

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

VIFOR (INTERNATIONAL) AG,
Petitioner,

v.

BIOFER S.p.A.,
Patent Owner.

IPR2022-01608
Patent 8,759,320 B2

Before ERICA A. FRANKLIN, GRACE KARAFFA OBERMANN,
and DEVON ZASTROW NEWMAN, *Administrative Patent Judges*.

OBERMANN, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Petitioner filed a Petition (Paper 1, “Pet.”) for *inter partes* review of claims 1–16, 19–21, and 23–25 of U.S. Patent No. 8,759,320 B2 (Ex. 1001, “the ’320 patent”). Patent Owner filed a Preliminary Response. Paper 9 (“Prelim. Resp.”). This Decision is based on the information presented in the Petition and the Preliminary Response.

Petitioner identifies itself and CSL Behring AG as real parties-in-interest. Pet. 1. Patent Owner identifies itself as the real party-in-interest. Paper 3, 2 (mandatory notice). The parties identify as the sole related matter a pending district court action in *Biofer, S.p.A. v. Vifor (International) AG*, Case No. 1:22-cv-02180 (E.D.N.Y., filed April 15, 2022). Pet. 1; Paper 3, 2.

II. BACKGROUND

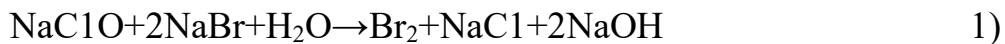
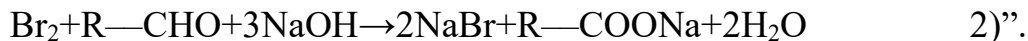
A. THE ’320 PATENT (EX. 1001)

1. Specification Overview

The ’320 patent is titled “Process for the Preparation of Trivalent Iron Complexes with Mono-, Di- and Polysaccharide Sugars.” *Id.* at code (54).¹ The claimed process relates to “the activation of” a “sugar by oxidation with nascent bromine generated in situ by reaction between an alkaline or alkaline earth bromine and an alkaline hypochlorite.” *Id.* at code (57). The activated sugar reacts with a ferric salt in solution to yield an iron-sugar complex via ultrafiltration. *Id.* The Specification states that the complex is useful for treating “functional iron deficiency in patients suffering from a renal chronic failure.” *Id.* at 1:6–15.

¹ Based on the preliminary record, for the sole purpose of deciding whether to institute review, we find that the ’320 patent has an effective filing date of March 15, 2005. Ex. 1001, code (30); Pet. 13; Prelim. Resp. 6.

In the method of the claimed invention, “[t]he bromine quantity needed for the sugar activation is produced *instant by instant* from the addition of the alkaline or alkaline earth hypochlorite, which is used in *a stoichiometric quantity* with respect to the number of end aldehydes according to the reactions:



Id. at 6:51–59 (Board’s emphasis); *see id.* at 16:44–56 (claim 1). According to the Specification, some prior art methods may hinder “a clean and complete reaction, as the hypochlorite is able to oxidize” sugars having undesirable oxidation positions, resulting in unwanted reaction products. *Id.* at 6:1–29 (describing prior art methods).

The Specification further states that “the use of bromine as an oxidizing agent” comes with disadvantages due to “its dangerousness and handling difficulty,” which “are overcome” in the claimed method by producing bromine “in situ” by “slowly introducing sodium hypochlorite” to an “aqueous solution containing an alkaline or alkaline earth bromide and the sugar.” *Id.* at 6:30–36. In addition, the Specification reports, “Surprisingly,” the claimed method produces an “absolutely clean reaction.” *Id.* at 6:60–65. The Specification indicates that sugar activation, when performed according to the method of the claimed invention, may be carried out on an industrial scale due to the ease “of handling of the reagents and the repeatability of the reaction itself. *Id.* at 6:36–43.

Critical to this Decision, claim 1 requires a “step of reacting a sugar having an aldehyde end group with bromine” carried out “in a solution *at a pH between 7.0 and 9.0*.” Ex. 1001, 16:45–46 (claim 1, the sole independent challenged claim) (Board’s emphasis). That pH range limitation is inherited by dependence in the other challenged claims. Ex. 1001, 16:57–18:29. This Decision

turns on whether Petitioner shows sufficiently, for purposes of institution, that the prior art would have suggested the method of the claimed invention and, in particular, the limitation that the reaction must occur in the specified pH range.

2. Relevant Prosecution History

During patent prosecution, the Examiner asserted obvious rejections based on prior art references that included Besemer I² and Besemer II³. Ex. 1004, 283–292.⁴ Regarding the pH range limitation of claim 1, the Examiner relied on Besemer I’s disclosure that the oxidation reaction of the aldehyde of the sugar in solution with sodium hypochlorite “in general can be carried out at a pH of 7–11,” a range that fully encompasses the specified range of between 7.0 and 9.0. Prelim. Resp. 6–7; Ex. 1004, 219. Although Besemer II does “not expressly teach” that the reaction occurs at a pH “between 7 and 9” as required by claim 1, the Examiner reasoned that its disclosure nonetheless suggests that range. Ex. 1004, 287–288.

In response to a Final Office Action, the applicant (Patent Owner) submitted the Declaration of Mr. Egidio Marchi, a co-inventor of the ’320 patent, which advances an opinion, supported by experimental data, that the reaction conditions, including the specified pH range of between 7.0 and 9.0, are critical to the method of the claimed invention. *Id.* at 432–440 (“the Marchi Declaration”); *see* Ex. 1001, code (75) (named inventors). Specifically, the Marchi Declaration indicates that

² U.S. Patent No. 5,326,864, issued July 5, 1994 (Ex. 1011). We follow the parties’ convention and refer to this reference as Besemer I.

³ Arie C. Besemer et al., *Dicarboxy-Starch by Sodium Hypochlorite/Bromide Oxidation and Its Calcium Binding Properties*, 45 STARK 95 (1994) (Ex. 1012). We follow the parties’ convention and refer to this reference as Besemer II. *See, e.g.*, Pet. ix, 14; Prelim. Resp. 7–11.

⁴ Throughout this Decision, we refer to page numbers added by Petitioner.

undesirable “side reactions” result in the “destruction of the main chain” of the sugar when the claimed method “takes place at pH 10,” however, when performed at pH 8, “successful suppression of degrading side reactions” is accomplished and “high selectivity” is achieved. Ex. 1004, 379, 432–440

On the strength of the Marchi Declaration, the applicant successfully argued to the Examiner that the claimed pH range of 7.0 to 9.0 is critical to the claimed process such that the specified pH range is non-obvious over the pH ranges disclosed or suggested in Besemer I and Besemer II. *Id.* at 379, 429–430. The Examiner allowed the claims specifically because the results reported in the Marchi Declaration “show the criticality of the conditions used in the instant process,” including the specified pH range of 7.0 to 9.0. *Id.* at 459-460.

B. CHALLENGED CLAIMS

The Petition challenges claims 1–16, 19–21, and 23–25 of the ’320 patent. Claim 1, reproduced below, is the only independent claim challenged.

1. A process for the preparation of an activated sugar comprising the step of reacting a sugar having an aldehyde end group with bromine in a solution ***at a pH between 7.0 and 9.0*** with the specific oxidation of the end aldehyde, wherein:

i) said sugar is selected from the group consisting of dextrans and dextrans and wherein

ii) said bromine is produced in situ through the addition of hypochlorite and an alkaline or earth alkaline metal bromide to said solution, said hypochlorite being added in stoichiometric quantities with respect to the aldehyde end groups, wherein said hypochlorite is added instant by instant, such that an excess of hypochlorite in solution is never present.

Ex. 1001, 16:44–56 (Board’s emphasis). The other challenged claims depend directly or indirectly from claim 1. *Id.* at 16:57–18:29.

C. ASSERTED GROUNDS OF UNPATENTABILITY

The Petition advances three grounds of unpatentability based on anticipation under 35 U.S.C. § 102 or obviousness under § 103.⁵ We provide below a chart that sets forth the grounds identified in the Petition.

Ground	35 U.S.C. §	Claims Challenged	Reference(s)/Basis
1	103	1–13, 19–21, 23, 25	Geisser ⁶ , Stoll ⁷
2	103	14–16, 24	Geisser, Stoll, Usher ⁸
3	102	1–7, 9–13, 19–21, 23, 25	Geisser

Pet. 3. The Petition is supported by the Declaration of Dr. Jeffrey D. Winkler (Ex. 1002). Patent Owner does not advance a declaration prepared specifically for this proceeding, however, in the Preliminary Response, Patent Owner relies on the Marchi Declaration, which was sufficient to persuade the Examiner to issue the claims during patent prosecution. Ex. 1004, 432–440.

III. ANALYSIS

A. LEVEL OF ORDINARY SKILL IN THE ART

The level of ordinary skill in the art at the time of the invention is a factual determination that provides a primary guarantee of objectivity in an obviousness

⁵ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112–29, 125 Stat. 284 (Sept. 16, 2011), includes revisions to Sections 102 and 103 that became effective on March 16, 2013. Because the challenged claims issued from an application filed before March 16, 2013, we apply pre-AIA law. *See* Ex. 1001, code (30); *see also supra* 2 n.1. Neither party, however, indicates that the result would change based on which version of the statute is applied.

⁶ WO 2004/037865 A1, published May 6, 2004 (Ex. 1006) (certified translation).

⁷ U.S. Patent No. 1,548,368, issued Nov. 8, 1927 (Ex. 1007).

⁸ CA 2,195,283, published July 16, 1998 (Ex. 1008).

analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1324 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Petitioner proposes that an ordinarily skilled artisan “would hold an advanced degree, such as an M.S. or doctorate, in chemistry, medicine, pharmacy, or a related degree,” as well as post-graduate experience “in areas of carbohydrate chemistry, synthetic chemistry, medicinal chemistry, inorganic chemistry, and/or metal carbohydrate complexes, or the clinical use of such complexes.” Pet. 16. Patent Owner does not contest Petitioner’s proposed definition in the Preliminary Response. Prelim. Resp. 17–18.

Based on the information presented, we find that the asserted prior art itself is sufficient to demonstrate the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (prior art itself can reflect the appropriate level of ordinary skill in the art). To the extent a more precise definition is required, we apply Petitioner’s unopposed proposed definition for purposes of determining whether to institute review because it is consistent with the disclosures of the asserted prior art references.

B. CLAIM CONSTRUCTION

In an *inter partes* review, the Board construes the terms of a patent claim “in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” 37 C.F.R. § 42.100(b). Under that standard, claim terms generally are given their plain and ordinary meaning as would have been understood by the ordinarily skilled artisan at the time of the invention and within the context of the entire patent disclosure. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). We construe terms in controversy only to the extent necessary to

resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

Petitioner proposes an express construction for one claim term, namely, the phrase “hypochlorite is added instant by instant,” arguing that this “refers to slow addition of hypochlorite.” Pet. 16–17 (citing Ex. 1002 ¶ 36). For the limited purposes of deciding whether to institute review, Patent Owner does not contest Petitioner’s construction or propose any constructions of its own. Prelim. Resp. 17. This Decision turns on the sufficiency of Petitioner’s showing as to the obviousness of a process that occurs “at a pH between 7.0 and 9.0.” Ex. 1001, 16:46. Under these circumstances, no express claim construction of the instant-by-instant limitation or any other claim term is necessary to this Decision.

C. THE PATENTABILITY CHALLENGES

1. Ground Based on Obviousness over Geisser and Stoll

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). In this section, we apply that standard to assess whether Petitioner shows sufficiently, for purposes of institution, that the subject matter of claims 1–13, 19–21, 23, and 25 would have been obvious over the combined disclosures of Geisser and Stoll. Pet. 35–57.

a. *Geisser*

Geisser is titled “Water-Soluble Iron-Carbohydrate Complexes, Their Production and Pharmaceuticals Containing These.” Ex. 1006, 1 (code (54)). Geisser relates to the production of water-soluble iron carbohydrate complexes that

“are obtainable from an aqueous solution of an iron (III) salt and an aqueous solution of the oxidation product of one or more maltodextrins.” *Id.* at 3:1–11. Geisser is concerned with water-soluble iron carbohydrate complexes useful for treating iron-deficiency anemia. *Id.* at 2:7–13. Petitioner directs us to information that Geisser discloses the oxidation of maltodextrin in a solution of hypochlorite at a pH range between 8 and 12. Pet. 39; *see* Ex. 1006, 3:3–7.

b. Stoll

Stoll is titled “Process for the Oxidation of Aldoses.” Stoll activates sugars, but does not mention the specific sugars—dextrins and dextrans—that are specified in claim 1. Ex. 1007, 1; *see* Ex. 1001, 16:48–49 (claim 1). Petitioner asserts Stoll to establish that the ordinarily skilled artisan would have understood the benefits of performing a slow addition, when combining strong oxidants, such as sodium hypochlorite, with sugar molecules. Pet. 25–26. In other words, Stoll is asserted in combination with Geisser to make out the obviousness of the limitation of claim 1 that specifies addition “instant by instant, such that an excess of hypochlorite in solution is never present.” *Id.* at 27. Petitioner also points out that, similar to Geisser, “Stoll describes oxidation of aldoses in ‘alkaline’ solutions,” that is, solutions having “a pH greater than 7.” *Id.* at 39; *see id.* at 29–30 and n.7 (citing Ex. 1002 ¶ 81 (Winkler Declaration)), 39.

c. The pH Range Limitation of Claim 1

Claim 1, and by dependence each other challenged claim, requires that the step of reacting a sugar with bromine occurs “in a solution at a pH between 7.0 and 9.0.” Ex. 1001, 16:46–47. A dispositive question arises, on this record, as to whether Petitioner’s information, directed to this pH range limitation, is sufficient to support institution of review. For reasons that follow, we determine that Petitioner’s information is not sufficient and deny the Petition on that basis.

We agree with Petitioner that Geisser discloses a pH range of between 8 and 12 and that Stoll suggests a pH range of 7 or greater. Pet. 29–30 and n.7, 39. Those prior art pH ranges overlap or encompass the specified pH range of “between 7.0 and 9.0.” Pet. 38–39 and n.10. Under these circumstances, the burden of production shifts to Patent Owner to come forward with evidence of the criticality of the specified pH range limitation. *See id.* at 39–40 (quoting *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1008 (Fed. Cir. 2018)).

Patent Owner meets that burden by directing us to the Marchi Declaration. Resp. 9–12; Ex. 1004, 432–440. That evidence contains experimental results that support Dr. Marchi’s opinion that the claimed method, when performed at a pH of 8, “can be run with equimolar amounts of oxidant without increasing depolymerization,” but when performed at a pH of 10, results in an undesirable “depolymerizing attack on the main chain, even employing only 0.9 equivalents of oxidant.” Ex. 1004, 434–435 (¶ 7). As Patent Owner points out, moreover, the oxidation reaction in each of the examples in Geisser is carried out at a pH of 10. *see* Prelim. Resp. 26 and n.8 (citing Ex. 1006, Examples 1–8).

The Marchi Declaration includes comparative experimental results, including chromatograms that compare light and heavy molecular-weight fractions in the reaction products of the experimental examples, which support Dr. Marchi’s opinion that “the lion’s share of” depolymerizing attack on the main chain occurs when the reaction is performed at pH 10, whereas the main chain is retained “almost entirely intact” when run at pH 8. Ex. 1004, 435 (¶ 6); *see* Prelim. Resp. 10–11 (quoting Ex. 1004, 429–430 (arguments presented during prosecution pertaining to the data set forth in the chromatograms, including information tending to support the view that, “outside the claimed [pH] range, even application of somewhat ‘under-stoichiometric’ reaction conditions” are “not effective in

preventing destructive attack” on the main sugar chain)). Petitioner does not challenge those experimental results or attempt to show how or why they reflect a difference in degree and not in kind. *See generally*, Pet.; *see especially id.* at 15, 40, 52, 68–69 (Petitioner’s arguments pertaining to the Marchi Declaration).

The Examiner allowed the claims to issue on the strength of the Marchi Declaration, finding that this evidence “show[s] the criticality of the conditions used in the instant process,” including the specified pH range of 7.0 to 9.0. *Id.* at 459-460 (allowance of claims); *see* Prelim. Resp. 10–13 (citing prosecution history). As even Petitioner acknowledges, the Examiner found that “the Marchi Declaration ‘show[s] the criticality of the conditions’ and ‘is seen to overcome the obviousness rejection of record.’” Pet. 15 (citing Ex. 1004, 451–461).

In a nutshell, the Examiner viewed the Marchi Declaration as sufficient to establish the criticality of the pH range specified in claim 1, and so do we based on the information presented in the Petition and the Preliminary Response. Petitioner does not explain adequately why we should reach a different result based on the facts at hand. Critically, Petitioner directs us to no evidence tending to undercut the opinions or experimental results reported in the Marchi Declaration, or that any experimental variable aside from the pH range accounts for the observed increase in efficiency of the experimental process. *See generally* Petition.

On that point, Petitioner does no more than point out that the ranges of Geisser and Stoll overlap or fully encompass the pH range specified in claim 1. *See* Pet. 15, 40, 52, 68–69. Petitioner ignores that Besemer I and Besemer II, which were before the Examiner, similarly disclosed or suggested pH ranges that overlap or fully encompass the claimed range. *See* Ex. 1004, 219, 287–288 (prosecution history). Petitioner’s only attempt to overcome the Marchi Declaration is to argue that Geisser, by virtue of its disclosure of a pH range between 8 and 12, “expressly

discloses the same pH level used by Dr. Marchi,” namely, a “pH of 8.” *Id.* at 40. That argument does not account adequately for the fact that Geisser, like Besemer I and Besemer II, discloses a pH *range* that includes 8, not a pH *value* of 8. The Marchi Declaration supports Patent Owner’s view that the *value* of pH 8 within the range is, in fact, critical to obtain optimal results from the claimed process.

As Patent Owner observes, all of the examples in Geisser are carried out at a pH of 10, the very pH value that, according to Dr. Marchi, produces undesirable results. Prelim. Resp. 26 and n.8 (citing Ex. 1006, Examples 1–8). Petitioner directs us to no particular pH values in Stoll, but relies exclusively on the reference’s disclosure that the reaction takes place in alkaline conditions. Pet. 29–30 and n.7 (citing Ex. 1002 ¶ 81 (Winkler Declaration)), 39. Under these circumstances, Patent Owner’s evidence, in the form of the Marchi Declaration, shows that a pH of 8 is critical over a pH of 10 and that claim 1 is non-obvious over the combined disclosures of Geisser and Stoll.

Petitioner did not seek authorization to file a reply to the Preliminary Response; therefore, the arguments raised by Patent Owner about the Marchi Declaration stand uncontested on this record. Against that backdrop, based on the information presented in the Petition and the Preliminary Response, we determine that the Marchi Declaration supports Patent Owner’s view that the specified pH range is “critical” and, when combined with the other conditions set forth in claim 1, produces clean and complete oxidation of the aldehyde end groups of the sugar by the hypochlorite as compared to the prior art. Ex. 1004, 435 (the Marchi Declaration, ¶ 7); *see generally id.* at 432–440 (the entirety of the Marchi Declaration); *compare* Ex. 1001, 6:21–24, 6:60–65 (Specification of the ’320 patent, explaining that, as compared to reaction conditions disclosed in the prior

art, the reaction conditions of the claimed invention “[s]urprisingly” produce “clean and complete” oxidation of the aldehyde end groups).

Accordingly, because Petitioner does not show sufficiently that the specified pH range would have been obvious over the combined disclosures of Geisser and Stoll, Petitioner fails to establish “a reasonable likelihood” of prevailing with respect to claim 1 based on this ground. 35 U.S.C. § 314(a). Our reasoning applies with equal force to the other claims challenged in this ground, because each inherits the pH limitation of claim 1 through direct or indirect dependence.

2. Petitioner’s Other Asserted Grounds of Unpatentability

The Petition sets forth two additional grounds of unpatentability. Pet. 57–63 (asserting obviousness over Geisser, Stoll, and Usher), 63–69 (asserting anticipation by Geisser). The ground that asserts Usher rests on the same arguments that Geisser and Stoll, taken together, would have suggested to an ordinarily skilled artisan the pH limitation of claim 1. *Id.* at 57. Usher is advanced for the sole purpose of establishing certain ultrafiltration or stability features of dependent claims. *Id.* at 57–63. Petitioner does not identify in Usher a disclosure that cures the deficiency in Petitioner’s evidence regarding the pH range limitation. Thus, our reasoning above applies with equal force to this obviousness ground.

We assess the ground based on anticipation by Geisser in view of the principle that a prior art reference anticipates a patent claim “if it discloses every claim limitation.” *In re Montgomery*, 677 F.3d 1375, 1379 (Fed. Cir. 2012). The ground based on anticipation by Geisser rests on a conclusory opinion that Geisser’s disclosure of a pH range between 8 and 12 “describes” an oxidation reaction that occurs “at a pH between 7.0 and 9.0.” Pet. 63 (citing Ex. 1002 ¶ 178, which repeats that conclusory opinion *verbatim* without objective evidence or

analysis). It is unclear on this record, and Petitioner does not explain adequately, how or why Geisser anticipates the pH range limitation of claim 1, which is “critical” for reasons explained above in our analysis of the ground based on obviousness over Geisser and Stoll. Ex. 1004, 435 (the Marchi Declaration, ¶ 7).

Accordingly, on this record, we determine that Petitioner does not establish a reasonable likelihood of prevailing “with respect to at least [one] of the claims” based on any ground asserted in the Petition. 35 U.S.C. § 314(a).

3. Patent Owner’s Request for Discretionary Denial

In view of our determination that Petitioner does not meet the threshold evidentiary showing necessary to support institution of review, we need not, and do not, resolve Patent Owner’s alternative request that we exercise our discretion to deny the Petition. *See* Prelim. Resp. 18–36. Although resolution of that request is not necessary to this Decision, we take note that Patent Owner’s arguments are not insubstantial. *See id.* (Patent Owner’s extensive arguments that discretionary denial is appropriate pursuant to 35 U.S.C. § 325(d) based on the considerations set forth in *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 (PTAB Feb. 13, 2020) (precedential) or pursuant to 35 U.S.C. § 314(a) based on the factors set forth in *Apple, Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 (PTAB Mar. 20, 2020) (precedential)).

IV. CONCLUSION

For the above reasons, we *deny* the Petition and do not institute an *inter partes* review.

V. ORDER

It is

ORDERED that the Petition is denied and no *inter partes* review is instituted.

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