we find that Petitioner persuasively established

that little to no quantity of experimentation would have been necessary to make Rhim's Compounds 20 and 22, or a pharmaceutical composition comprising either of those compounds, given the detailed disclosures by Rhim. Pet. Reply 13. Petitioner explains persuasively that, to the extent purification of the compounds would have been required for administration to a mammal, Rhim discloses a means for purification, i.e., refining reaction products using column chromatography, and that if additional purification had been necessary, it would have required no more than routine experimentation to develop and employ such purification steps. Pet. Reply 5 (citing Ex. 1005, 12–18, 20–23); Pet. Reply 13 (citing Ex. 1011 ¶ 30).

We find also that Petitioner established persuasively that the amount of direction and guidance presented in Rhim included step-by-step synthesis routes for Compounds 20 and 22. Pet. Reply 14 (citing Ex. 1005, 12, 19, 20, 22; Ex. 1011 ¶¶ 22–25). Dr. Crimmins prepared Appendix A, depicting, in sequential order, the process disclosed for Compounds 20 and 22. Ex. 1011, App'x A. Petitioner and Dr. Crimmins explain that in Rhim, “[o]nce the final product was obtained according to Preparation 6-1, the residue was refined, or purified, by column chromatography.” Pet. Reply 14; Ex. 1011 ¶ 28, App'x A. Further, Petitioner explains that, as Patent Owner's declarant, Dr. Hunt testified, Rhim discloses that acute toxicity testing revealed no severe toxic symptoms after administration of the compounds. Pet. Reply 14–15 (citing Ex. 1010, 69:16–70:2).

Regarding the presence or absence of working examples, Petitioner and Dr. Crimmins satisfactorily establish that Rhim provided working examples of Compounds 20 and 22, as just discussed, and characterized

those examples by NMR analysis, and confirmed that administering those compounds did not cause severe toxicity. Pet. Reply 15; Ex. 1011 ¶¶ 22, 25.

We find that Petitioner accurately characterized the nature of the invention as relating to chemical compounds, particularly those useful as BACE inhibitors. Pet. Reply 15 (citing Ex. 1011 ¶ 35). Petitioner and Dr. Crimmins described the state of the prior art as well-developed with respect to the body of knowledge regarding organic chemistry reactions and purification processes useful for the manufacture of pharmaceutical compounds such as Compounds 20 and 22. *Id.* at 15–16 (citing Ex. 1011 ¶ 36). Patent Owner has not argued or established otherwise with persuasive evidence.

We agree with Petitioner and Dr. Crimmins that the relative skill of those in the art is “quite high.” *Id.* at 16 (citing Ex. 1011 ¶ 37). We agree also with Dr. Crimmins’ opinion that persons of ordinary skill in the art “would have experience in the synthesis of compounds that were intended to be used as pharmaceuticals.” Ex. 1011 ¶ 37.

Further, Petitioner and Dr. Crimmins persuasively described the predictability in the art relating to organic chemical reactions for making Compounds 20 and 22 as “quite predictable.” Pet. Reply 21 (citing Ex. 1011 ¶¶ 38, 61). Finally, regarding the breadth of the subject matter that must be enabled, we agree with Petitioner’s assertion that such breadth is “very narrow,” as it involves only enabling making a pharmaceutical composition comprising Rhim’s Compound 20 or 22. *Id.* (citing Ex. 1011 ¶ 34).

Based on those findings, we agree with Petitioner that, on balance, the *Wands* factors tend to show that the level of experimentation required to make Rhim’s pharmaceutical composition comprising either Compound 20

or 22 would not have been undue. In particular, great weight is given to the facts that Rhim disclosed a method of making the compounds, including a purification step, the high level of skill in the art, and that persons of ordinary skill in the art would have had experience synthesizing compounds and compositions intended to be used as pharmaceuticals. Thus, based on the record as a whole, we determine that the preponderance of the evidence demonstrates that undue experimentation would not have been required to make and use the full scope of Rhim's invention relied upon by the Petitioner.

Accordingly, we determine that Rhim is enabling prior art properly considered as an anticipatory reference. We further determine that Rhim's Compounds 20 and 22 both satisfy each required claim element of the compounds recited in claims 1–7 for the reasons set forth in the Petition and the Declaration of Dr. Crimmins. *See* Pet. 35–40; Ex. 1002 ¶¶ 64–84. Additionally, we find that Rhim discloses a pharmaceutical composition comprising such compounds and a pharmaceutically acceptable carrier, as required by claim 12. Ex. 1005, 10–11, and 26 (Examples 2–4); Ex. 1002 ¶ 86. As Rhim discloses each limitation of claims 1–7 and 12, we determine Petitioner has shown by a preponderance of the evidence that claims 1–7 and 12 are anticipated by Rhim.

3. *Claims 13-16*

Claims 13–16 are directed to method claims. As previously discussed, we have determined that the preambles of claims 13 and 15, along with the wherein clauses of claims 14 and 16, are claim limitations. Thus, we turn to Petitioner's arguments addressing those claim phrases as limitations. According to Petitioner, Rhim inherently anticipates

antagonizing the NK receptor(s) set forth in claims 13–16 by teaching the administration of a pharmaceutical composition comprising Rhim’s Compounds 20 and 22. Pet. 41–43. Petitioner asserts that, although claims 13–16 vary with respect to which NK receptors are antagonized, “the operative step remains the same: administration of a pharmaceutical composition of claim 12 to a mammal.” *Id.* at 41. Petitioner contends that the antagonism of NK receptors disclosed by the ’454 patent is merely an inherent property of the compound of claim 1, such that administration to a mammal of a pharmaceutical composition comprising that compound would necessarily result in each receptor antagonism recited by claims 13–16. *Id.* at 42 (citing Ex. 1002 ¶¶ 87–89). Therefore, Petitioner asserts that Rhim’s teaching to administer a pharmaceutical composition that includes the same elements as the pharmaceutical composition of claim 12 meets each limitation of claims 13–16, wherein the “antagonizing” limitations are met inherently. *Id.* at 42.

We agree with Petitioner. As discussed in the analysis of Shibayama, the phrases in claims 13–16 requiring antagonizing NK receptor(s) merely explain the effect the compounds have in the body, at any dose. Upon performing the method step of administering the pharmaceutical composition of claim 12 to a mammal, the active compound is expected to antagonize NK1, NK2, and NK3 receptors. The claims do not recite any other step for this effect to occur. Indeed, the claims do not even require a specific dose for this function. Rhim teaches administering to a mammal a pharmaceutical composition that reads on claim 12. Therefore, administration of the active compound in Rhim’s composition necessarily achieves the same effect as administration of the compound claimed in the

'454 patent. *See* Ex. 1001, 9:58–65 (explaining that the chemical structure of the disclosed compounds enables strong NK1, NK2, and NK3 receptor antagonistic action). It is not significant that the inherent property of the compound to antagonize NK1, NK2, and NK3 receptors upon administration to a mammal may not have been appreciated by the inventors of the prior art. *See MEHL/Biophile*, 192 F.3d at 1366.

In the Patent Owner's Response, Patent Owner's arguments relating to claims 13–16 are the same non-enablement arguments asserted with respect to claims 1–7 and 12. PO Resp. 15. Accordingly, we remain unpersuaded by Patent Owner's non-enablement argument with respect to claims 13–16 for similar reasons discussed regarding claim 12.

Therefore, we find that Rhim discloses each required element of claims 13–16 for the reasons set forth above and in the Petition. *See* Pet. 41–43; Ex. 1002 ¶¶ 86–89. As Rhim discloses each limitation of claims 13–16, we determine that Petitioner has shown by a preponderance of the evidence that each of those claims are anticipated by Rhim.

For the foregoing reasons, we conclude that Petitioner has established by a preponderance of the evidence that claims 1–7 and 12–16 are unpatentable under 35 U.S.C. § 102 as anticipated by each of Shibayama and Rhim.

III. MOTION TO EXCLUDE

Patent Owner moves to exclude Petitioner's Exhibits 1011, 1012, 1020–1026, 1032, and 1033. Exclude Mot. 1. Petitioner opposes the motion. Exclude Opp. 1. As the moving party, Patent Owner has the burden of proof to establish that it is entitled to the requested relief. 37 C.F.R. § 42.20(c).

1. *Exhibit 1011*

Exhibit 1011 is the Declaration of Michael Crimmins in Support of Petitioner's Reply Brief. Patent Owner objects to the exhibit asserting that it "presents evidence belatedly which could have and should have been offered in support of its Petition," and "is contrary to prior sworn testimony under FRE [Federal Rule of Evidence] 806." Exclude Mot. 2. Regarding the timing of the submission of Exhibit 1011, Patent Owner takes issue with the fact that Petitioner and Dr. Crimmins relied on the presumption that the references cited for the anticipation challenges were enabling references. *Id.* at 3. Patent Owner states that Petitioner "was not free to wait and see if [Patent Owner] challenged that presumption, which it did, before presenting affirmative evidence of enablement." *Id.* at 3–4.

We disagree with Patent Owner. The presumption of enablement relied upon by Petitioner places the burden of proof on the party challenging that presumption. Petitioner had no burden of production regarding enablement of the cited references at the time it filed its Petition. Indeed, as discussed in the preceding analysis, we have determined that Patent Owner failed to shift that burden to Petitioner at all. In any event, Petitioner appropriately submitted Exhibit 1011 as rebuttal evidence to Patent Owner's enablement challenge raised after the submission of the Petition.

Regarding FRE 806 (declarant's credibility), Patent Owner asserts that Dr. Crimmins states in his declaration testimony, Ex. 1011, that it "took a few hours" to sketch a synthesis route for Compound 3 of Shibayama, and that doing so was "routine." *Id.* at 8 (citing Ex. 1011 ¶¶ 50–52). According to Patent Owner, that testimony contradicts Dr. Crimmins' earlier deposition testimony where he responded to a request to sketch the synthesis route for Compound 3, explaining, "I would have access to the scientific literature and be able to sit quietly at my desk to think about this for probably multiple days to come up with a reasonable approach" *Id.* (quoting Ex. 2032, 24:3–9). We disagree. In the deposition testimony, it is clear that Dr. Crimmins was explaining in general terms what his normal practice would involve in a normal setting, as opposed to the setting of a deposition. In his declaration, he was able to describe the effort that sketching the synthesis route took, in specific terms, as he had at that point actually completed the task.

Patent Owner objects also to Exhibit 1011 by asserting that it does not meet the requirements of FRE 702 (expert witness testimony) and 703 (bases of an expert's testimony). Exclude Mot. 2. Patent Owner acknowledges that Dr. Crimmins "is unquestionably a noted medicinal chemist," but argues that he is unqualified to provide testimony regarding the enablement of the cited references, Rhim's disclosure of acute toxicity testing, or the removal of the metal catalyst from Rhim's synthesis products. *Id.* at 8.

To begin, we note that "[e]nablement is a question of law based on underlying factual findings." *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012) (citing *Wands*, 858 F.2d at 735). The *Wands* factors, used to analyze whether undue experimentation

would have been required, and discussed by Dr. Crimmins in Exhibit 1011, are fact-based inquiries. *See Wands*, 858 F.2d at 735–37. As such, we find it appropriate for Petitioner to have offered expert testimony regarding the facts involved in an enablement analysis. Thus, we are not persuaded by Patent Owner’s assertion that Dr. Crimmins was not qualified to provide such testimony because he is not a legal scholar. Exclude Mot. 8.

Further, we are unpersuaded by Patent Owner’s remaining contentions, as they represent attorney argument and not evidence. For example, Patent Owner asserts that Dr. Crimmins lacked the expertise and experience to rely upon Rhim’s disclosure that its compounds were subjected to “acute toxicity testing.” *Id.* at 7. In support of that contention, Patent Owner states, “one of skill in the art would have recognized that acute toxicity testing has nothing to do with metal catalyst poisoning.” *Id.* Patent Owner, however, has not provided any citation for that position or explained persuasively how that assertion disqualifies Dr. Crimmins’ reliance on Rhim’s disclosure relating to toxicity or the admissibility of his declaration testimony. Indeed, as Patent Owner notes, Dr. Crimmins confirmed that he is not a toxicologist and avoided offering answers to questions posed to him that were not within his scope of expertise. *Id.* (citing Ex. 2053, 53:1–4) (Dr. Crimmins identifying a deposition question as “not within the scope of my expertise” and offering that he is “not a toxicologist.”).

Therefore, having considered the evidence and arguments, we determine that Patent Owner has not established that it is entitled to have Exhibit 1011 excluded from the evidence of record.

2. Exhibits 1012 and 1032

Exhibit 1012 is the version of the Declaration of Peter Bernstein that Petitioner seeks to seal. Exhibit 1032 is the redacted version of that exhibit. Patent Owner acknowledges that Dr. Bernstein is an expert in the field of antagonizing NK-1 receptors. Exclude Mot. 13. Patent Owner, however, challenges the entirety of his declaration by asserting that, in some instances, Dr. Bernstein goes beyond offering testimony within his field of expertise by addressing the breadth and written description support for Patent Owner's proposed claims. *Id.*

Petitioner asserts that in Dr. Bernstein's declaration, "Dr. Bernstein is offering scientific testimony concerning the issues of written description, enablement and anticipation of the proposed amended claims," such as what a person of ordinary skill in the art would understand upon reviewing the '454 patent. Exclude Opp. 8.

We agree with Petitioner that Patent Owner has not established persuasively that it is entitled to the relief requested. In particular, we view Patent Owner's criticism of Dr. Bernstein's declaration testimony as challenging the weight that should be accorded to select portions of it, rather than the admissibility of the declaration. Indeed, Patent Owner does not recite a FRE upon which it challenges Exhibits 1012 and 1032 until the last sentence of its Reply Brief. See Exclude Mot. 13–15; Exclude Reply 5.

Therefore, having considered the evidence and arguments, we determine that Patent Owner has not established that it is entitled to have Exhibits 1012 and 1032 excluded from the evidence of record.

3. *Exhibits 1020–1025, and 1033*

Patent Owner asserts that Petitioner submits Exhibits 1020–1025 and 1033 as notebook pages of various researchers at Array. Exclude Mot. 9. According to Patent Owner, Petitioner relies on those exhibits as evidence that, prior to Patent Owner’s filing date, Array reduced to practice the subject matter of Patent Owner’s proposed claims and did not suppress the invention prior to filing a patent application. *Id.* (citing Paper 29, 23–25). Patent Owner challenges the exhibits as unauthenticated hearsay under FRE 802 (inadmissible hearsay) and 901 (authenticating evidence). Additionally, Patent Owner asserts that because the exhibits contain pages from notebooks, they are not eligible for consideration as business records under FRE 803(6) (business records hearsay exception). *Id.* at 9–10 (citing *Chen v. Bouchard*, 347 F.3d 1299, 1308 (Fed. Cir. 2003)).

Because we have not considered or relied upon Exhibits 1020–1025 and 1033 in this Decision, we dismiss, as moot, Patent Owner’s request to exclude those exhibits.

4. *Exhibit 1026*

Exhibit 1026 is titled, “[Sealed] Summary Chart of Compounds Synthesized and Tested.” Patent Owner asserts that Mr. Steven Andrews prepared Exhibit 1026 and selected the records he summarized in it. Exclude Mot. 12–13. Patent Owner challenges the exhibit because Petitioner and Mr. Stevens did not make the originals available, as required by FRE 1006 (summaries to prove content). *Id.* at 13.

Because we have not considered or relied upon Exhibit 1026 in this Decision, we dismiss, as moot, Patent Owner’s request to exclude Exhibit 1026.

IV. MOTION TO AMEND

Having concluded that claims 1–7 and 12–16 are unpatentable under 35 U.S.C. § 102 as anticipated by Shibayama or Rhim, we consider Patent Owner’s Contingent Motion to Amend the claims of the ’454 patent. Proposed amended claims are set forth on pages vi–xvii of the motion. Patent Owner supports its motion with the declaration of Dr. David Hunt (Ex. 2033) and the original disclosure of the ’454 patent (U.S. Appl. No. 13/119,743) (Ex. 2031). Amend Mot. 4, 8.

As the moving party, Patent Owner bears the burden of proving that it is entitled to the relief requested. *See* 37 C.F.R. § 42.20(c); *Microsoft Corp. v. Proxyconn, Inc.*, 789 F.3d 1292, 1307 (Fed. Cir. 2015) (“The Board has reasonably interpreted these provisions as requiring the patentee to show that its substitute claims are patentable over the prior art of record.”). Entry of proposed amendments is not automatic, but occurs only upon the patent owner having met the requirements of 37 C.F.R. § 42.121 and demonstrating, by a preponderance of the evidence, the patentability of the proposed substitute claims. *Nike, Inc. v. Adidas AG*, 812 F.3d 1326, 1334 (Fed. Cir. 2016) (“[T]he Board did not err by placing the burden on [Patent Owner] to establish patentability over the prior art of [Patent Owner]’s proposed substitute claims.”); *see Idle Free Sys., Inc. v. Bergstrom, Inc.*, IPR2012-00027, slip op. at 7–8 (PTAB June 11, 2013) (Paper 26, “*Idle Free*”) (Informative). For the reasons explained below, we conclude that Patent Owner has not met its burden with respect to proposed substitute and new claims.

A. *Reasonable Number of Substitute Claims*

“A motion to amend may . . . propose a reasonable number of substitute claims. The presumption is that only one substitute claim would be needed to replace each challenged claim, and [that presumption] may be rebutted by a demonstration of need.” 42 C.F.R. § 42.121(a)(3). Patent Owner’s proposed claims 18–29 represent a one-for-one substitution for original claims 1–7 and 12–16, respectively. Amend Mot. 1, vi–xvi; *see Idle Free*, slip op. at 3–6. Thus, those proposed substitutions satisfy 37 C.F.R. § 42.121(a)(3).

Patent Owner asserts that its proposed new claim 30 also corresponds with original claim 1, and proposed new claim 31 also corresponds with original claim 12. Amend Mot. 1, xvi–xvii. Patent Owner asserts that proposed claim 18 limits ring D in a manner that excludes three compounds within the scope of original claim 1. *Id.* at 3–4. “Specifically, when ring D is ‘(b)’ a ‘C6-14 aryl group’, then it must have a substituent selected from groups (1)–(54), but the three excluded species have an ‘unsubstituted’ phenyl ring corresponding to ring D.” *Id.* at 4. Claim 30 recites that compound and claim 31 recites a pharmaceutical composition comprising that compound. Thus, according to Patent Owner, proposed claims 30 and 31 are needed “to maintain the scope of original claims 1 and 12 with respect to the three excluded species.” *Id.* Patent Owner asserts that the proposed two-for-one substitute claims are patentably distinct from each other. *Id.* (citing *U.S. Dep’t of Homeland Sec. v. Golden*, Case IPR2014-00714, 2015 WL 5818910, at *8 (PTAB Oct. 1, 2015)); *Idle Free*, slip op. at 5.

Petitioner challenges the two-for-one substitutions by asserting that Patent Owner has not identified a “special reason” for proposed claim 18, or for proposing to claim the three excluded compounds separately. Amend Opp. 4 (quoting *Idle Free*, slip op. at 6 (“A desire to obtain a new set of claims having a hierarchy of different scope typically would *not* constitute a sufficient special circumstance.”)). Petitioner asserts also that “there is no apparent connection between the subject matter allegedly invented by the patentee, and the arbitrary sub-genus of compounds now recited in claim 18.” *Id.*

During the initial conference for this *inter partes* proceeding, Patent Owner indicated that it planned to file a motion to amend. Paper 15, 3. In response to that notice, we directed the parties’ attention to certain guidance regarding motions to amend, including *Idle Free*. *Id.* Prior to filing its Motion to Amend, Patent Owner did not discuss a desire to rebut the presumption that only one substitute claim would be needed to replace each challenged claim. See *Idle Free*, slip op. at 6. It is apparent, however, that Patent Owner has considered the guidance provided during the initial conference, including the Rule explaining the presumption that only one substitute claim would be needed for each challenged claim may be rebutted, 37 C.F.R. § 42.121(a)(3), and the discussion of that Rule in *Idle Free*, as Patent Owner cites those references in its Motion when addressing proposed claims 30 and 31. See Amend Mot. 2–4.

According to Patent Owner, there is a special need to replace original claim 1 with claims 18 and 30 so that proposed claim 30 may recite a compound or salt selected from a group consisting of the three compounds that it chooses to exclude from the genus of compounds included in

proposed claim 18. Amend Mot. 3–4. That explanation, however, does not demonstrate a need to propose separate claims to cover each of the desired compounds. As Petitioner has correctly noted, the Board explained in *Idle Free* that “[a] desire to obtain a new set of claims having a hierarchy of different scope typically would *not* constitute a sufficient special circumstance.” *Idle Free*, slip op. at 6. Patent Owner has not addressed or established persuasively why its proposed hierarchy of different scope represented by proposed claims 30 and 31 should constitute a special circumstance. As the Board has explained, “[i]f a patent owner desires a complete remodeling of its claim structure according to a different strategy, it may do so in another type of proceeding before the Office.” *Id.* Accordingly, we are not persuaded that Patent Owner has met the requirements of 37 C.F.R. § 42.121(a)(3) with regard to proposed claims 30 and 31 as additional substitutions for original claims 1 and 12.

B. No Broadening of Scope

Proposed substitute claims in an *inter partes* review “may not enlarge the scope of the claims of the patent.” 35 U.S.C. § 316(d)(3); see 37 C.F.R. § 42.121(a)(2)(ii). In the Motion to Amend, each of the proposed substitute claims 18–29 add to the limitations of each corresponding original claim.⁴ No original limitations are removed.

⁴ We address the effect of one of those limitations with regard to the scope of the claim 18 in our following discussion of written description support.

C. Written Description Support

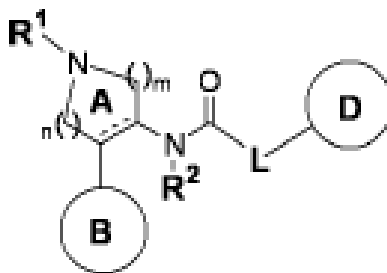
Pursuant to 37 C.F.R. § 42.121(b), a motion to amend in an *inter partes* review must set forth “[t]he support in the original disclosure of the patent for each claim that is added or amended,” and “[t]he support in an earlier-filed disclosure for each claim for which benefit of the filing date of the earlier filed disclosure is sought.” In particular, the limitations added to the challenged claims must be supported *individually* by the application, from which Patent Owner claims priority, and the substitute claims also must be supported *as a whole* by that application. *Nichia Corp. v. Emcore Corp.*, Case IPR2012-00005, slip op. at 4 (PTAB June 3, 2013) (Paper 27) (Representative).

The language of the proposed substitute claims does not need to be described *in ipsius verbis* in the original disclosure to support the proposed substitute claims. *Id.*; *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000); *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996). However, if the original disclosure does not use the precise terminology recited in a proposed claim, “mere citation to the original disclosure without any explanation as to why a person of ordinary skill in the art would have recognized that the inventor possessed the claimed subject matter as a whole may be similarly inadequate.” *Nichia Corp.*, slip op. at 4. In other words, in such case, the question remains whether the disclosure reasonably would lead persons of ordinary skill in the art to the subject matter recited in the proposed claims. *See Fujikawa*, 93 F.3d at 1570.

Patent Owner asserts that each proposed claim finds written description support in the disclosure of U.S. Application No. 13/119,743 (Ex. 2031) (“the original disclosure”) that later issued as the ’454 patent.

Amend Mot. 5–6. Petitioner disagrees. Amend Opp. 2–12. Having considered the arguments and the evidence, and for the reasons set forth below, we agree with Petitioner that Patent Owner has failed to demonstrate that there is adequate written description in the original disclosure for the proposed substitute claims.

We begin by considering Patent Owner’s proposal to substitute claim 18 for original independent claim 1. *See* Amend Mot. vi–xi (setting forth proposed substitute claim 18, wherein the added limitations are underlined, and the removed portions are bracketed). Among the proposed amendments to original claim 1 are added limitations for ring D of the compound represented by the following formula:



Id. at vi. Patent Owner explains that “[p]roposed claim 18 limits ring D to ‘(a)’ an aromatic ‘heterocyclic’ ring optionally having substituents, wherein 6-quinolyl is excluded, or ‘(b)’ a ‘C₆₋₁₄ aryl group having ‘at least one substituent’ selected from substituent groups (1) to (54).” *Id.* at 3.

Patent Owner states that “[s]upport for ‘(b)’ of ring D can be found in ¶¶ [0084]-[0089] of Ex. 2031,” without any further discussion for that limitation or any citation to declaration testimony. Amend Mot. 5.

Petitioner asserts that Patent Owner has failed to meet its burden of proving that the proposed claims are supported by the original disclosure because the language of those claims does not appear *in ipso verbis* in the

paragraphs cited by Patent Owner. Amend Opp. 1–2. Petitioner asserts also that Patent Owner has not provided any explanation how or why a person of ordinary skill in the art would have recognized from the cited portion of the original disclosure that the inventor possessed the claimed subject matter.

Id. (citing *Nichia Corp.*, slip. op. at 4).

In particular, Petitioner asserts that the '454 patent discloses (1) that ring D can be an “aromatic ring optionally having substituents”; (2) the aromatic ring may be an aryl or aromatic heterocycle, and that the aryl group may be a C₆₋₁₄ aryl group; (3) “[e]xamples of the substituents on Ring B and Ring D include 1 to 3 substituents selected from” 55 groups of potential substituents. Amend Opp. 8 (citing Ex. 1001, 13:31–32, 33–35, 54–55, 13:56–27:11). Petitioner assert that the “specification never states that Ring D can be a ‘C₆₋₁₄ aryl group having at least one substituent selected from the group consisting of [substituent groups (1) through (54),’ as recited in the amended claim.” *Id.* According to Petitioner, “[a] person of ordinary skill in the art would not understand the specification’s disclosure of ‘1 to 3 substituents’ as describing a Ring D with ‘at least one substituent.’” *Id.* (citing Ex. 1032, Bernstein Decl. ¶ 42) (further explaining that “the amended claims encompass compounds with four or more substituents on an aryl ring that can contain as many as 14 carbons”)). Petitioner asserts that “[t]here are no blazemarks reasonably leading the skilled artisan to contemplate that the invention includes C₆₋₁₄ aryl groups with more than three substituents.” *Id.*; Ex. 1032 ¶ 43. Petitioner and Dr. Bernstein note further that of the 432 exemplary compounds disclosed in the Specification, “not one of those compounds has more than three substituents on Ring D.” Amend Opp. 8–9 (citing Ex. 1032 ¶ 43).

In the Reply, Patent Owner acknowledges that “the only recitation not literally appearing in the specification as originally filed but appearing in the proposed amended claims is the definition for ring D.” Amend Reply 2. Patent Owner asserts that the Specification describes compounds where ring D is an aryl group with none, one and multiple substituents. *Id.* at 3. Based on that assertion, Patent Owner reasons that “it is [an] inescapable conclusion that the ’454 Patent inventors had possession of the subgenus of compounds, within original claim 1, where ring D is in fact (and not optionally) substituted,” as set forth in substitute claim 18. *Id.* Patent Owner asserts, “This omission of the one set of compounds, where ring D is not substituted, is the only departure from the scope of original claim 1 not expressly recited in the specification as filed.” *Id.* According to Patent Owner, “[s]urely, one of skill in the art would recognize that a genus of compounds containing those where ring D is ‘optionally’ substituted would include those where ring D is substituted.” *Id.*

We are not persuaded by Patent Owner’s argument as it misses the point. In the Reply, Patent Owner has not addressed Petitioner’s assertion that the original disclosure provides “no blazemarks reasonably leading the skilled artisan to contemplate that the invention includes C₆₋₁₄ aryl groups with *more than three substituents*.” Amend Opp. 8 (emphasis added). In other words, Patent Owner has not addressed or explained how the original disclosure of ring D including “1 to 3 substituents” supports the recitation in the amended claim of ring D including “at least one substituent,” as a skilled artisan would understand the phrase “at least one” may include more than three. That modification effectively increases the number of ring D substituents that may be applied, which exceeds what the Specification

describes. Absent that discussion, and in view of the original disclosure, and persuasive argument by Petitioner, supported by the credible testimony from Dr. Bernstein that a person of ordinary skill in the art would not have concluded from the original disclosure that the inventors were in possession of a compound with a ring D having more than 1 to 3 substituents, Ex. 1032 ¶ 43, we conclude that a preponderance of the evidence compels a determination that Patent Owner has failed to demonstrate that there is adequate written description in the original disclosure to support proposed substitute independent claim 18. Because proposed claims 19–29 depend from independent claim 18, claims 19–29 are also unsupported for at least the same reasons discussed regarding claim 18.

Regarding claims 30 and 31, even if Patent Owner had shown good cause to include those substitute claims, we are unpersuaded that Patent Owner has established adequate written description for claims directed to only three species of the genus of compounds described by original disclosure. In particular, Patent Owner has not established that the original disclosure provided any blazemarks reasonably leading a skilled artisan to selectively choose and claim the three recited compounds. *See Fujikawa*, 93 F.3d at 1571 (affirming the Board’s denial of a motion to amend where there was no indication in the original disclosure that a particular subgenus of the disclosed genus of compounds would be a better candidate than any other); *see also In re Ruschig*, 379 F.2d 990, 994 (CCPA 1967) (“Specific claims to single compounds require reasonably specific supporting disclosure . . .”).

Therefore, based on the foregoing discussion, we determine that Patent Owner has not demonstrated adequate written description support for

any of the proposed substitute or new claims. Accordingly, the Motion to Amend is *denied*.

V. CONCLUSIONS

For the foregoing reasons, we conclude that Petitioner has established by a preponderance of the evidence that claims 1–7 and 12–16 of the ’454 patent are unpatentable under 35 U.S.C. § 102 as anticipated by each of Shibayama and Rhim. Additionally, we conclude that Patent Owner has not established that it is entitled to have Exhibits 1011, 1012, and 1032 excluded. We dismiss Patent Owner’s request to exclude Exhibits 1020–1026 and 1033, as moot. We conclude further that Patent Owner has not met the requirements of 37 C.F.R. § 42.121 for amending claims.

ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1–7 and 12–16 of the ’454 patent are unpatentable under 35 U.S.C. § 102 as anticipated by each of Shibayama and Rhim;

FURTHER ORDERED that Patent Owner’s Motion to Exclude is *denied* as to Exhibits 1011, 1012, and 1032, and *dismissed* as moot as to Exhibits 1020–1026 and 1033;

FURTHER ORDERED that Patent Owner’s Contingent Motion to Amend is *denied*; and

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

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Patent 8,592,454 B2

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