No. 21-2121

In the United States Court of Appeals for the Federal Circuit

MYLAN PHARMACEUTICALS INC.,
Appellant,
v.
MERCK SHARP & DOHME CORP.,
Appellee.

Appeal from the Patent Trial and Appeal Board
No. IPR2020-00040

COMBINED PETITION FOR PANEL REHEARING OR REHEARING EN BANC

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November 14, 2022

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 2021-2121

Short Case Caption Mylan Pharmaceuticals Inc. v. Merck Sharp & Dohme Corp.

Filing Party/Entity Mylan Pharmaceuticals Inc.

Instructions: Complete each section of the form. In answering items 2 and 3, be specific as to which represented entities the answers apply; lack of specificity may result in non-compliance. **Please enter only one item per box; attach additional pages as needed and check the relevant box**. Counsel must immediately file an amended Certificate of Interest if information changes. Fed. Cir. R. 47.4(b).

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: 10/24/2022

Signature: /s/ Deepro R. Mukerjee

Name: Deepro R. Mukerjee

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	**2. Real Party in Interest.** Fed. Cir. R. 47.4(a)(2).	**3. Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☑ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
Mylan Pharmaceuticals Inc.		Mylan Inc.; Viatris Inc.

☐ Additional pages attached

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

☐ None/Not Applicable ☐ Additional pages attached

Alissa M. Pacchioli (Katten Muchin Rosenman)		
Christopher W. West, Ph.D. (Katten Muchin Rosenman)		
Heike S. Radeke, Ph.D. (Katten Muchin Rosenman)		

5. Related Cases. Provide the case titles and numbers of any case known to be pending in this court or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. Do not include the originating case number(s) for this case. Fed. Cir. R. 47.4(a)(5). See also Fed. Cir. R. 47.5(b).

☐ None/Not Applicable ☐ Additional pages attached

Merck Sharp & Dohme, LLC v. Mylan Pharmaceuticals Inc., CAFC No. 2023-1013		

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

☑ None/Not Applicable ☐ Additional pages attached

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STATEMENT OF COUNSEL CONCERNING REHEARING EN BANC

Based on my professional judgment, I believe the panel decision is contrary to the following decision(s) of the Supreme Court of the United States or the precedent(s) of this Court: *Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368 (Fed. Cir. 2005); *In re Gleave*, 560 F.3d 1331 (Fed. Cir. 2009); *Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356 (Fed. Cir. 2012).

Date: November 14, 2022 /s/ Deepro R. Mukerjee

POINTS OF LAW OVERLOOKED OR MISAPPREHENDED BY THE COURT

The panel in this case concluded that a prior-art reference could not anticipate or disclose an invention formed from two elements contained in defined lists that the art invited the skilled artisan to combine because the art contained "no direction to select" either element from their respective lists. In doing so, the panel overlooked and misapprehended this Court's controlling decisions in *Perricone*, *Gleave*, and *Wm. Wrigley Jr. Co.*

INTRODUCTION

Nearly two decades ago, this Court rejected the notion that a reference cannot anticipate merely because the relevant teachings "appear[] without special emphasis in a longer list." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005). It has reaffirmed that holding several times. *In re Gleave*, 560 F.3d 1331, 1337 (Fed. Cir. 2009); *Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1361 (Fed. Cir. 2012). And the Court's position makes sense. Anticipation is not obviousness. All that is required to anticipate is disclosure and enablement. *Perricone*, 432 F.3d at 1376. Motivation, emphasis, and other obviousness-like doctrines are out-of-place in a § 102 analysis.

The panel decision in this case embraced precisely what *Perricone* rejected, and it did so without even mentioning (let alone distinguishing) earlier precedent. It held that a prior-art reference (WO '498) did not anticipate a salt made of sitagliptin and phosphoric acid ("sitagliptin DHP") claimed in a later patent (the '708 Patent), despite the fact that both elements were disclosed in two narrow lists that the art invited the skilled artisan to

combine to create pharmaceutically acceptable salts.[1] That was not enough, per the panel decision, because the reference contained "no direction to select" either sitagliptin or phosphoric acid from the lists in which they appeared. Op. 9.

Respectfully, that's error and Mylan urges the panel to correct it. The starting point for the anticipation analysis in this case should have been the disclosure of sitagliptin and its pharmaceutically acceptable salts created using phosphoric acid. The fact that sitagliptin and phosphoric acid appear in longer lists of elements is not relevant in a § 102 analysis, per *Perricone* and its progeny. The panel's error infected not only its treatment of anticipation, but also its assessment of antedation. Key there was whether Merck had reduced to practice as much of the alleged invention as the prior art showed. Because the panel believed the prior art did not show sitagliptin DHP (let alone hydrates thereof), it answered the question in the negative. The panel's failure to follow *Perricone* was case dispositive of multiple issues that

[1] This case involves two materially identical pieces of prior art: WO 03/004498 ("WO '498") and U.S. Patent No. 6,699,871 ("the '871 Patent"). For the sake of brevity, they are collectively referred to as WO '498, unless noted otherwise. The patent challenged in the underlying *inter partes* review is U.S. Patent No. 7,326,708 ("the '708 Patent"). Appellant is referred to as "Mylan," and Appellee is referred to as "Merck."

touched almost every claim challenged by Mylan. Panel rehearing is therefore warranted.

If the panel declines the opportunity for rehearing, then en banc review is warranted. The error here will not be a one-off issue. The precedential panel decision creates an intracircuit split, erases the distinction between list and genera disclosures, and blurs the lines between anticipation and obviousness. The en banc court should review and correct this issue to prevent future confusion and conflict.

BACKGROUND

A. The '708 Patent and Prior Art.

The '708 Patent claims a dihydrogen phosphate salt of sitagliptin in a 1:1 stoichiometry, as well as various compositions and methods of using sitagliptin DHP to treat Type 2 diabetes. Appx00078 (Abstract). Claims 1-3 broadly claim a sitagliptin phosphate salt or a hydrate thereof in the (R) or (S) configuration. Appx00091 (15:64-16:46). Claim 4 is specifically directed to "a crystalline monohydrate" of the (R)-sitagliptin phosphate salt of Claim 2. Appx00091 (16:47-48). Claim 17 is directed to a pharmaceutical composition containing a therapeutically effective amount of (R)-sitagliptin phosphate salt. Appx00092 (17:21-24). Claim 19 is directed to a method for the treatment

of type 2 diabetes using a therapeutically effective amount of (R)-sitagliptin phosphate salt or its hydrate. Appx00092 (17:29-32). Claims 21 and 22 are process claims for preparing (R)-sitagliptin phosphate salt, and Claim 23 is a product-by-process claim for Claim 21. Appx00092 (17:37-18:12). Each claim requires the claimed sitagliptin phosphate salt to have a 1:1 stoichiometry. Appx00027.

The '708 Patent acknowledges WO '498 as prior art and admits that "[p]harmaceutically acceptable salts of [sitagliptin] are generically encompassed within the scope" of the application. Appx00084 (1:49-52, 1:55-57). WO '498 teaches formulas for various DP-IV inhibitors, the class of compounds to which sitagliptin belongs. The reference exemplifies and claims sitagliptin and its pharmaceutically acceptable salts. Appx00422 (bottom compound), Appx00427 (60:5), Appx00523 (37:35-40), Appx00524 (40:48). This disclosure appears in a list of 32 other compounds created from Formula I in the prior art. Appx00421-00427; Appx00522-00524.

Further, WO '498 instructs that the term "'pharmaceutically acceptable salts' refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids." Appx00376 (9:27-29), Appx00507(6:38-41). Significantly, the prior art

identifies eight "[p]articularly preferred" acids for preparing pharmaceutically acceptable salts: "citric, hydrobromic, hydrochloric, maleic, **phosphoric**, sulfuric, fumaric, and tartaric acids." Appx00377 (10:14 15), Appx00508 (7:2-4) (emphasis added). In the same discussion, WO '498 states that "[s]alts in the solid form may exist in more than one crystal structure, and may also be in the form of hydrates." Appx00376 (9:33-34), Appx00507 (6:46-48).

B. Procedural History.

Mylan filed abbreviated new drug applications for generic versions of Merck's Januvia® and Janumet® products, which included Paragraph IV certifications to the '708 Patent. Appx01623. Merck sued Mylan for patent infringement in February 2019. *See* Compl., *Merck Sharp & Dohme Corp. v. Mylan Pharms. Inc.*, No. 1:19-cv-00315, ECF No. 1 (D. Del. Feb. 13, 2019). Mylan thereafter petitioned the Patent Trial and Appeal Board for *inter partes* review in October 2019, which the Board instituted. Appx01738-01801.

Among other things, Mylan argued that Claims 1-3, 17, 19, 21-23 of the '708 Patent were separately anticipated by WO '498 and the '871 Patent, because they disclosed the elements of sitagliptin DHP in two narrow lists and a skilled artisan could readily envisage the 1:1 stoichiometry of the salt.

Appx00019-00021. It further asserted that Claims 1-4, 17, 19, 21-23 were obvious over WO '498 and the '871 Patent in view of additional pieces of prior art. Appx00177-00258.

The Board denied Mylan's petition, and a panel of this Court affirmed. Relevant here, the Board did not start its anticipation analysis with the express disclosure of sitagliptin and its pharmaceutically acceptable salts. It instead formed a nearly 1000-member genus by combining the 33 compounds disclosed alongside sitagliptin with the eight particularly preferred salts disclosed in the specification. Appx00029-00030. From there, the Board rejected Mylan's anticipation argument because it did not believe a skilled artisan would immediately envisage every member of this genus. Appx00029-00030. A panel of this Court agreed and further elaborated on the reasoning: "As Merck asserted, and as the Board considered, the list of 33 compounds, ***with no direction to select sitagliptin from among them***, plus the eight 'pharmaceutical preferred' acids and various stoichiometric possibilities, results in 957 salts[.]" Op. 9 (emphasis added).

This flawed analysis also infected the Board's treatment of obviousness. Merck tried to short-circuit Mylan's obviousness argument as to Claims 1-2, 17, 19, and 21-23 by antedating WO '498. The critical issue here

was whether Merck had reduced to practice as much of these claims as was shown by WO '498. *See In re Clarke*, 356 F.2d 987, 991 (C.C.P.A. 1966). Based on the conclusion that the prior art did not reveal sitagliptin salts made from phosphoric acid, the Board held that WO '498 revealed less than what was claimed by the '708 Patent. Appx00047-00048. It further concluded that WO '498 did not enable hydrates of sitagliptin DHP, and therefore Merck did not need to show reduction to practice of this element either. Appx00048-00052. The Board accordingly disqualified WO '498 as prior art under § 103. Appx00052. Based solely upon its antedation analysis, the Board rejected Mylan's obviousness argument as to Claims 1-2, 17, 19, and 21-23. On appeal, the panel affirmed this decision based exclusively upon its conclusion that the prior art did not disclose sitagliptin DHP. Op. 11-12.

ARGUMENT

Motivation to Select Is Not Required for a List Disclosure Under § 102, and the Panel's Decision to the Contrary Warrants Reconsideration.

A. The Panel Decision Conflicts With Circuit Precedent.

WO '498 explicitly discloses sitagliptin and its pharmaceutically acceptable salts. In defining what a "pharmaceutically acceptable salt" is, the specification states that phosphoric acid is a "[p]articularly preferred" reactant. Appx00377 (10:14 15); Appx00508 (7:2-4). Putting these two

elements together—as the reference invites the skilled artisan to do—results in a sitagliptin-phosphoric acid salt.

That should have been the starting point for the anticipation analysis in this case. But it wasn't. Instead, the panel treated all 33 compounds listed in the prior art as a genus and asked how many different salts could be formed from this genus using the particularly preferred acids disclosed in the specification. It did so because WO '498 contains "no direction to select sitagliptin from among" the 33 listed compounds. Op. 9. Starting from this broader genus (instead of starting with sitagliptin), the Court concluded that 957 different salts would result from the combination of this genus with the particularly preferred acids listed in the specification. Op. 9. This result was fatal to Mylan's anticipation argument. Op.9-10. It was also dispositive of Mylan's obviousness argument on Claims 1-2, 17, 19, and 21-23, because the panel affirmed the Board's decision on antedation on the same grounds. Op.11-12.

Respectfully, the panel's decision is wrong. This Court has repeatedly held that anticipation through a list disclosure does not have a selection requirement. *Perricone* is the clearest example. The patent owner in *Perricone* argued that two skin benefit ingredients could not anticipate because they

appeared in a list with "an additional twelve ingredients." 432 F.3d at 1376. This Court unequivocally "reject[ed] the notion that one of these ingredients cannot anticipate because it appears without special emphasis in a longer list." *Id.* "To the contrary, the disclosure is prior art to the extent of its enabling disclosure." *Id.*

Gleave is similar. The applicant there argued that when an anticipatory disclosure "is only a small part of a much larger and exhaustive listing and there is no basis in the art for selecting some individual members of the listing over others," the disclosure amounts to "no more than the generic concept underlying the list." 560 F.3d at 1336. The Court dismissed this as an argument "rooted in policy" rather than law. *Id.* In doing so, it reaffirmed *Perricone*'s statement that no "special emphasis" is needed when an anticipatory disclosure appears in a list. *Id.*

The fact that reaching sitagliptin-phosphoric acid salts requires combining two lists in the prior art is of no moment. "[E]ven when a reference discloses elements in different locations in the disclosure, the relevant question is whether the reference is sufficiently clear in disclosing the combinability of those elements such that a skilled artisan would 'at once

envisage' the claimed combination." *Chamberlain Grp., Inc. v. Techtronic Indus. Co.*, 935 F.3d 1341, 1350 (Fed. Cir. 2019).

Wm. Wrigley demonstrates this. The Court found anticipation of a claimed chewing gum's combination of menthol and a chemical coolant called WS-23, based on their disclosure in lists in the prior art. 683 F.3d at 1362. The anticipating reference broadly disclosed chemical combinations in many potential oral compositions, like chewing gum, lozenges, toothpaste, and mouth rinses. *Id.* at 1360. In one list of 23 flavoring agents, the patent's written description listed menthol. *Id.* In a separate list, the patent disclosed WS-23 as a "preferred cooling agent." *Id.* Here, it's hard to see how 33 (the number of compounds disclosed in the prior art, including sitagliptin) is materially different than 23 (the number of flavoring agents listed in *Wm. Wrigley*, including menthol). And certainly it would be "immediately apparent" to combine the "particularly preferred" acids listed in the specification (including phosphoric acid) to create the claimed "pharmaceutically acceptable salts" of sitagliptin.

If the prior art both discloses and enables, then the prior art can anticipate. Nothing more is required. By imposing the additional requirement that the prior art provide "direction to select" a teaching from

a list disclosure, the panel contravened settled precedent and improperly narrowed the scope of § 102.

B. Correcting the Conflict Is Important.

The perceived absence of "direction to select" sitagliptin and phosphoric acid from the prior art was dispositive of both anticipation and antedation in this case. Op. 9-12. For all the reasons discussed in the panel merits briefing, both issues would have gone Mylan's way with the proper framing. On anticipation, all that would have been left to show is that a skilled artisan would readily envisage a 1:1 stoichiometry for sitagliptin DHP. Appellant Br. 29-33. The record shows there are only a finite number of stoichiometries that for sitagliptin DHP, and 1:1 would be the first and most likely arrangement that a skilled artisan would obtain. *Id*. As for antedation, getting past the disclosure of the salt itself would have allowed the panel to engage the principal dispute between the parties: whether the prior art enabled hydrates and, specifically, whether Merck overcame the presumption of enablement that attached to the prior art. *Id*. at 47-51. Merck didn't even try to overcome that presumption before the Board or in its briefing to this Court, which should have been dispositive. Given this, Mylan therefore respectfully requests that the panel reconsider its decision.

Short of panel reconsideration, the error laid out above is important enough to warrant review by the en banc court. That's so for three reasons:

First, the panel decision creates an intractable conflict in circuit precedent. There is no way to reconcile the panel opinion with this Court's prior decisions in *Perricone*, *Gleave*, and *Wm. Wrigley*. The panel decision and *Perricone* are squarely at odds. If left to stand, the panel decision here will leave future litigants and panels of this Court to argue over which line of cases controls.

Second, injecting a selection requirement into § 102 vitiates a critical distinction between list disclosures and genus disclosures. Again, the Court has repeatedly said as much. In *Perricone*, the Court pointed out that "specific disclosure[s], even in a list, make[] this case different from cases involving disclosure of a broad genus without reference to the potentially anticipating species." 432 F.3d at 1377. That is because specific disclosures lead the skilled artisan "to derive a class of compounds of lesser scope than the genus actually disclosed in the reference on the basis of preferences ascertainable from the remainder of the disclosure." *In re Schaumann*, 572 F.2d 312, 316 (C.C.P.A. 1978). The Court reiterated this distinction in *Gleave*. 560 F.3d at 1337 ("For the purposes of whether they are anticipatory, lists and genera

are often treated differently under our case law."). If an express disclosure of a compound and its pharmaceutically acceptable salts is not enough to narrow an anticipation analysis down from a broader genus, then it is difficult to see what relevance remains of the list/genus distinction.

Third, and finally, the panel's "direction to select" rule significantly constrains the scope of the anticipation doctrine, to the point of jeopardizing its ongoing utility. Motivation—whether to select or combine teachings—is a familiar concept in obviousness analyses under § 103. But it is totally foreign to anticipation under § 102. *See Callaway Golf Co. v. Acushnet Co.*, 576 F.3d 1331, 1347 (Fed. Cir. 2009) (observing that, unlike obviousness, "motivation to combine is not an issue" in anticipation). That's because "[t]he anticipation analysis asks solely whether the prior art reference discloses and enables the claimed invention, and not how the prior art characterizes that disclosure or whether alternatives are also disclosed." *Hewlett–Packard Co. v. Mustek Sys., Inc.*, 340 F.3d 1314, 1324 n.6 (Fed. Cir. 2003). Indeed, the Court in *Perricone* distinguished obviousness cases in forming its no-need-for-emphasis rule. 432 F.3d at 1376-77.

If anticipation required litigants to vault over the same hurdles they'd have to in order to prove obviousness—and do it all with only a single

reference—why would anyone turn to anticipation at all? Requiring litigants to demonstrate motivation to select a teaching out of a list in order to prevail on anticipation blurs a critical line between § 102 and § 103. Cases like *Perricone*, *Gleave*, and *Wm. Wrigley* recognize this. The panel decision here regretfully does not. For that reason, rehearing is warranted.

CONCLUSION

The petition should be granted.

Date: November 14, 2022

Respectfully submitted,

/s/ Deepro R. Mukerjee

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ADDENDUM

United States Court of Appeals for the Federal Circuit

MYLAN PHARMACEUTICALS INC.,
Appellant

v.

MERCK SHARP & DOHME CORP.,
Appellee

2021-2121

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2020-00040.

Decided: September 29, 2022

ERIC THOMAS WERLINGER, Katten Muchin Rosenman LLP, Washington, DC, argued for appellant. Also represented by JITENDRA MALIK, Charlotte, NC; DEEPRO MUKERJEE, LANCE SODERSTROM, New York, NY.

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Before LOURIE, REYNA, and STOLL, *Circuit Judges*.

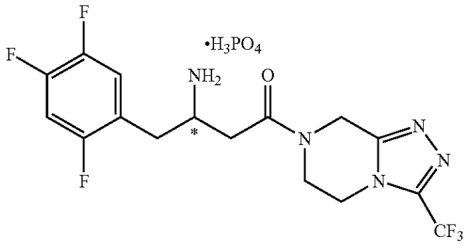
LOURIE, *Circuit Judge*.

Mylan Pharmaceuticals Inc. ("Mylan") appeals from the final written decision of the U.S. Patent and Trademark Office Patent Trial and Appeal Board (the "Board") holding that it failed to show that claims 1–4, 17, 19, and 21–23 of U.S. Patent 7,326,708 (the "'708 patent") were anticipated or would have been obvious over the cited prior art at the time the alleged invention was made. *See Mylan Pharms. Inc. v. Merck Sharp & Dohme Corp.*, No. IPR2020-00040, 2021 WL 1833325 (P.T.A.B. May 7, 2021) ("*Decision*"). For the reasons provided below, we affirm.

BACKGROUND

Merck Sharp & Dohme Corp. ("Merck") owns the '708 patent, which describes sitagliptin dihydrogenphosphate ("sitagliptin DHP"). Sitagliptin DHP is a dihydrogenphosphate salt of 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro [1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine. Sitagliptin DHP belongs to the class of dipeptidyl peptidase-IV ("DP-IV") inhibitors, which can be used for treating non-insulin-dependent (i.e., Type 2) diabetes. Independent claim 1 recites a sitagliptin DHP salt with a 1:1 stoichiometry, and reads as follows:

> 1. A dihydrogenphosphate salt of a 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro [1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine of Formula I:



or a hydrate thereof.

'708 patent col. 15 l. 64–col. 16 l. 15.

Sitagliptin contains a single asymmetric carbon, indicated by the asterisk in the above chemical structure. The (R)-configuration and (S)-configuration of sitagliptin DHP are recited in dependent claims 2 and 3, respectively. A crystalline monohydrate form of the (R)-configuration is recited in dependent claim 4.

Mylan petitioned for *inter partes* review ("IPR") of claims 1–4, 17, 19, and 21–23 of the '708 patent. J.A. 177. Mylan argued that claims 1–3, 17, 19, and 21–23 were anticipated by International Patent Publication WO 2003/004498 (the "'498 publication"), a Merck-owned publication, and the equivalent U.S. Patent 6,699,871 (the "'871 patent") (collectively, "Edmondson").[1]

Edmondson "is directed to compounds which are inhibitors of the dipeptidyl peptidase-IV enzyme ('DP-IV inhibitors') and which are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes." *Decision*, 2021 WL 1833325, at *6. Specifically, Edmondson discloses a genus of DP-IV inhibitors and 33 species, one of which is sitagliptin. '498 publication col. 54 l. 16–col. 60 l. 5. Edmondson further discloses that pharmaceutically acceptable salts can be formed using one of eight "[p]articularly preferred" acids. *Id.* at col. 10 ll. 14–15. Phosphoric acid is in the list of "particularly preferred" acids. Edmondson also discloses that the salts may

[1] The parties agree that the '498 publication and the '871 patent are identical in relevant part. Appellant's Br. 1; Appellee's Br. 5, n.1. The Board also treated them as identical in relevant part. *Decision*, 2021 WL 1833325, at *1, n.4.

exist in crystalline forms, including as hydrates. *Id.* at col. 9 ll. 32–34.

Mylan also argued that claims 1–4, 17, 19, and 21–23 would have been obvious over Edmondson and two additional publications titled "Structural Aspects of Hydrates and Solvates" ("Brittain")[2] and "Salt Selection and Optimisation Procedures for Pharmaceutical New Chemical Entities" ("Bastin").[3]

Brittain describes the pharmaceutical importance and prevalence of crystalline hydrates of pharmaceutical compounds. J.A. 438–94. Specifically, Brittain teaches that approximately one third of studied pharmaceutical active ingredients could form crystalline hydrates, and half of those one-third were monohydrates. J.A. 441. In other words, Brittain illustrates that approximately one sixth of the analyzed pharmaceutical compounds formed crystalline monohydrates. Brittain also cites various challenges that arise during the manufacturing and development of hydrates, including lower solubility, chemical instability, and discoloration. J.A. 440.

Bastin teaches salt selection and optimization procedures during the development of pharmaceutical compounds. J.A. 495–97. Specifically, Bastin teaches that a range of possible salts should be prepared for each new substance to compare adequately the properties of each salt during the development process. J.A. 495. Bastin also

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[2] Kenneth R. Morris, *Structural Aspects of Hydrates and Solvates*, *in Polymorphism in Pharmaceutical Solids* 125–181 (Harry G. Brittain ed., 1999).

[3] Richard J. Bastin, Michael J. Bowker, & Brian J. Slater, *Salt Selection and Optimisation Procedures for Pharmaceutical New Chemical Entities*, 4 *Organic Process Rsch. & Dev.* 427 (2000).

discloses disadvantages of certain salts used in drug formulations, including hydrochloric acid ("HCl"). J.A. 496.

First, the Board determined that there was no express disclosure of all of the limitations of the 1:1 sitagliptin DHP salt in Edmondson, and that Mylan could not fill in the gaps by arguing that a skilled artisan would "at once envisage" what is missing. *Decision*, 2021 WL 1833325, at *10, *12. The Board also concluded that Mylan had not proven an inherent disclosure of the 1:1 sitagliptin DHP salt in Edmondson, and that evidence, both experimental and from the technical literature, undeniably showed that 1:1 sitagliptin DHP does not form every time sitagliptin and DHP were reacted. *Id.* at *15–16. The Board concluded that claims 1–3, 17, 19, and 21–23 were neither expressly nor inherently anticipated by Edmondson. *Id.* at *16.

Next, the Board determined that claims 1–4, 17, 19, and 21–23 would not have been obvious in view of Edmondson, Bastin, or Brittain. First, the Board considered the threshold issue whether Merck could antedate Edmondson with evidence that it had reduced to practice the subject matter of claims 1, 2, 17, 19, and 21–23 before Edmondson had been published on January 16, 2003. *Id.* at *16–20. The Board concluded that Merck had reduced to practice at least as much, and in fact more, of the claimed subject matter than was shown in Edmondson. *Id.* at *20. Thus, Merck could successfully antedate the subject matter of claims 1, 2, 17, 19, and 21–23, and thus Edmondson was not a 35 U.S.C. § 102(a) reference, but merely a 35 U.S.C. § 102(e) (pre-AIA) reference. *Id.* Because it was undisputed that the inventions claimed in the '708 patent and the subject matter of Edmondson were commonly owned by Merck, or under obligation of assignment to Merck, at the time of the invention, the Board determined that the 35 U.S.C. § 103(c)(1) (pre-AIA) exception applied to claims 1, 2, 17, 19, and 21–23. *Id.* Merck did not assert a prior-reduction-to-practice argument for claims 3 and 4. *Id.*

The Board considered whether claim 3, which recites the (S)-configuration of sitagliptin DHP, and claim 4, which recites the crystalline monohydrate form of (R)-sitagliptin, would have been obvious in view of Edmondson, Bastin, and Brittain. The Board found that neither Edmondson nor Bastin disclosed anything related to (S)-sitagliptin or even a racemic mixture of any sitagliptin salt. *Id.* at *21. The Board thus concluded that Mylan did not show that claim 3 would have been obvious to a skilled artisan at the time the invention was made. *Id.* at *22. The Board also found that Mylan provided no rationale to explain why a person of ordinary skill would have been motivated to make the claimed crystalline monohydrate form of 1:1 sitagliptin DHP of claim 4 and failed to show that a skilled artisan would have had a reasonable expectation of success in making the crystalline monohydrate form of the 1:1 sitagliptin DHP salt. *Id.* at *24, *26. The Board thus concluded that Mylan failed to show that claim 4 would have been obvious to a person of ordinary skill at the time the invention was made. *Id.* at *26.

In summary, the Board concluded that Mylan had not demonstrated that claims 1–4, 17, 19, and 21–23 were anticipated or would have been obvious at the time the invention was made. Mylan appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(4).

DISCUSSION

Mylan raises three challenges on appeal. First, Mylan contends that the Board erred in determining that a 1:1 stoichiometry of sitagliptin DHP was not anticipated, either expressly or inherently, by Edmondson. Second, Mylan contends that the Board erred in determining that the '708 patent antedates Edmondson.[4] Third, Mylan

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[4] The '498 publication was published on January 16, 2003, and the '871 patent was published on May 29, 2003.

contends that the Board erred in determining that it failed to prove that claims 3 and 4 of the '708 patent would have been obvious over Edmondson, Brittain, and Bastin. We address each argument in turn.

We review the Board's legal determinations *de novo*, *In re Elsner*, 381 F.3d 1125, 1127 (Fed. Cir. 2004), but we review the Board's factual findings underlying those determinations for substantial evidence. *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). A finding is supported by substantial evidence if a reasonable mind might accept the evidence as adequate to support the finding. *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938). And "[i]f two 'inconsistent conclusions may reasonably be drawn from the evidence in the record, [the PTAB]'s decision to favor one conclusion over the other is the epitome of a decision that must be sustained upon review for substantial evidence.'" *Elbit Sys. of Am., LLC v. Thales Visionix, Inc.*, 881 F.3d 1354, 1356 (Fed. Cir. 2018) (alteration in original) (quoting *In re Cree, Inc.*, 818 F.3d 694, 701 (Fed. Cir. 2016)).

Anticipation is a question of fact. *Genentech, Inc. v. Hospira, Inc.*, 946 F.3d 1333, 1337 (Fed. Cir. 2020). The prior art may be deemed to disclose each member of a genus when, reading the reference, a person of ordinary skill can "at once envisage each member of this limited class." *In re Petering*, 301 F.2d 676, 681 (C.C.P.A. 1962).

Obviousness is a "mixed question of law and fact," and we review "the Board's ultimate obviousness determination *de novo* and underlying fact-findings for substantial evidence." *Hologic, Inc. v. Smith & Nephew, Inc.*, 884 F.3d 1357, 1361 (Fed. Cir. 2018).

Since the '498 publication was published earlier, we consider Edmondson, for purposes of antedation, to have been published on January 16, 2003.

I

We first consider Mylan's challenge to the Board's determination that it failed to prove that Edmondson anticipates claims 1–3, 17, 19, and 21–23. Mylan argues that Edmondson anticipates the claims because it discloses sitagliptin in a list of 33 compounds. Mylan further asserts that Edmondson discloses acids forming "pharmaceutically acceptable salts," including phosphoric acid in a list of eight "particularly preferred" acids. Mylan, therefore, asserts that sitagliptin DHP is effectively disclosed in Edmondson, and Edmondson thus anticipates the challenged claims.

Mylan further asserts that a skilled artisan would "at once envisage" a 1:1 stoichiometry of the sitagliptin DHP salt for two reasons. First, Example 7 of Edmondson discloses a sitagliptin hydrochloride salt ("sitagliptin HCl") having a 1:1 stoichiometry. Second, experimental data presented by Mylan's expert Dr. Chorghade illustrate that only a 1:1 sitagliptin DHP stoichiometry forms under conditions allegedly similar to those disclosed in Edmondson. Mylan contends that the Board thus erred in holding that a 1:1 stoichiometry was not anticipated by Edmondson.

Merck responds that the Board's holding that the claims are not anticipated by Edmondson was supported by substantial evidence. Merck asserts that a skilled artisan would not "at once envisage" all members of the entire genus of DP-IV-inhibitor salts disclosed in Edmondson. Merck further contends that the combined list of 33 compounds and eight preferred salts, taking into account various stoichiometric possibilities, would result in 957 salts, some of which may not even form under experimental conditions. That, Merck asserts, does not meet the standard set by the "at once envisage" theory. Merck argues that Mylan seeks to expand the theory inappropriately, improperly focusing on whether skilled artisans could have envisaged 1:1 sitagliptin DHP among the members of the class instead of envisaging each member of the disclosed class.

In essence, Merck asserts that Mylan uses hindsight to single out one compound from the large class. Merck further argues that Mylan's own expert conceded that Edmondson does not direct a skilled artisan to sitagliptin from among the 33 DP-IVs, nor does it disclose a phosphate salt of any DP-IV inhibitor.

We agree with Merck that the Board's decision was supported by substantial evidence. The Board did not err in determining that Edmondson does not expressly disclose a 1:1 sitagliptin DHP salt. The Board grounded its finding in the testimony from Mylan's own expert, Dr. Chorghade, stating that nothing in Edmondson directs a skilled artisan to sitagliptin from among the 33 listed DP-IV inhibitors. J.A. 2342, 2373–74; Chorghade Dep. 61:7–62:9, 188:6–189:8. Further, nothing in Edmondson singles out phosphoric acid or any phosphate salt of any DP-IV inhibitor, and the list of "pharmaceutically preferred" salts comes 44 pages earlier in the specification. The Board reasonably concluded that Edmondson does not expressly disclose the 1:1 sitagliptin DHP salt.

We also agree with Merck that the Board did not err in determining that Edmondson does not inherently disclose a 1:1 sitagliptin DHP salt. *In re Petering* stands for the proposition that a skilled artisan may "at once envisage each member of [a] *limited* class, even though the skilled person might not at once define in his mind the formal boundaries of the class." 301 F.2d at 681 (emphasis added). The key term here is "limited." As Merck asserted, and as the Board considered, the list of 33 compounds, with no direction to select sitagliptin from among them, plus the eight "pharmaceutically preferred" acids and various stoichiometric possibilities, results in 957 salts, some of which may not exist. That is a far cry from the 20 compounds "envisaged" by the narrow genus in *Petering*. *Id.* Mylan's own expert, Dr. Chorghade, even stated that salt formation is an unpredictable art that requires a "trial and error

process." *Decision*, 2021 WL 1833325, at *8; J.A. 2355–56; Chorghade Dep. 116:22–117:3.

We cannot provide a specific number defining a "limited class." *In re Petering*, 301 F.2d at 681. It depends on the "class." But we agree with Merck and hold that the Board did not err in finding that a class of 957 predicted salts that may result from the 33 disclosed compounds and eight preferred acids, some of which may not even form under experimental conditions, is insufficient to meet the "at once envisage" standard set forth in *Petering*.

II

We next consider Mylan's challenge to the Board's determination that Mylan failed to prove that claims 1–4, 17, 19, and 21–23 would have been obvious to a person of ordinary skill in the art at the time the invention was made.

A

We must first consider the threshold issue of Mylan's antedation challenge and application of the 35 U.S.C. § 103(c)(1) exception. Under 35 U.S.C. § 102(a) (pre-AIA), "[a] person shall be entitled to a patent unless the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent." But a party can overcome the § 102(a) barrier if it can antedate a reference "by showing that the invention was conceived before the effective date of the reference, with diligence to actual or constructive reduction to practice." *In re Steed*, 802 F.3d 1311, 1320 (Fed. Cir. 2015). To prove antedation, the patent owner must show that it reduced to practice at least as much as "the reference shows of the claimed invention" before the reference's publication date. *In re Clarke*, 356 F.2d 987, 991 (C.C.P.A. 1966).

Mylan does not dispute that Merck reduced 1:1 (R)-sitagliptin DHP salt to practice before Edmondson was

published, nor does it dispute that Merck commonly owned Edmondson and the '708 patent. Mylan, instead, argues that the Board erred in finding that Merck's reduction to practice of the 1:1 (R)-sitagliptin DHP salt antedates Edmondson, because Edmondson discloses sitagliptin hydrates, and Merck had not made hydrates of 1:1 sitagliptin DHP until March 2003, about two months after the January 16, 2003 Edmondson publication date. Mylan also argues that the Board erred in finding that Edmondson does not disclose hydrates of sitagliptin phosphate.

Merck responds that the Board did not err in finding that Merck's work on the subject matter in claims 1, 2, 17, 19, and 21–23 of the '708 patent antedated Edmondson. Merck argues that it had reduced to practice the subject matter of these claims before Edmondson had been published on January 16, 2003. As a result, Merck asserts, Edmondson could not serve as 35 U.S.C. § 102(a) prior art and would merely be a 35 U.S.C. § 102(e) reference. Because it is undisputed that the invention claimed in the '708 patent and the subject matter of Edmondson were commonly owned by Merck at the time of the invention, the exception in § 103(c)(1) applies. Section 103(c)(1) (pre-AIA) provides that "[s]ubject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f), and (g) of section 102, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person." Merck therefore argues that Edmondson cannot serve as an obviousness reference for claims 1, 2, 17, 19, and 21–23. Without Edmondson, the obviousness challenge to these claims fails. *Decision*, 2021 WL 1833325, at *20.

We agree with Merck that the Board's antedation determination was supported by substantial evidence. As Merck asserts, and as the Board considered, Merck showed that it developed a 1:1 sitagliptin DHP salt in December

2001 with experimental confirmation in early 2002. As Merck highlights, Mylan did not argue that claim 4, directed to a crystalline monohydrate, was anticipated by Edmondson, which it could have done had it believed that Edmondson disclosed a crystalline monohydrate. The Board's finding that Edmondson does not disclose 1:1 sitagliptin DHP was supported by substantial evidence; thus, the Board's finding that it does not disclose a hydrate of that salt was likewise supported by substantial evidence. We therefore agree with the Board that Merck reduced to practice "more . . . than what is shown in [Edmondson] for the claimed subject matter." *Decision*, 2021 WL 1833325, at *18.

B

We next turn to whether the Board erred in holding that Mylan failed to prove that claims 3 and 4 of the '708 patent would have been obvious to a skilled artisan at the time the invention was made.

Mylan argues that the Board erred in holding that it failed to prove that claim 3, which recites the (S)-configuration of 1:1 sitagliptin DHP, would have been obvious. Mylan argues that Edmondson, in combination with Bastin, would have allowed a skilled artisan to envisage and create 1:1 (S)-sitagliptin DHP. According to Mylan, Bastin, which cites disadvantages of hydrochloric acid in pharmaceutical formulations, would encourage a skilled artisan to replace the hydrochloric acid in Example 7 of Edmondson. Furthermore, Mylan states that sitagliptin has one asymmetric carbon, and a skilled artisan would thus have a reasonable expectation of success in creating both (R)-sitagliptin and (S)-sitagliptin.

Mylan further argues that the Board erred in holding that it failed to prove that claim 4, which recites the crystalline monohydrate form of (R)-sitagliptin, would have been obvious. Mylan asserts that a skilled artisan would have had a reasonable expectation of success in creating a

crystalline monohydrate in view of Edmondson in combination with Brittain. First, Mylan argues that Edmondson states that the described salts exist in more than one crystal structure and in the form of a hydrate. Second, Mylan argues that Brittain's discussion of hydrates would have provided motivation for a skilled artisan to explore hydrates in the development process.

Merck argues that the Board did not err in holding that claim 3 would not have been obvious, and that the Board's underlying factual findings were supported by substantial evidence. As the Board considered, Bastin does not provide a specific motivation, including any screening or optimization protocol that, combined with Edmondson, would lead to 1:1 sitagliptin DHP, the (S)-configuration, or even a racemic mixture.

Merck also argues that the Board did not err in holding that claim 4 would not have been obvious, and that the Board's underlying factual findings were supported by substantial evidence. Merck argues that the Board was correct in finding that Mylan did not provide a persuasive motivation for making the crystalline monohydrate form of sitagliptin. Merck asserts evidence that skilled artisans would avoid making hydrates due to solubility and stability challenges during the drug-production process. Merck also contends that the monohydrate has unexpectedly favorable properties, and that these properties are objective indicia of nonobviousness.

We agree with Merck that the Board's decision that Mylan failed to show that claims 3 and 4 of the '708 patent would have been obvious to a skilled artisan at the time the invention was made was supported by substantial evidence.

With respect to claim 3, the Board found that there was no motivation to combine Edmondson and Bastin to make sitagliptin DHP, that the two cited references did not provide motivation to make (S)-sitagliptin, and that there was

no reasonable expectation of success in combining the references. The Board adequately credited Dr. Chorghade's testimony, which stated that the (S)-enantiomer was not disclosed in Edmondson. *Decision*, 2021 WL 1833325, at *21. The Board further highlighted that Mylan advanced no expected or theoretical benefit to making the (S)-enantiomer of 1:1 sitagliptin DHP, and that the general disclosure on diastereomers in Edmondson encompasses millions of potential compounds and salts with no motivation to make the (S)-enantiomer with a reasonable expectation of success, particularly in an unpredictable activity like salt formation. *Id.* at *22. We thus agree with Merck that the Board's decision was supported by substantial evidence.

With respect to claim 4, the Board found that there was no motivation to combine Edmondson, Bastin, and Brittain, and that a person of ordinary skill would have had no reasonable expectation of success in doing so. The Board credited Dr. Chorghade's testimony, which stated that a skilled artisan "couldn't predict with any degree of certainty" hydrate formation. *Id.* at *21; Chorghade Dep. 238:8–18. The Board also addressed the numerous downsides of hydrates reported in the literature, including those stating that a skilled artisan would have several reasons for avoiding hydrates. *Decision*, 2021 WL 1833325, at *23. The Board also credited Merck's expert, Dr. Myerson, who stated that a skilled artisan would have sought to avoid hydrates, *Decision*, 2021 WL 1833325, at *22; Myerson Decl., ¶¶ 127–38, and that forming crystalline salts, including hydrates, is highly unpredictable. *Decision*, 2021 WL 1833325, at *24; Myerson Decl., ¶¶ 146–49. We thus agree with Merck that the Board's decision was supported by substantial evidence.

Finally, the Board did not err in its evaluation of purported objective indicia of nonobviousness. Although the Board did not consider in detail the alleged unexpected properties of the claimed crystalline monohydrate of claim 4, the Board stated that such unexpected results

served as further evidence undermining Mylan's challenge to claim 4. *See Hamilton Beach Brands, Inc. v. f'real Foods, LLC*, 908 F.3d 1328, 1343 (Fed. Cir. 2018) (holding that there is no need to reach objective indicia of nonobviousness where the petitioner has not made a showing necessary to prevail on threshold obviousness issues).

CONCLUSION

We have considered Mylan's remaining arguments, but we find them unpersuasive. The Board's decision was supported by substantial evidence and not erroneous as a matter of law. For the foregoing reasons, the decision of the Board is affirmed.

AFFIRMED

CERTIFICATE OF COMPLIANCE

I hereby certify that the foregoing complies with the word limitation of Fed. R. App. P. 40 (b) because it contains 2,715 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(f) and Fed. Cir. R. 32(b)(2). This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type-style requirements of Fed. R. App. P. 32(a)(6) because it was prepared in Microsoft Word 2016 using a proportionally spaced typeface (Book Antiqua) in 14-point font.

Date: November 14, 2022 /s/ Deepro R. Mukerjee

CERTIFICATE OF SERVICE

I hereby certify that I caused a copy of the foregoing to be filed on November 14, 2022, with the Clerk of the Court for the United States Court of Appeals for the Federal Circuit using the Court's electronic filing system, which will send a notice of electronic filing to all attorneys appearing in this matter.

/s/ Deepro R. Mukerjee