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Paper No. 10
Entered: February 22, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COALITION FOR AFFORDABLE DRUGS IX LLC,
Petitioner,

v.

BRISTOL-MYERS SQUIBB COMPANY,
Patent Owner.

Case IPR2015-01723
Patent 6,967,208 B2

Before GRACE KARAFFA OBERMANN, BRIAN P. MURPHY, and TINA E. HULSE, *Administrative Patent Judges.*

MURPHY, *Administrative Patent Judge*.

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

I. INTRODUCTION

Coalition For Affordable Drugs IX LLC ("Petitioner") filed a Petition requesting *inter partes* review of claims 1–13, 20–27, and 34–61 of U.S. Patent No. 6,967,208 B2 ("the '208 patent"). Paper 1 ("Pet."). Bristol-Myers Squibb Company ("Patent Owner") filed a Preliminary Response to the Petition. Paper 8 ("Prelim. Resp."). We have statutory authority under 35 U.S.C. § 314(a), which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition."

Petitioner challenges claims 1–13, 20–27, and 34–61 of the '208 patent as unpatentable for alleged anticipation under 35 U.S.C. § 102 and obviousness under 35 U.S.C. § 103. Pet. 15. Based on the information presented in the Petition and Preliminary Response, we are not persuaded there is a reasonable likelihood Petitioner would prevail with respect to at least one of the claims challenged in the Petition. Therefore, we decline to institute *inter partes* review.

A. Related Proceedings

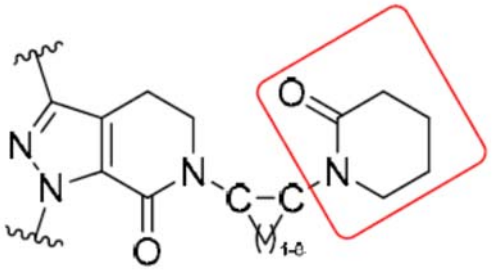
The parties do not identify any related matters. Pet. 2–3; Paper 6, 1.

B. The '208 Patent

The '208 patent, titled "Lactam-Containing Compounds and Derivatives Thereof as Factor Xa Inhibitors," issued November 22, 2005 from an application filed September 17, 2002, which claims priority to provisional applications filed September 21, 2001 and August 9, 2002. Ex. 1001, (22), (45), (60). The '208 patent is directed to genus, sub-genus, and species claims for lactam-containing compounds, pharmaceutical compositions, and methods of treatment, particularly

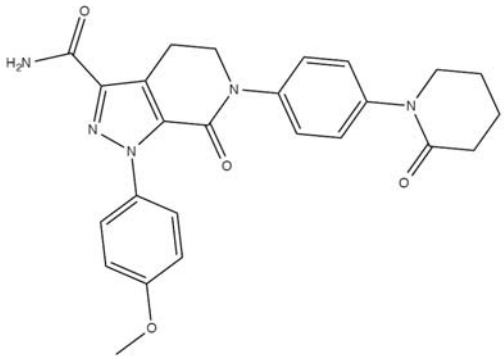
including a compound called "apixaban." *Id.* at 5:53–67. Apixaban is the active ingredient in ELIQUIS®, a lactam-containing compound used as an anticoagulant (blood factor Xa inhibitor) to reduce the risk of blood clots that can cause strokes and heart attacks. Ex. 1001, 1:20–25, 174:21–25; Ex. 1009. A lactam is a cyclic amide (O=C–N–) that includes a nitrogen in the ring structure. Prelim. Resp. 10 n.3; Ex. 1003, 79, 83–84.

Claim 1 of the '208 patent is directed to lactam genera—that is, compounds (or pharmaceutically acceptable salts thereof) having the lactam-containing core structure below:



Prelim. Resp. 12. The portion of the structure identified within the box, above, is a lactam ring. *Id.* In claim 1 of the '208 patent (reproduced below), the lactam ring at issue is defined as "M_4" substituent "B."

Claims 2 through 8 are claims to progressively smaller subgenera of claim 1. Claim 8 depends from claim 1 and is limited to 65 enumerated compounds (and their pharmaceutically acceptable salts). The ninth compound listed in claim 8 is apixaban. Claim 13 claims apixaban as a single species, dependent from claim 8. The chemical structure of apixaban is reproduced below.

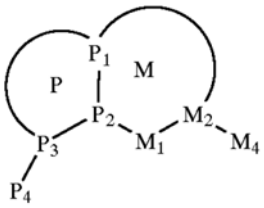


Pet. 14 (citing Ex. 1008 ¶¶ 51, 52); Prelim. Resp. 16 (noting the synthesis of apixaban is described in Example 18 of the '208 patent (Ex. 1001, 174:21–175:51)).

C. The '208 Patent Claims

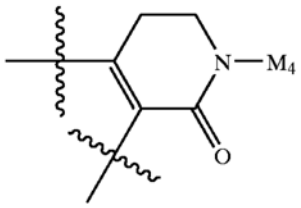
Abbreviated forms of claims 1 and 8, and claim 13 of the '208 patent are illustrative and reproduced below (emphasis added):[1]

1. A compound of Formula I:

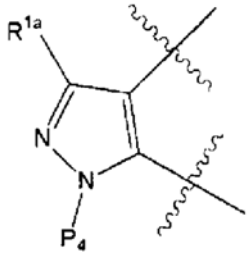


or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;
ring M, including P_1, P_2, M_1, and M_2 is substituted with 0–2 R^{1a} and is[2]

[1] Claim 1 comprises over five columns of text in the '208 patent and includes numerous Markush group substitutions. The claims of the patent were corrected by a thirteen-page Certificate of Correction issued December 2, 2008, which can be located in Exhibit 1001 following column 276. The claims reproduced here incorporate the changes identified in the Certificate of Correction. *See* Ex. 1001, Certificate of Correction, 1–2 (claim 1), 7 (claim 8), 10 (claim 13).
[2] We note ring M does not contain an R^{1a} substitution group. *See* Ex. 1001, Certificate of Correction, 1–2.



ring P, including P_1, P_2, and P_3, is



M_4 is –A–B;

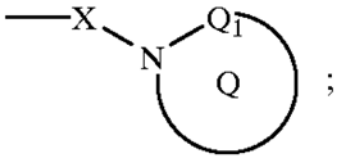
P_4 is $–G_1–G$;

. . .

A is selected from:

$C_{3\text{-}10}$ carbocycle substituted with 0–2 R^4,

B is



;

. . .

Q_1 is C=O;

ring Q is a 6 membered monocyclic ring, wherein: 0 double bond is present within the ring and the ring is substituted with 0–2 R^{4a};

X is absent; . . . .

8. A compound according to claim 1, wherein the compound is selected from the group:

[first 8 compounds] . . .

1-(4-methoxypheny1)-7-oxo-6-[4-(2-oxo-l-piperidinyl)

phenyl]-4,5,6,7-tetrahydro-1H-pyrazo1o-[3,4-c]
pyridine-3-carboxamide; . . .;
or a pharmaceutically acceptable salt form thereof.

13. A compound according to claim 8, wherein the
compound is:
1-(4-methoxyphenyl)-7-oxo-6-[4-(2-oxo-1-piperidinyl)
phenyl]-4,5,6,7-tetrahydro-1H-pyrazolo-[3,4-c] pyridine-3-carboxamide
or a pharmaceutically acceptable salt form thereof.

D. Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–13, 20–27, and 34–61 of the '208 patent are unpatentable as i) anticipated by Fevig I[3] or Fevig II[4] or ii) obvious over Fevig I or Fevig II. Pet. 15. Petitioner relies on the Declaration of Dr. George Burton in support of its arguments. Ex. 1008.[5] Patent Owner opposes. Prelim. Resp. 14–47.

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, we construe claim terms of an unexpired patent according to their broadest reasonable interpretation in light of the patent specification. 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, 793 F.3d

[3] PCT Publication No. WO 00/39131 published July 6, 2000 on an application filed December 17, 1999 by Fevig et al. ("Fevig I"). Ex. 1003.
[4] U.S. Patent No. 6,413,980 B1 issued July 2, 2002 on an application filed December 22, 1999 by Fevig et al. ("Fevig II). Ex. 1004.
[5] The Burton Declaration is unsworn and technically inadmissible. Prelim. Resp. 29 n.13 (citing Ex. 1008 at 70 (unsworn signature page); 37 C.F.R. §§ 41.2, 1.68); *see also* 37 C.F.R. §§ 42.53(a), 42.61(a) (uncompelled direct testimony "must be submitted in the form of an affidavit," otherwise it is not admissible).

1268, 1279–81 (Fed. Cir. 2015), *cert. granted sub nom. Cuozzo Speed Techs., LLC v. Lee*, 84 U.S.L.W. 3218 (U.S. Jan. 15, 2016) (No. 15-446). Under the broadest reasonable interpretation standard, we assign claim terms their ordinary and customary meaning, as understood by one of ordinary skill in the art, in the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definition for a claim term must be set forth in the specification with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

We determine that no claim terms require express construction for purposes of this Decision.

B. Asserted Anticipation of 1–13, 20–27, and 34–61 over Fevig I or Fevig II

Petitioner alleges that species claim 13 (apixaban) and genus/sub-genus claims 1–8 are anticipated by Fevig I and Fevig II because apixaban is "specifically disclosed in *Fevig* I." Pet. 21, 30, 43.[6] Petitioner reasons that "[d]emonstration of the presence of this single compound in any of claims 1-8 is sufficient to invalidate each of those claims since each is a Markush-style claim and anticipation of a single member anticipates the entire group." *Id.* at 21 (citing *In re Ruff*, 256 F.2d 590, 593 (C.C.P.A. 1958); *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1346 (Fed. Cir. 1999) ("In chemical compounds, a single prior art species within the patent's claimed genus reads on the generic claim and anticipates.")). Petitioner also argues, however, that a "broad prior art genus anticipat[es] specific compounds or render[s] later generic claims obvious." Pet. 21–22 (citing *In re Susi*, 440 F.2d 442 (C.C.P.A. 1971); *Merck v Biocraft Labs.*,

[6] Claims 9-12, 20-27 and 34–61 are addressed derivatively in claim charts. Pet. 51–54.

874 F2d 1843, 1846 (Fed. Cir. 1989)).

Patent Owner opposes, arguing that Petitioner incorrectly asserts that apixaban and the challenged lactam genera claims are specifically disclosed in Fevig I and Fevig II. Prelim. Resp. 3. Patent Owner asserts:

> [T]here can be no dispute that neither Fevig reference specifically identifies apixaban, the lactam ring, or the compounds making up the lactam genera. At best, such compounds can be derived from the Fevig references only by selecting particular substituent groups from among numerous alternative choices at a number of different locations on the generic chemical structure identified by Petitioner (i.e., structure 4, or the "Fevig genus"). To get from the compounds in the Fevig genus to apixaban, one must piece together the lactam ring, which is not specifically disclosed in the Fevig references. Indeed, as Petitioner acknowledges, the genera disclosed in the Fevig references encompass an "enormous number of compounds." [Pet.] at 16.

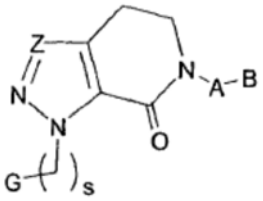
Id. Patent Owner also argues that, as a matter of well-established law, disclosure of a prior art genus "'is not necessarily a disclosure of every species that is a member of that genus,'" rather a genus only anticipates a specific compound if a person of ordinary skill would "'at once envisage'" the specific compound or class of compounds, for example, by "following 'a pattern of preferences' disclosed in the art." *Id.* at 3–5 (citations omitted).

1. Fevig I and Fevig II

Petitioner provides a brief overview of Fevig I and Fevig II in the Petition. Pet. 16–19. Petitioner represents that "the specification of Fevig II is identical to Fevig I," and Patent Owner does not dispute the point, so we will refer and cite to Fevig I. Pet. 38; Prelim. Resp. 18 n.9. A review of the dozens of compound genera in Fevig I indicates a disclosure of "an enormous number of compounds claimed to be Factor Xa inhibitors." Pet. 16 (citing Ex. 1003 *passim*; Ex. 1008 ¶

55). Each structural genus alone bears numerous Markush group substitutions. *Id.* Fevig I was disclosed in the background section of the '208 patent and is a cited reference on the cover page of the '208 patent. Ex. 1001, 2:49–64. The '208 patent further states that "[c]ompounds specifically described in WO00/39131 [Fevig I] are not considered to be part of the present invention." *Id.* at 2:63–64.

One structural formula representing a genus of compounds, referred to by Petitioner as "Structure 4" and by Patent Owner as the "Fevig genus," is disclosed in the upper left corner of page 4 in Fevig I. Ex. 1003, 4; Ex. 1008 ¶¶ 66–67. Structure 4 of Fevig is reproduced below:



Id. Substituents A, B, G, and Z are, in turn, defined by innumerable Markush group substitutions. Ex. 1003, 9–15. Petitioner bases its arguments of anticipation and obviousness on the disclosure of Structure 4 in Fevig I.

2. Analysis

a. The law of genus-species disclosures for chemical compounds

"It is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus." *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006). Rather, "whether a generic disclosure necessarily anticipates everything within the genus . . . depends on the factual aspects of the specific disclosure and the particular products at issue." *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1083 (Fed. Cir. 2008). Of "critical importance" in conducting this analysis is "how one of ordinary skill in the art would understand the relative size of a genus or species in a particular

technology." *OSRAM Sylvania, Inc. v. Am. Induction Techs., Inc.*, 701 F.3d 698, 706 (Fed. Cir. 2012). On the one hand, "when the class of compounds that falls within the genus is so limited that a person of ordinary skill in the art can '*at once envisage* each member of this limited class,' . . . a reference describing the genus anticipates every species within the genus." *In re Gleave*, 560 F.3d 1331, 1338 (Fed. Cir. 2009) (quoting *Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1376 (Fed. Cir. 2006)) (emphasis added). However, where "the number of compounds actually disclosed by [the asserted prior art] numbers in the millions (including all proposed alternative substituents)," the prior art genus cannot anticipate a later species claim. *Eli Lilly*, 471 F.3d at 1376. A person of ordinary skill in the art would understand to look at any expressed "pattern of preferences" in the prior art, such as preferred embodiments, in assessing the scope of the generic disclosure. *See, e.g.*, *Sanofi-Synthelabo*, 470 F.3d at 1377. Therefore, to anticipate a later-claimed species, a pattern of preferences or other related teaching or suggestion must lead to a genus small enough that a person of ordinary skill in the art would at once envisage the claimed species. *Sanofi-Synthelabo*, 550 F.3d at 1083; Prelim. Resp. 19–21.

b. Claims 8 and 13 – Petitioner has not shown that apixaban is specifically disclosed in Fevig I

Petitioner's factual assertion that apixaban is "specifically disclosed in *Fevig* I" is based solely on Dr. Burton's hindsight reconstruction of the apixaban structure from "the appropriately disclosed alternative for each variable of [Structure 4 that] results in" apixaban. Pet. 23; *see also id.* at 24–27, 29–33 (citing Ex. 1008 ¶¶ 66–75 and describing the "appropriate" Markush group selections). Neither the Petition nor Dr. Burton's Declaration, however, contains a citation to a disclosure of the apixaban species in Fevig I. Petitioner and Dr. Burton also

acknowledge that Structure 4 is a "general formula" (Pet. 23 (citing Ex. 1008 ¶ 66)), and they do not provide persuasive evidence that Fevig I discloses any preference or suggestion for selecting a lactam ring as substituent B in Structure 4 (*id.* at 26), much less for selecting the other required substituents necessary to derive the apixaban species (*id.* at 23–27). In short, a person of ordinary skill "would be required to make many specific selections without any guidance from the Fevig specifications pointing to the selection of the particular combination of variables required to arrive at apixaban."[7] Prelim. Resp. 19 n.10.

Dr. Burton derives a lactam ring for substituent B by making hindsight-based Markush group selections, including the selection of a carbonyl oxygen from a "long list of alternatives," without citing anything in Fevig I that discloses or teaches one of ordinary skill to make such selections. Ex. 1008 ¶ 74 (citing Ex. 1003, 12:27–28, 13:24). As Patent Owner notes, the preferred general compound structures identified in Fevig I do not indicate any preference for a lactam ring as substituent B, and Petitioner has not cited evidence to suggest such a preference. Prelim. Resp. 4; Ex. 1003, 12:24–13:29.[8] We agree with Patent Owner that Petitioner has not shown Fevig I discloses apixaban or the claimed lactam genera. Prelim. Resp. 3–4, 19 n.10, 22–24. Petitioner also has not provided evidence of a reason why a person of ordinary skill would at once envisage apixaban, or the

[7] For purposes of this Decision, we accept Petitioner's definition of a person of ordinary skill in the art as someone with "either a Pharm. D. or a Ph.D. in organic chemistry, pharmacy, pharmacology, or a related discipline; or a Bachelor's or Master's degree in organic chemistry or a related field with at least four years of experience relating to compounds that are or may be Factor Xa inhibitors." Pet. 19–20 (citing Ex. 1008 ¶ 61).

[8] A word search of "lactam" in Fevig I reveals discussion of lactams in various compounds corresponding to ring "M" recited in claim 1, but not corresponding to substituent B. Ex. 1003, 79–83.

lactam genera claimed in the ’208 patent, from the disclosures in Fevig I. Therefore, we find that Petitioner has not established a reasonable likelihood that Fevig I anticipates claims 8 and 13.

c. Claim 1 – Petitioner has not shown the claimed genus is disclosed in Fevig I

Regarding the huge genus of compounds recited in claim 1 of the ’208 patent, Petitioner does little more beyond showing how a single species, apixaban, could be derived in hindsight from the general formula of Structure 4 in Fevig I. Pet. 28–33, 45–50 (claim chart), 59; Prelim. Resp. 45 n.17. For example, Petitioner does not attempt to show that Fevig I discloses, suggests, or indicates a preference for a lactam ring as substituent B in Structure 4, where “Q_1 is C=O” and “ring Q is a six membered monocyclic ring wherein 0 double bond is present within the ring,” as recited in claim 1. *Compare* Ex. 1001, 238:33–35 *with* Pet. 50 (citing Ex. 1003, 12:24–28, 13:24). Petitioner’s Markush group selections, made from the enormous number of compounds represented by each genus disclosed in Fevig I, are hindsight-based presumptions. Petitioner has not shown such selections to be rational selections that would have been made by one of ordinary skill in the art of medicinal chemistry based on the disclosures and teachings of Fevig I. Pet. 28–33, 45–50 (claim chart), 59. The Petition and Dr. Burton’s Declaration, moreover, do not provide any meaningful technical analysis of the synthetic chemistry disclosed in Fevig I with respect to lactam-containing compounds, from which we might conclude that Dr. Burton’s Markush group selections were based on something more than a hindsight reconstruction of apixaban as described and claimed in the ’208 patent.

Therefore, Petitioner has not made a sufficient showing that Fevig I anticipates the genus recited in claim 1 of the ’208 patent.

d. Petitioner's legal arguments

As indicated previously, Petitioner argues that a "broad prior art genus anticipat[es] specific compounds." Pet. 21, 22. Petitioner's argument is contrary to the law of genus-species anticipation, set forth above in Section B.2.a.

The case of *Eli Lilly & Co. v. Zenith Goldline Pharmaceuticals, Inc.*, 471 F.3d 1369, 1376–77 (Fed. Cir. 2006) is particularly instructive in the present case. The prior art reference in *Eli Lilly* disclosed millions of potential compounds (including all Markush group alternative substituents) and listed several "preferred compounds and substituents, none of which resemble [the claimed compound]." *Id.* at 1376; *see also Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1376–77 (Fed. Cir. 2006) (prior art disclosure of hydrochloride salt of racemic compound insufficient to anticipate later-claimed bisulfate salt of the compound's d-enantiomer, in the absence of a "pattern of preferences" that would further limit the prior art disclosure); *Impax Labs., Inc. v. Aventis Pharm. Inc.*, 468 F.3d 1366, 1383 (Fed. Cir. 2006) (disclosure of prior art genus (formula 1) included "hundreds of compounds" and was insufficient to anticipate later-claimed treatment method using single compound). *Eli Lilly* also distinguished *In re Petering*, 301 F.2d 676, 681–82 (C.C.P.A. 1962) and *In re Schaumann*, 572 F.2d 312, 315 (C.C.P.A. 1978), two seminal cases in the art of medicinal chemistry not cited or addressed by Petitioner. "[I]n contrast to this case, the prior art in *Petering* did more than make a broad generic disclosure. In *Petering*, the prior art disclosed a limited number of specific preferences from a specifically defined group of isoalloxazines . . . a limited class of only 'some 20 compounds.'" *Eli Lilly*, 471 F.3d at 1376. "[T]he prior art in both *Petering* and *Schaumann* expressly spelled out a definite and limited class of compounds that enabled a person of ordinary skill in the art to at once envisage each member of this limited class." *Id.* (citing *Petering*, 301 F.2d at

681–82; *Schaumann*, 572 F.2d at 315).

In contrast to *Petering* and *Schaumann*, Petitioner and Dr. Burton do not make a showing that Fevig I discloses a limited and defined group of compounds within the scope of the challenged patent claims, or that Fevig I indicates any preference for lactam rings as substituent B in Structure 4. The Petition and Dr. Burton's Declaration do not indicate a disclosure in Fevig I that would lead one of ordinary skill in the art to "at once envisage" the claimed lactam genera or the apixaban species. The Petition and Dr. Burton's Declaration do no more than show that "[a]t most, apixaban is encompassed by the enormous genera described in the Fevig references." Prelim. Resp. 19. For example, "they do not offer helpful analyses of the size or scope of the earlier-disclosed genera; and they do not offer any insights about whether a person of ordinary skill in the art would at once envisage apixaban or the other lactam-genera claims in the '208 patent from the Fevig genus." *Id.* at 23.

Petitioner also acknowledges that i) the Fevig I genus is "enormous" and "enormously complicated," ii) the selection of substituents in Fevig I is a "puzzle," and iii) one of ordinary skill would have to "piece together apixaban via a labyrinth of nested components with variations on variations." Prelim. Resp. 24 (citing Pet. 16, 17, 25, 60; Ex. 1008 ¶¶ 55–56). Petitioner's hindsight reconstruction of the apixaban structure is not supported by citations to particular teachings, preferences, suggestions, or other reasons derived from Fevig I and the level of skill in the art that otherwise would limit the enormous number of disclosed compounds or solve the self-described apixaban puzzle. Petitioner's evidence, therefore, is insufficient to satisfy the relevant legal standard for anticipation of genus and species claims directed to chemical compounds.

Petitioner relies on *Atlas Powder*, 190 F.3d at 1346 and *In re Ruff*, 256 F.2d

at 593 to support its position that "when one member of a Markush group is anticipated, the entire group is anticipated." Pet. 27, 44. Neither case is apposite to the present case.

In *Atlas Powder*, the patent claimed blasting compositions consisting of several components within recited ranges by weight percent. *Atlas Powder*, 190 F.3d at 1344. The prior art disclosed blasting compositions having the same components in ranges overlapping the claimed ranges, but there was an issue of whether a limitation regarding "sufficient aeration" was inherently disclosed by the prior art compositions. *Id.* at 1345. Inherency is not at issue here. Petitioner also misapplies the court's statement that "[i]n chemical compounds, a single prior art species within the patent's claimed genus reads on the generic claims and anticipates" (*id.* at 1346), because apixaban is not a disclosed prior art species in Fevig I or Fevig II. Pet. 27–28, 33–34, 44. Therefore, we are not persuaded that *Atlas Powder* supports Petitioner's anticipation argument.

The citation to *In re Ruff* is not explained by Petitioner, and we fail to see its relevance to the facts of the present case. *In re Ruff* stands for the proposition that a patent claim is invalid where the prior art teaches the functional equivalency between the claimed compound(s) and the prior art compounds. *In re Ruff*, 256 F.2d at 593–94. Petitioner has not made a showing of functional equivalency here. Therefore, we are not persuaded by Petitioner's citation to *In re Ruff* in support of its anticipation argument.

In conclusion, we determine Petitioner has failed to show a reasonable likelihood of prevailing on its assertion that the challenged claims in the '208 patent are anticipated by Fevig I or Fevig II.[9]

[9] Claims 9–12, 20–27, and 34–61 of the '208 patent are composition and method of treatment claims that depend from claims 1–8 and 13. Petitioner does not argue

C. Asserted Obviousness of Claims 1–13, 20–27, and 34–61 over Fevig I or Fevig II

Petitioner asserts that either Fevig I or Fevig II, "each in its own right," renders the challenged claims of the '208 patent obvious under 35 U.S.C. § 103. Pet. 54–58. Petitioner's argument, however, relies in part on the rejection of patent application claims in Fevig II over another prior art reference, the relevance of which is not sufficiently articulated by Petitioner, apart from Petitioner's discussion of *Merck v. Biocraft Labs.*, 874 F.2d 804, 807 (Fed. Cir. 1989). *Id.* at 56–57. More fundamentally, Petitioner's obviousness argument neither analyzes the facts of the present case in view of the *Graham* factors nor explains sufficiently why the challenged patent claims would have been obvious to one of ordinary skill in the art. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417–420 (2007). Petitioner does not offer a proper obviousness analysis, relying instead on a perfunctory reference to its anticipation argument, and arguing that the facts of the present case are "directly analogous to the facts in *Merck*." Pet. 56–58.

The claims in *Merck* recited a pharmaceutical composition comprising a combination of two known active compounds, amiloride hydrochloride and hydrochlorothiazide, within a range of weight ratios. *Merck*, 874 F.2d at 805–06. The prior art taught a limited genus of 1200 effective drug combinations that included the claimed combination. *Id.* at 806–07. The claims were found to be obvious because the claimed composition was used for "the identical purpose taught by the prior art," and because the patent owner failed to prove any unexpected synergistic effect from the claimed combination of known active

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claims 9–12, 20–27, and 34–61separately from claims 1–8 and 13. Pet. 38, 51–54. Therefore, Petitioner fails to show a reasonable likelihood of prevailing on its assertion of anticipation of those claims for the same reasons explained above.

compounds. *Id.* at 807–08.

The facts of *Merck* bear little relevance to the facts of the present case. The claimed compounds in the '208 patent are not combinations of known species disclosed in the prior art, where evidence of synergistic effect of the claimed combination is often a determinative consideration. Furthermore, Petitioner's evidence does not establish that either Fevig I or Fevig II discloses apixaban or any of the claimed lactam genera. Rather, Petitioner's selection of the claimed species (apixaban) and lactam genera from the disclosed Fevig I and Fevig II genus is "dependent upon random variation of numerous parameters." *Merck v. Biocraft*, 874 F.2d at 807.

Petitioner's argument also is inconsistent with the substantial authority declining to apply *Merck v. Biocraft* in the way Petitioner suggests. The Federal Circuit has held that showing a prior art genus encompasses a later-claimed species is not sufficient, by itself, to render the later-claimed species obvious. *See, e.g.*, *In re Baird*, 16 F. 3d at 382 (claims to bisphenol A not obvious over prior disclosure of a genus of diphenols encompassing bisphenol A); *In re Jones*, 958 F.2d 347, 350 (Fed. Cir. 1992) ("We decline to extract from *Merck* the rule that the Solicitor appears to suggest—that regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it."). Prelim. Resp. 41–42. Consistent with *Baird* and *Jones*, Petitioner has not provided sufficient evidence that one of ordinary skill would have been motivated to make the necessary selections in the disclosed Fevig I and Fevig II genus (Structure 4) to achieve apixaban or the lactam genera recited in the challenged '208 patent claims.[10]

For the reasons given above, we are not persuaded by Petitioner that Fevig I

[10] In view of our Decision, we need not consider the parties' arguments regarding secondary considerations of nonobviousness or whether 35 U.S.C. § 103(c)

or Fevig II discloses the genera, sub-genera, or species of compounds recited in claims 1–13, 20–27, and 34–61 of the '208 patent. We also are not persuaded that Petitioner has provided sufficient evidence to show a reasonable likelihood of prevailing on its assertion that at least one claim would have been obvious to one of ordinary skill in the art over Fevig I or Fevig II, at the time the '208 patent claims were filed.

III. CONCLUSION

Petitioner has failed to demonstrate a reasonable likelihood of prevailing with respect to at least one of the claims challenged in this Petition, based on the grounds asserted and information presented therein.

IV. ORDER

For the reasons given, it is

ORDERED that the Petition is denied.

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precludes consideration of Fevig II as a reference for purposes of Petitioner's obviousness challenge. Pet. 58–59; Prelim. Resp. 44–47.

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