No. 18-1933

In the United States Court of Appeals for the Federal Circuit

GENENTECH, INC.,
APPELLANT

v.

HOSPIRA, INC.,
APPELLEE

UNITED STATES,
INTERVENOR

ON APPEAL FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE PATENT TRIAL AND APPEAL BOARD IN NO. IPR2016-01837

REPLY BRIEF OF APPELLANT GENENTECH, INC.

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CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rule 47.4, undersigned counsel for appellant certifies the following:

1. The full name of the party represented by me is Genentech, Inc.

2. The name of the real party in interest represented by me is the same.

3. Genentech, Inc. is a wholly-owned subsidiary of Roche Holdings Inc. Roche Holdings Inc.'s ultimate parent, Roche Holdings Ltd, is a publicly held Swiss corporation traded on the Swiss Stock Exchange. Upon information and belief, more than 10% of Roche Holdings Ltd's voting shares are held either directly or indirectly by Novartis AG, a publicly held Swiss corporation.

4. The following attorneys appeared for Genentech, Inc. in proceedings below or are expected to appear in this Court and are not already listed on the docket for the current case: Adam Perlman, Christopher Suarez, and Teagan Gregory of Williams & Connolly LLP, 725 Twelfth Street, N.W., Washington, D.C. 20005.

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in this pending appeal are *Genentech, Inc. and City of Hope v. Amgen, Inc.*, No. 17-1407 (D. Del.); *Genentech, Inc. and City of Hope v. Amgen, Inc.*, No. 17-1471 (D. Del.); *Genentech, Inc. et al. v. Pfizer, Inc.*, No. 17-1672 (D. Del.); *Genentech, Inc., et al. v. Sandoz, Inc., et al.*, No. 17-13507 (D.N.J.); *Genentech, Inc. et al. v. Celltrion, Inc., et al.*, No. 18-574 (D.N.J.); *Genentech, Inc. et al. v. Celltrion, Inc., et al.*, No. 18-00095 (D. Del.); *Genentech, Inc. et al. v. Celltrion, Inc. et al.*, No. 18-01025 (D. Del.); *Genentech, Inc. et al. v. Celltrion, Inc. et al.*, No. 18-11553 (D.N.J.); *Genentech, Inc. et al. v. Samsung Bioepis Co., Ltd.*, No. 18-1363 (D. Del.).

DECEMBER 12, 2018

/s/ Paul B. Gaffney
PAUL B. GAFFNEY

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INTRODUCTION

Genentech's opening brief identified critical errors in the Board's decision arising from its failure to consider particular cases or support particular conclusions. Hospira's responsive brief is a microcosm of this proceeding, amplifying the Board's errors by repeating the same mistakes. For example:

-- Genentech's very first argument concerning the correct construction of "about 18°C" cites the Board's failure to address this Court's controlling precedent on construing "about." Genentech's Opening Brief ("Br.") at 25-27. Hospira's responsive brief ("Hospira Br.") nowhere addresses this argument or the cited precedent. *See* Hospira Br. at 20-28.

-- One of Genentech's main points concerning anticipation was that the Board credited Hospira's expert's reply declaration but not his contradictory deposition testimony. Br. at 34-38. Hospira alleges that "the Board took into account evidence that could justify or detract from its factual determinations," Hospira Br. at 33-34, yet notably does not cite the Board's decision, let alone provide a pin cite to where the Board purportedly reconciled Hospira's expert's irreconcilable testimony.

-- As for obviousness, Genentech emphasized the absurdity of deeming "routine" a type of experiment for which the record contained one example. Br. at 46-50. Hospira's response alleges that this example "is just one example of published research," yet fails to cite another, and that "there is no evidence that skilled artisans in the field never varied temperature," yet again fails to cite any other such instance. Hospira Br. at 49-50.

The Board's failures to engage with the law and facts resulted in an erroneous decision. It should be vacated.

ARGUMENT

I. THE BOARD INCORRECTLY CONSTRUED "ABOUT 18°C."

The Board's determination that van Sommeren anticipates claims 1, 2, and 5 turns on claim construction. If this Court adopts Genentech's proposed construction of "about 18°C," Hospira does not dispute that the Board's determination should be reversed. *See* Hospira Br. at 20-25. And under this Court's precedent, Genentech's proposed construction is the correct one.

A. The Board Did Not Make Any Findings Requiring Deference.

As an important preliminary matter, Hospira urges that the Board's rejection of Genentech's claim construction arguments is

"entitled to deference." Hospira Br. at 23 (citing Appx14-15). The cited portion of the Board's decision recounts the Board's interpretation of the specification and prosecution history and its disagreement with Genentech's interpretations. *See* Appx14-15. The interpretation of intrinsic evidence is not a "fact finding" that is entitled to deference; rather "the determination of the meaning of the term in the claim in light of the patent's intrinsic record" is "the *legal* part of claim construction." *Perfect Surgical Techniques, Inc. v. Olympus Am., Inc.*, 841 F.3d 1004, 1012-13 (Fed. Cir. 2016) (emphasis added). This Court's review of the Board's construction of "about 18°C" is *de novo*. *See id.* at 1012.

B. Both the Board and Hospira Have Ignored Federal Circuit Precedent Regarding the Ordinary Meaning of "About."

The ordinary meaning of "about" under this Court's precedent is "approximately." Br. at 25-27. This ordinary meaning controls unless "about" has been "defined either explicitly or by implication by the specification." *Ferring B.V. v. Watson Labs., Inc.*, 764 F.3d 1382, 1389 (Fed. Cir. 2014). The *Ferring* decision is just part of a line of precedent on this issue. *See* Br. at 26 (citing *Pall Corp. v. Micron Separations,*

Inc., 66 F.3d 1211, 1217 (Fed. Cir. 1995), *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1369-70 (Fed. Cir. 2005)).

The Board disregarded this precedent. *See* Appx11-15. It did not bother even to cite it, let alone distinguish it. *See id.* The Board's conduct is indefensible, as evidenced by Hospira's decision to say nothing in response on this issue. *See* Hospira Br. at 20-25.

The claim construction analysis here, when actually applying *Ferring*, is simple. Hospira concedes there is no "explicit" definition of "about" in the patent. Hospira Br. at 22-23. It also does not try to argue that the specification has defined the term by implication; it merely quotes one line of the specification that does not even use the word "about." *See id.* Absent such an explicit or implicit definition, the correct construction of "about" under *Ferring* is "approximately."

Rather than engage this precedent (or stipulate that the Board had erred), Hospira urges that "the meaning of the term 'about' is context dependent," citing *Atlas IP, LLC v. Medtronic, Inc.*, 809 F.3d 599, 605 (Fed. Cir. 2015). Hospira Br. at 24. In view of how often this Court has been asked to address the term "about" and how Hospira presented this case, one might think the *Atlas* case discusses the

construction of the term "about." It does not. The *Atlas* case concerns the construction of various words but does not purport to address this Court's guidance regarding the ordinary meaning of "about." That ordinary meaning should control here, and there is no dispute that under such a construction, van Sommeren does not anticipate.

C. The Specification Reinforces the Ordinary Meaning of "About 18°C," not the Board's Construction.

1. The specification is most useful in interpreting claim language when it, in fact, uses the claim language. *See Eon-Net LP v. Flagstar Bancorp*, 653 F.3d 1314, 1320 (Fed. Cir. 2011). The specification here does so in column 18, explaining that "preferably, the method comprises reducing the temperature of the composition subjected to protein A chromatography, e.g., where the temperature of the composition is reduced *below room temperature*, for instance in the range from about 3°C to about 20°C, e.g., from about 10°C to about 18°C." Appx68 (emphasis added). Claim 1's method is drawn to this narrowest preferred embodiment in which the composition being purified is at a temperature in the range of "about 10°C to about 18°C."

By describing these temperature ranges as "below room temperature," the specification illustrates what is meant by the phrases

"about 18°C" and "about 20°C." Because room temperature is commonly understood to encompass 21°C, "about" in this context must mean *no more than* ± 1°C; otherwise "about 20°C" would overlap with 21°C.[1] In its response, Hospira alleges that Genentech "argues that 'about 18°C' should mean '18±1°C.'" Hospira Br. at 26 (citing Br. at 27). This is a misrepresentation of Genentech's position. Genentech's position is, as stated in its opening brief, "to the extent that 'about' is being defined by implication here [i.e., in the specification passage about "below room temperature], it must mean *no more than* ±1°C." Br. at 27 (emphasis added). To the extent the ordinary meaning of "about" has been altered by an implied definition, this is the passage of

[1] Hospira alleges that "there is no consensus when it comes to the meaning of room temperature." Hospira Br. at 27. It then identifies various *ranges* that have been described as "room temperature," all of which include 21°C. *Id.* (citing Appx522, Appx570, Appx1165-1166). But there is no dispute that 21°C is "room temperature," as Hospira's expert testified. Appx1600. In any event, what matters is the meaning of "room temperature" in the context of this patent's specification, where the temperature of "about 20°C" is described as being "below room temperature." Hospira notes that in European Patent Office proceedings, a third party uncovered a reference suggesting that "room temperature" could span "between 15°C and 25°C." *Id.* Hospira declined to note that the same third party then argued to the EPO that the specification "indirectly defines room temperature as above about 20°C, i.e. starting at 21°C." Appx1166.

the specification that did so, and that implied definition of "about" cannot be broader than ±1°C. Again, there is no dispute that van Sommeren would not anticipate under such a construction.

2. Hospira argues that "the specification demonstrates that ±3°C is a normal fluctuation for temperatures in these types of processes." Hospira Br. at 23. Hospira supports this contention by citing to full-scale experiments in the patent in which 12,000 liters of cell culture fluid were maintained at "15 ± 3 °C." Hospira Br. at 22-24 (citing Appx70-71).

Hospira nowhere argues that this passage impliedly defines "about," *see* Hospira Br. at 22-23, nor could it. This passage does not use the word "about," so arguing that it impliedly defined the term would make as much sense as suggesting that one can look up the word "about" in the dictionary under the sections for words starting with B through Z. This passage does not refer to these experiments as being conducted at "about 15 °C." It does not purport to speak to the variability of the end points of a range. To the extent the example bears on the construction of claim 1, it exemplifies a process that falls within the claimed range of "about 10°C to about 18°C." Simply put, to the

extent any portion of the specification impliedly defines "about" to depart from its ordinary meaning, it is the passage that uses the word, not the one that does not.

D. Prosecution History Cannot Broaden Ordinary Meaning.

1. Based on the ordinary meaning of the word "about" and the specification discussed above, the broadest reasonable construction of "about 18°C" is "approximately 18°C," which can be no broader than "18±1°C" lest it contradict the specification.

The prosecution history cannot "trump the plain language of the claims and the direct teaching of the specification." *Telcordia Techs., Inc. v. Cisco Sys., Inc.*, 612 F.3d 1365, 1375 (Fed. Cir. 2010). Genentech emphasized this maxim of claim construction law, Br. at 31, yet Hospira says nothing in response, *see* Hospira Br. at 24-26. Given that the construction of "about" compelled by its ordinary meaning and the context in which it is used in the specification is narrower than the meaning Hospira alleges was "implicitly acknowledged" during prosecution, the prosecution history is irrelevant. *Telcordia*, 612 F.3d at 1375; *see also Phillips v. AWH Corp.*, 415 F.3d 1303, 1316-17 (Fed. Cir. 2005) (en banc).

2. To the extent the prosecution history is relevant, it is undisputed that Genentech stated its disagreement with the Examiner's position, but narrowed the claims to expedite prosecution. Hospira contends that despite Genentech's stated disagreement, it "implicitly acknowledged" a broad meaning of the term "about."[2] Hospira cites no case endorsing such an approach to claim construction. The only case it cites, *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, supports Genentech, not Hospira. In *Biogen*, this Court explained: "If an applicant chooses, she can challenge an examiner's characterization in order to avoid any chance for disclaimer[.]" 713 F.3d 1090, 1096 (Fed. Cir. 2013). Genentech did exactly what it was supposed to do under *Biogen*. The *Biogen* case is inapposite for the additional reason that it concerns *disclaimer* of scope. Here, Hospira urges the unprecedented position that an applicant's "implicit" actions during prosecution can compel *broadening* a claim's scope. It should be

[2] Hospira also claims the Board's analysis of the prosecution history relied on amendments made during prosecution of both the "'704 Patent and *EP '940*." Hospira Br. at 25 (emphasis added) (citing Appx14). It would have been unusual for the Board to have relied upon ex-US prosecution in claim construction, and that did not happen here. *See* Appx14.

rejected, and, under the correct construction of "about 18°C," the Board's determination that claims 1, 2, and 5 are anticipated by van Sommeren should be reversed.

II. THE BOARD ERRED IN INFERRING THAT THE '389 APPLICATION DISCLOSED PURIFYING A COMPOSITION THAT WAS AT "ABOUT 10°C TO ABOUT 18°C."

The claimed methods arise from the observation that chilling cell culture fluid to a range below room temperature can improve purification processes by reducing the leaching of protein A. The '389 Application has nothing to do with this. It discloses the routine performance of protein A purification in a room temperature setting. More specifically, its example states: "All steps are carried out at room temperature (18 - 25 °C)." Appx522. The Board's conclusion that claims 1 and 5 are not novel turns on this sentence. But the Board's conclusions based upon it are erroneous.

1. This sentence concerns the temperature of the laboratory, not the temperature of the composition being purified. Hospira's expert confirmed this fact during his deposition:

> Q. [I]t says, "all steps carried out at room temperature (18 to 25 degrees Celsius); do you see that?
>
> A. I do see that, yes.

> Q. Okay. So, that is referring to the temperature of the lab where this experiment was conducted; correct?
>
> A. Yes.

Appx1547. Genentech's expert agreed. Appx1350-1353.

Other portions of the '389 Application confirm this. Hospira notes that the '389 Application specifically identified the temperature of the fluid during steps where its temperature was important. Hospira Br. At 31-32 (citing Appx523-524, where the fluid was held at 4°C or -70°C). If the statement "All steps are carried out at room temperature (18 - 25 °C)" referred to the temperature of the fluid in addition to the temperature of the laboratory, it would be false. As the Application states, "all steps" were not in fact carried out at room temperature; some were carried out where the composition was cold or frozen. The sentence only makes sense as referring to the temperature of the laboratory, just as both experts testified.

The Board nevertheless inferred that this disclosure of the laboratory's temperature also described the temperature of the composition being purified. This Court has previously pointed out that inferences of this sort are legally inappropriate. Br. at 34-37 (citing *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 851 F.3d 1270,

1274 (Fed. Cir. 2017) (citing *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1381 (Fed. Cir. 2015)).[3] Hospira defends the Board's inference-making on the ground that "here there is no missing element." Hospira Br. at 36. But Hospira cannot wish away the gap in the '389 Application's disclosure—the Board expressly acknowledged that "we agree with Patent Owner that WO '389 does not expressly call out the temperature of the HCCF[.]" Appx20. The Board filled this acknowledged gap in the application's disclosure, improperly, with its inference that "such specificity would be redundant." Appx20.

Disclosure of *every* limitation of the claimed invention is the bedrock principle of anticipation, even the niggling, purportedly "redundant" limitations. The Board in this case should have held that the '389 Application did not anticipate claims 1 and 5 and proceeded to focus on whether those claimed methods would have been obvious. *Cf. Structural Rubber Prods. Co. v. Park Rubber Co.*, 749 F.2d 707, 716

[3] Hospira also alleges that Genentech "does not provide any reason why the Board's logical inference could be wrong." Hospira Br. at 35. This is false. Genentech cited both experts' agreement that the cell culture fluid would have been warmer than room temperature when harvested, that the '389 Application makes no disclosure as to how long such fluid should be held, and that a POSA would have had reason to purify it quickly. Br. at 34.

(Fed. Cir. 1984) ("A prior art disclosure that 'almost' meets that standard may render the claim invalid under § 103; it does not 'anticipate.'"). It instead committed legal error by purporting to find anticipation by inference. It should be reversed.

2. Even if the Board's legal rubric were proper, its analysis of the record is not supported by substantial evidence. As Genentech explained, the Board ignored the conflict between Hospira's expert's deposition testimony (that the composition would not necessarily have cooled to room temperature) and his contrary reply declaration testimony (that the POSA would have understood that it would have). Br. at 37-38. This failure to account for the evidence detracting from the Board's determination was erroneous. *See In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000).

Hospira's argument that the deposition testimony "does not contradict" the rebuttal declaration testimony is specious. Hospira Br. at 32-33. In his deposition, Dr. Todd Przybycien testified that it was "not inevitable" that the cell culture fluid used in '389 Application's methods would have cooled to the laboratory's ambient temperature. Appx1555. In the reply declaration submitted by Hospira and quoted

by the Board, he claimed that "[n]o POSA would understand WO '389 as teaching a practitioner to use HCCF having a temperature above 18ºC – 25º C°[.]" Appx21. These statements cannot both be true. The Board's decision to adopt the latter without even acknowledging the former represents a failure to consider the evidence that detracts from the Board's conclusion. Its resulting finding is therefore not supported by substantial evidence and the Board's determination that the '389 Application anticipates claims 1 and 5 should be vacated.

III. THE BOARD ERRED IN ITS OBVIOUSNESS ANALYSIS.

Hospira's responsive brief largely avoids Genentech's points and instead raises several irrelevant arguments. Each of these issues is addressed below.

A. Genentech Challenged Each of the Board's Obviousness Determinations.

Hospira twice argues that Genentech somehow limited its appeal to two of the Board's six obviousness determinations. Hospira Br. at 37 (alleging Genentech "does not challenge the Board's separate findings regarding Grounds 4-6 and 8"); 51 ("As noted above, Genentech has not appealed . . .").

It would have been rather bizarre for Genentech to appeal only some of the Board's obviousness determinations, and of course Genentech's opening brief did not seek partial, pointless relief. *See*, *e.g.*, Br. at 40 (arguing for reversal on "each of these six grounds"). The Board lumped its analysis of the obviousness grounds together—*e.g.*, Appx42 ("Patent Owner's arguments with respect to Ground 3 apply equally with respect to Ground 4, as does our analysis."); Appx43 (Genentech's "arguments with respect to Grounds 3 and 4 apply equally with respect to Ground 5, as does our analysis."); Appx44 (Genentech's arguments "apply equally with respect to Ground 6, as does our analysis"); Appx48 (as to Ground 8, adopting Petitioner's obviousness argument based "the same reasons discussed above")—and Genentech organized its appellate challenge to match. Hospira's waiver argument is specious.

B. Criticality Is Irrelevant to this Appeal.

Hospira devotes a considerable portion of its brief to arguing that the claims are *prima facie* obvious based on the alleged overlap between the claimed methods and the prior art methods in van Sommeren and the '389 Application. Hospira Br. at 39-42. Hospira criticizes

Genentech for "not address[ing] that its failure to show criticality renders claims 1, 2 and 5 obvious over WO '389 and van Sommeren." Hospira Br. at 38.[4]

Hospira's argument assumes that the prior art's methods and the claimed methods in fact overlap, a point Genentech disputes vigorously. As explained above in sections I and II, there is no overlap. If this Court agrees with Genentech, there is no basis to analyze validity by starting with the presumption of obviousness urged by Hospira. The Court should instead proceed to address the merits of the Board's determinations.

C. The Board's Conclusions Based on "Routine Optimization" Were Erroneous.

The Board articulated two rationales for why the claimed methods would have been obvious based upon "routine experimentation." Appx39. First, the Board determined that the POSA would have been

[4] Genentech presented evidence on criticality below, substantiating the patent's data and running new experiments showing the benefits of the claimed methods compared to the prior art methods. Appx208-212. The Board rejected this evidence "for the reasons set forth on pages 13 through 16 of Petitioner's Reply brief, and further detailed in paragraphs 37-45 of Dr. Przybycien's second declaration." Appx23. Given the number of issues already on appeal, Genentech did not separately appeal this finding.

motivated to chill the liquid being purified to the claimed temperature range based on a routine desire to reduce protein A leaching. Appx38-39. Second, the Board determined that the POSA would have been motivated to chill the liquid being purified to the claimed range based on a routine desire to improve binding capacity. Appx46-47. Both of these rationales are flawed, Br. at 40-50, and Hospira's response does not meaningfully address the flaws.

1. The Board's Findings on Proteolysis Are Incompatible.

a. With supporting testimony from its purification expert, Genentech explained that the nanograms of leached protein A generated during purification procedures are of concern only in the manufacture of drugs that will be given to humans. Br. at 41. Hospira responds that this "is not the only reason a person of ordinary skill in the art would have for reducing protein A leaching." Hospira Br. at 46. It then cites to two scientific papers—not testimony—that discuss how a column can be affected by leaching. *Id.* (citing Appx903-904, Appx932).

This Court reviews for error the obviousness rationale the Board actually articulated. *See In re Hounsfield*, 699 F.2d 1320, 1324 (Fed. Cir. 1983) ("We review the Board's decision on the basis of what the

Board said, not on the basis of counsel's theory concerning what the Board really meant. . . . [C]ourts may not accept appellate counsel's *post hoc* rationalizations for agency action." (internal quotation marks omitted)). Hospira does not cite any discussion of this purported rationale in the Board's decision, making Hospira's argument on this point irrelevant.

b. Hospira emphasizes the Board's rejection of Genentech's argument as "irrelevant because the claims are not limited to commercial-scale applications." Hospira Br. at 47 (citing Appx20). The Board's statement reflects its fundamental misapprehension of the argument.

While the claimed methods are not limited to a particular scale, the issue is whether the claims embrace subject matter that would have been obvious to the POSA. The alleged basis for obviousness was that the POSA would have been motivated to practice the claimed methods to achieve "increasing purity." Appx38 (quoting Hospira's expert). But the desire for "increasing purity" is applicable only at a particular scale, namely, in the industrial manufacture of a therapeutic product. Br. at 41-42 (citing Appx1337-1338, Appx1375, Appx1607). The large

scale at which the POSA intended to operate is therefore not just *directly* relevant to what the POSA would (or would not) have been motivated to do but critical to that analysis, regardless of whether the claimed methods encompass operating at other, smaller scales. The Board's cursory rejection of Genentech's argument based on its misunderstanding on this point was error.

Hospira also argues that not all protein A chromatography occurs at industrial scale, alleging that there are "smaller scale or academic applications" of Protein A chromatography. Hospira Br. at 46. This is irrelevant to the obviousness rationale articulated by Dr. Przybycien and adopted by the Board. Dr. Przybycien testified that the claimed methods are "aimed at production-scale operation" and that the POSA would have been "looking to develop a process . . . for commercial scales." Appx1607.

c. Genentech pointed out that the record lacked any evidence from which the Board could conclude that the POSA would have been motivated to control temperature at an industrial scale. Hospira Br. at 47. Disputing this point, Hospira argues "it would have been routine before 2003 for a skilled artisan in the field of protein purification to

control or vary the temperature of compositions intended for purification, at both laboratory and industrial scales." *Id.* No citations follow that sentence.

As Genentech explained, chilling thousands of liters of water to the claimed temperature range involves substantial expense and specialized equipment. Br. at 42. Rather than cite evidence, Hospira suggests this must not be true because the patent "does not describe any means for chilling HCCF at commercial scale." Hospira Br. at 48. This misses the point. Genentech does not claim to have invented refrigeration. The point is that, in the absence of Genentech having demonstrated the benefits that flow from undertaking this substantial expense, the POSA would not have been motivated to do so. Nothing Hospira cites in response supports the notion that chilling at an industrial scale "would have been routine before 2003." No reference cited exemplifies doing this.

d. Finally, Hospira suggests that "techniques that require expense, time, and effort to carry out may nevertheless be routine." Hospira Br. at 47. Hospira's argument defies the ordinary meaning of "routine," and the sole case cited by Hospira—*Velander v. Garner*—is

inapposite. *Velander* concerned whether the POSA could have had a reasonable expectation of success at carrying out a method that was "expensive, technically challenging, and laborious." 348 F.3d 1359, 1378 (Fed. Cir. 2003). Critically, there was no dispute in *Velander* that the POSA would have had a motivation to undertake such painstaking research. *Id.* at 1374 ("Velander does not dispute . . . that there was a motivation to combine those elements."). The case does not purport to suggest that the POSA is "routinely" motivated to undertake experiments that are expensive, challenging, and laborious.

* * *

Here, the Board's obviousness rationale required a finding that the POSA would have been motivated to vary routinely the temperature of the fluid being purified at industrial scale. The Board did not make such a finding at that scale, and given the undisputed technical challenges involved in doing so, it could not have made such a finding. Its actual finding—that temperature could be controlled routinely at the lab bench—is irrelevant to an obviousness rationale based on the need to remove a contaminant generated during industrial manufacture. Its determination on this point should be reversed.

2. The Board Failed to Analyze Obviousness as of the Time of the Invention.

The Board's second obviousness rationale was that the POSA would have performed the claimed methods as part of the routine optimization of a protein A column's binding capacity. Appx46-47. The Board's conclusion that such methods would have been developed "routinely" was based on a single paper published in 1992. As Genentech showed, as of the priority date in 2003, intervening review articles demonstrated that parameters other than temperature were the key to optimizing binding capacity. Br. at 46-48.

Hospira ridicules this argument, stating that "there is no such thing as prior art that is 'too early.'" With respect to anticipation, Hospira is certainly correct. *Cf. In re Cruciferous Sprout Litig.*, 301 F. 3d 1343, 1350 (Fed. Cir. 2002) (citing prior art cookbook describing uses of the claimed methods in 2939 B.C.). But it cites no support for its argument as it pertains to an obviousness analysis, and the precedent cited by Genentech in its opening brief—which Hospira ignores—holds otherwise. *See* Br. at 49-50 (citing *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346 (Fed. Cir. 2013)). In *Leo*, this Court emphasized how "this considerable time lapse suggests instead that the

Board only traverses the obstacles to this inventive enterprise with a resort to hindsight." 726 F.3d at 1356.

Hospira also insists that the 1992 van Sommeren article "is just one example of published research that placed the concept of temperature-dependent binding in the public domain." Hospira Br. at 49. One would think Hospira might have offered another "example," but no citations follow the assertion that van Sommeren was only one of many disclosing the same thing.[5] *Id.*

Hospira next suggests "there is no evidence that skilled artisans in the field have never varied temperature in order to affect binding since the publication of van Sommeren. This is mere speculation on Genentech's part." *Id.* at 50. Respectfully, the evidence of such absence is shown by Hospira's failure to cite a single example of this allegedly routine development work having occurred. The evidence of such absence also comes from Dr. Przybycien, who testified that he had never

[5] Perhaps Hospira's other "examples" were intended to refer merely to how van Sommeren was cited later on in two review papers, which Hospira accuses Genentech of having "mischaracterized." Hospira Br. at 50. Hospira does not say *how* Genentech mischaracterized these papers. As previously explained, they demonstrate how the art had developed methods for optimizing binding capacity that did not involve modifying temperature. *See* Br. at 8-10.

seen anyone do the experiment he alleged to be routine. Br. at 48 (citing Appx1666-1668).

Finally, Hospira mocks Genentech's argument that "a 'routine' development process is one that has been performed dozens of times." Hospira Br. at 45 (citing Br. at 50). Hospira does not engage with the support for Genentech's argument, which is the ordinary meaning of the word "routine." So that there is no ambiguity on this point, "routine" means "a customary or regular course of procedure" or "commonplace tasks, chores, or duties as must be done regularly . . . typical or everyday activity." Random House Webster's Unabridged Dictionary, Second Edition (2001). It defies common sense to call experimentation that has been done once "routine."

3. The Board's Overarching Conclusion that Genentech's Research Was "Routine" Cannot Be Reconciled with Objective Evidence.

It is undisputed that the research underlying the patent was selected for and presented at the American Chemical Society's National Meeting in 2005. Hospira frames its response around the notion that a "showing of secondary considerations must be commensurate to the showing of obviousness." Hospira Br. at 51. Hospira and the Board

misapprehended the significance of the National Meeting evidence to this case.

As Learned Hand explained:

> Courts, made up of laymen as they must be, are likely either to underrate, or to overrate, the difficulties in making new and profitable discoveries in fields with which they cannot be familiar; and, so far as it is available, they had best appraise the originality involved by the circumstances which preceded, attended and succeeded the appearance of the invention.

Safety Car Heating & Lighting Co. v. Gen. Elec. Co., 155 F.2d 937, 939 (2d Cir. 1946). What succeeded the appearance of the invention here? It was chosen for presentation at the National Meeting of the American Chemical Society. As one of the meeting organizers Dr. Steven Cramer, explained, the purpose of the meeting is for the field "to learn about cutting edge developments in our field." Appx1391-1392.

Yet the Board concluded that this invention would have been the obvious result of "routine" work. That conclusion is irreconcilable with the objective evidence of what actually happened in 2005. It proves in a nutshell that the Board's rationale was infected by hindsight and should be reversed.

IV. THE RETROACTIVE APPLICATION OF INTER PARTES REVIEW IS UNCONSTITUTIONAL.

A. The Challenge Was Not Waived and, as the Government Concedes, Should Be Reached Regardless.

Genentech's failure to raise its constitutional challenge before the Board did not waive the argument in this Court. As this Court has recognized, "waiver is generally inapplicable to significant questions of general impact or of great public concern." *Amgen Inc. v. Sandoz Inc.*, 877 F.3d 1315, 1325 (Fed. Cir. 2017) (internal quotation marks omitted). The PTAB has declined to address issues of exactly this type, acknowledging that it does not "have jurisdiction to decide the constitutionality of congressional enactments." *Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-00366, 2018 WL 3326806, at *16 (July 6, 2018); *Apple, Inc. v. Realtime Data LLC*, IPR2016-01737, 2018 WL 1326656, at *19 (Mar. 13, 2018) (same).[6] And a party is not required to raise "arguments that . . . would have been futile to raise

[6] *See also Nebraska v. E.P.A.*, 331 F.3d 995, 997 (D.C. Cir. 2003) ("Agencies do not ordinarily have jurisdiction to pass on the constitutionality of federal statutes. Petitioners would have accomplished nothing if they had presented these objections to EPA." (citations and quotation marks omitted)).

before the agency," including because the agency's views "are already known" or were "recently addressed." *Wash. Ass'n for Television & Children v. F.C.C.*, 712 F.2d 677, 682 & n.9 (D.C. Cir. 1983) (collecting cases in the footnote); *see also* Harry T. Edwards & Linda A. Elliott, *Federal Standards of Review* § XI.E.4 (3d ed. 2018). As the Government's brief makes clear, the PTAB's views on this matter are well known.[7]

In any event, the Government itself invites this Court "to exercise its discretion to address the challenge here in order to avert unwarranted uncertainty regarding the constitutionality of inter partes review." Gov't Br. at 10; *id.* at 15 (recognizing "the growing number of retroactivity challenges" may indicate "that the interests of justice warrant addressing the retroactivity question quickly to avert further uncertainty regarding the constitutionality of inter partes review," and

[7] The Government relies heavily on *In re DBC*, 545 F.3d 1373, 1378-79 (Fed. Cir. 2008), but that case involved a constitutional objection to the appointment of two particular administrative law judges to hear the matter before the agency, an issue the Board "could have evaluated and corrected" by the agency including by changing the judges on the panel. *Id.* at 1379. The PTO does not have the authority to consider the retroactivity problem or to hold its congressionally mandated responsibilities unconstitutional.

that "Genentech's retroactivity challenge presents a question of law" that "would not require this Court to make factual findings" (internal quotation marks omitted)). Because this issue is fully briefed, there is no prejudice to any party to hear it, and it is a purely legal question, the Court should resolve it. *See Icon Health & Fitness, Inc. v. Strava, Inc.*, 849 F.3d 1034, 1040 (Fed. Cir. 2017).[8]

B. The AIA Unquestionably Applies Retroactively.

There is no question that the AIA applies inter partes review retroactively to pre-AIA patents. The AIA says explicitly that the inter partes review "'shall apply to any patent issued *before*, on or after' the effective date of the AIA." Gov't Br. at 16 (quoting Pub. L. No. 112-29, § 6(c)(2), 125 Stat. at 304) (emphasis added). That is the end of the analysis of whether the AIA applies retroactively; the remaining question is whether that retroactive application is constitutional.

[8] Hospira and the Government argue that Genentech elsewhere has "availed itself of the IPR process," Hospira Br. at 55 n.13, and "accepted and relied on the constitutionality" of this statute in other litigation, Gov't Br. at 16 n.2. For the reasons stated below and in its opening brief, Genentech believes that the process is unconstitutional when it is applied retroactively, but unless and until courts have so held, Genentech will exercise its rights in IPRs.

Hospira and the Government contort Supreme Court precedent to suggest otherwise, relying either (1) on the factors set forth by the Supreme Court in *Landgraf v. USI Film Products*, 511 U.S. 244, 269-70 (1994) to determine whether Congress intended a statute to apply retroactively or (2) on a test for retroactivity set out in a separate *Landgraf* opinion and rejected by the Court. Neither test applies to this case. The *Landgraf* factors do not apply where, as here, Congress has expressly answered the retroactivity question. *Id.* at 280 (statute determinative if clear). "When a statute, on its face, applies retroactively, it is unnecessary for us to rely on the factors identified by *Landgraf*[.]" *Schaeffler Grp. USA, Inc. v. United States*, 786 F.3d 1354, 1360 (Fed. Cir. 2015).

Nor does Justice Scalia's *Landgraf* concurrence advance the analysis. The Government relies on Justice Scalia's view that retroactivity should be determined by answering "what is the relevant activity that the rule regulates": activity that occurred before or after the enactment. *Id.* at 291 (Scalia, J., concurring in the judgment). Because IPR review, itself, has only been available since the AIA was enacted, the Government argues the law does not apply retroactively at

all. *See* Gov't Br. at 17-24. But the *Landgraf* majority rejected Justice Scalia's narrow definition of retroactivity, 511 U.S. at 291, in favor of a broader inquiry of whether a law "impairs vested rights acquired under existing law . . . or attaches a new disability," *id.* at 269 (majority opinion), recognizing that even changes to future procedures could have retroactive effect, *id.* at 275 n.29. That is the case here.

C. Retroactive Inter Partes Review Violates Due Process and Is an Unconstitutional Taking.

The Government and Hospira acknowledge that *Oil States Energy Services, LLC v. Greene's Energy Group, LLC*, 138 S. Ct. 1365, 1379 (2018) recognized and reserved the constitutional question. Their arguments on the merits rest on two fundamentally flawed premises: first, that Genentech did not have a valid property interest in its patent; and second, that inter partes review is not meaningfully different from reexamination.

1. The Government and Hospira argue that, because the Board cancelled the patent, Genentech never had a valid property interest in it and therefore no taking occurred. This misapprehends the law.

There is no question that patents are valid property interests for purposes of a taking and due process analysis. *See Oil States*,

138 S. Ct. at 1379; *see also Horne v. Dep't of Agric.*, 135 S. Ct. 2419, 2427 (2015). And in the years since this patent issued, Genentech has justifiably treated it as property, possessing a substantial reliance-backed interest in it. Genentech could have enforced, licensed, or assigned this patent, as it was and still is a property right. As the Government acknowledges, only after inter partes review and the resolution of any appeal will the Board issue a certificate "canceling" the patent claims. Gov't Br. at 33 (citing 35 U.S.C. § 318(b)). Even today, Genentech may still enforce the patent to exclude others.

This distinguishes this case from those cited in the Government's brief, where in each instance it was found that no property right existed at the time of government action. In *Wyatt v. United States*, 271 F.3d 1090, 1096-97 (Fed. Cir. 2001) a plaintiff's "voluntary relinquishment" of a property interest meant it did not possess a valid property interest for purposes of taking. In *CRV Enterprises, Inc. v. United States*, 626 F.3d 1241, 1250 (Fed. Cir. 2010), the takings claim accrued and ripened "before" plaintiffs' acquired the property, *i.e.*, they did not have a valid property interest at the time in question. In *Karuk Tribe of California v. Ammon*, 209 F.3d 1366, 1380 (Fed. Cir. 2000), the plaintiff

tribes never possessed a property interest in the reservation at issue. In *Rogers v. United States*, 814 F.3d 1299, 1303 (Fed. Cir. 2015), the plaintiffs had no property interest because their predecessors had transferred title and possession of their land to a railroad company. The Government's remaining cases either show that the property interest was valid or that its validity was "undisputed." *See Love Terminal Partners, L.P. v. United States*, 889 F.3d 1331, 1339 (Fed. Cir. 2018) (noting that property interest for issue before Court is "undisputed"); *Huntleigh USA Corp. v. United States*, 525 F.3d 1370, 1378 (Fed. Cir. 2008) (property interest "undisputed); *Cienega Gardens v. United States*, 331 F.3d 1319, 1329 (Fed. Cir. 2003) (plaintiffs retained valid property interest for purposes of taking claim).

Genentech is and has been the owner of this patent, with a right to enforce it. The Board's determination that the patent was improvidently issued, and its decision to *cancel* that right through inter partes review, does not change the fact that Genentech has possessed and to this day still possesses an enforceable property right.

2. As for their takings and due process arguments, Hospira and the Government contend that inter partes review is not meaningfully

different than reexamination procedures whose constitutionality has previously been upheld. But inter partes review differs in crucial ways from reexamination and other procedures that came before it. Reexamination, an "inquisitorial process for reconsidering patents," is inherently different from inter partes review, a "party-directed, adversarial process," which has "many of the usual trappings of litigation," *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1354-55 (2018), notwithstanding fewer protections than civil litigation, including a less stringent standard for proving invalidity. Nor does inter partes review allow "the kind of iterative amendment process" that existed in reexamination—IPR severely curtails possibilities for amendment. *See In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1288 (Fed. Cir. 2015) (Newman, J., dissenting). During reexamination, a patent holder engages in a dialogue with the examiner; in inter partes review, a patent owner has a single shot to respond to an adversarial challenge in very contained proceedings. *Patlex Corp. v. Mossinghoff*, 758 F.2d 594, 603 (Fed. Cir. 1985), which concerned a Fifth Amendment challenge to

the ex parte reexamination process, therefore does not foreclose this challenge to inter partes review.[9]

For the reasons stated in Genentech's opening brief, applying the AIA's inter partes review process to pre-AIA patents violates the Taking and Due Process Clauses of the Constitution.

CONCLUSION

For the foregoing reasons, Genentech respectfully requests that the Board's determination be reversed.

DECEMBER 12, 2018

Respectfully submitted,

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[9] *Joy Technologies, Inc. v. Manbeck*, 959 F.2d 226, 228 (Fed. Cir. 1992), cited by the Government and Hospira, merely incorporates *Patlex* without any analysis on these Fifth Amendment issues.

PROOF OF SERVICE

I, Paul B. Gaffney, counsel for appellant and a member of the Bar of this Court, certify that, on December 12, 2018, a copy of the attached Reply Brief of Appellant was filed with the Clerk and served on the parties through the Court's electronic filing system. I further certify that all parties required to be served have been served.

/s/ Paul B. Gaffney
PAUL B. GAFFNEY

CERTIFICATE OF COMPLIANCE WITH TYPEFACE AND WORD-COUNT LIMITATIONS

I, Paul B. Gaffney, counsel for appellant and a member of the Bar of this Court, certify, pursuant to Federal Rule of Appellate Procedure 32(a)(7)(B), that the attached Reply Brief of Appellant is proportionately spaced, has a typeface of 14 points or more, and contains 6,681 words.

/s/ Paul B. Gaffney
PAUL B. GAFFNEY

DECEMBER 12, 2018