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Paper 27
Date: February 23, 2022

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FRESENIUS KABI USA, LLC, and
FRESENIUS KABI SWISSBIOSIM GMBH
Petitioners,

v.

CHUGAI SEIYAKU KABUSHIKI KAISHA and
HOFFMANN-LA ROCHE INC.,
Patent Owners.

IPR2021-01336
Patent 10,874,677 B2

Before ERICA A. FRANKLIN, JOHN G. NEW, and ZHENYU YANG, *Administrative Patent Judges.*

FRANKLIN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Fresenius Kabi USA, LLC, Fresenius Kabi SwissBioSim GmbH. ("Petitioners") filed a Petition requesting*inter partes* review of claim 1 of U.S. Patent No. 10,874,677 B2 (Ex. 1006, "the '677 patent"). Paper 3 ("Petition" or "Pet."). Chugai Seiyaku Kabushiki Kaisha, Inc. and Hoffmann-La Roche Inc. ("Patent Owners") filed a Preliminary Response to the Petition. Paper 8 ("Prelim. Resp."). With our authorization, Ex. 3001, Petitioners filed a Reply to the Preliminary Response. Paper 13 ("Pet. Reply). Patent Owners filed a Sur-reply in response. Paper 23 ("PO Sur-reply").

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314 (2018). Upon considering the parties' arguments and evidence, we determine that Petitioners have demonstrated a reasonable likelihood that they would prevail in showing the unpatentability of the one claim challenged in the Petition. Accordingly, we institute an *inter partes* review.

A. Real Parties-in-Interest

Petitioners identify the real parties-in-interest as Fresenius Kabi USA, LLC, Fresenius Kabi SwissBioSim GmbH, Fresenius Kabi AG, Fresenius Kabi Pharmaceuticals Holding, Inc., Fresenius Kabi Deutschland GmbH and Fresenius SE & Co. KGaA. Pet. 6. Patent Owners identify themselves as the real party-in-interest, noting that Chugai Seiyaku Kabushiki Kaisha, Inc. is also called Chugai Pharmaceutical Co., Ltd. Paper 5, 1. Patent Owners further identify Genentech, Inc., as a real party-in-interest. *Id.*

B. Related Matters

Petitioners assert that the '677 patent is not currently the subject of any litigation or post-grant proceedings. Pet. 4. Petitioners note that they are seeking *inter partes* review of US Patent No. 5, 580,264 ("the '264 patent"). *Id.*; *see* IPR2021-01288, Paper 3 (petition seeking *inter partes* review of the '264 patent). The '677 patent claims priority to the application that issued as the '264 patent. Pet. 4.

Patent Owners identify a number of patent applications and issued patents that relate to US Patent Application No. 16/254,105, which issued as the '677 patent. Paper 5, 1–2. Patent Owners also note that the '264 patent is the subject of IPR2021-01288. *Id.* at 2.

C. The '677 Patent

In one aspect, the '677 patent relates to methods for treating interleukin-6 (IL-6) related diseases, such as rheumatoid arthritis (also referred to as "RA"), with subcutaneously administered antibody that binds interleukin-6 receptor (anti-IL-6R antibody). Ex. 1006, 1:29–35. The '677 patent also relates to "devices useful for subcutaneous administration of an anti-IL-6R antibody." *Id.* at 1:39–40, 4:65–5:3.

IL-6 is a "proinflammatory, multifunctional cytokine produced by a variety of cell types," and "exerts it s effects through a ligand-specific receptor (IL-6R) present both in soluble and membrane-expressed forms." *Id.* at 2:1–2, 16–18. It has been known in the art that "[e]levated IL-6 levels have been reported in the serum and synovial fluid of RA patients, indicative of production of IL-6 by the synovium." *Id.* at 2:19–21. It is also known in the art that "IL-6 levels correlate with disease activity in RA . . . and clinical efficacy is accompanied by a reduction in serum IL-6 levels." *Id.* at 2:23–25.

Tocilizumab (also referred to as "TCZ") is a recombinant humanized monoclonal antibody of the immunoglobulin IgG1 subclass which binds to human IL-6R." *Id.* at 2:27–29. Tocilizumab has been approved for use in treating a number of diseases, including rheumatoid arthritis and juvenile idiopathic arthritis. *See id.* at 2:34–43. In one aspect, the '677 patent relates to identification of a fixed dose of anti-IL-6R antibody such as tocilizumab. *Id.* at 1:35–36.

D. Challenged Claims

Petitioners challenge claims 1–8 in the '677 patent. Claims 1 and 5, the independent claims, are illustrative and set forth below.

> 1. An article of manufacture comprising a subcutaneous administration device, which contains and delivers to a patient a 162 mg fixed dose of tocilizumab.
>
> 5. An article of manufacture comprising a subcutaneous administration device, which contains and delivers to a patient a 162 mg fixed dose of an anti-IL-6R antibody, wherein the anti-IL-6R antibody comprises the light chain and heavy chain amino acid sequences of SEQ ID Nos: 1 and 2, respectively.

Ex. 1006, 63:45–47, 63:57–64:47.

E. Asserted Grounds of Unpatentability

Petitioners assert that the challenged claims are unpatentable on the following five grounds:

Claims Challenged	35 U.S.C. §[1]	Reference(s)
1, 5	102	NCT00965653[2]
1–8	103(a)	NCT00965653 and Kivitz[3]
1, 5	102	Georgy[4]
1–8	103(a)	Georgy and Kivitz
1–8	103(a)	Maini 2006,[5] Kivitz, Bonilla,[6] and Wang[7]

[1] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112–29, 125 Stat. 284 (2011), amended 35 U.S.C. §§ 102 and 103, effective March 16, 2013. Because the application from which the '677 patent issued has an effective filing date prior to March 16, 2013, the pre-AIA version of §§ 102 and 103 applies.

[2] ClinicalTrials.gov, *A Study of Subcutaneously Administered Tocilizumab in Patients with Rheumatoid Arthritis*, NCT00965653, available at https://clinicaltrials.gov/ct2/show/NCT00965653 (first posted August 21, 2009) (Ex. 1038) (last update posted Nov. 2, 2016) (Ex. 1028), (collectively, "NCT00965653").

[3] Kivitz et al., *HUMIRA® Pen: a novel autoinjection device for sub-cutaneous injection of the fully human monoclonal antibody adalimumab*, EXPERT REV. MED. DEVICES 4(2):109–16 (2007) (Ex. 1070, "Kivitz").

[4] Georgy et al., *A Clinical Study to Assess the Pharmacokinetics and Pharmacodynamics of Tocilizumab After a Single Dose of Administration by Subcutaneous and Intravenous Routs to Healthy Subjects*, CLINICAL PHARM. & THERAPEUTICS 87 Supp. 1 (2010) (Ex. 1044, "Georgy").

[5] Maini et al., *Double-Blind Randomized Controlled Clinical Trial of the Interleukin-6 Receptor Antagonist, Tocilizumab, in European Patients with Rheumatoid Arthritis Who Had an Incomplete Response to Methotrexate*, ARTHRITIS & RHEUMATISM 54(9) 2817–29 (2006) (Ex. 1025, "Maini 2006").

[6] Bonilla, *Pharmacokinetics of Immunoglobulin Administered via Intravenous or Subcutaneous Routes*, 28 IMMUN. AND ALLERGY CLINICS OF NORTH AMERICA 803–19 (2008) (Ex. 1021, "Bonilla").

[7] Wang et al., *Fixed Dosing Versus Body Size-Based Dosing of Monoclonal Antibodies in Adult Clinical Trials*, 49 J. CLIN. PHARM. 1012–24 (2009) (Ex. 1022, "Wang").

Petitioners also rely upon the Declarations of Thomas M. Zizic, M.D. (Ex. 1002) and Howard L. Levine, Ph.D. (Ex. 1003). Petitioners rely on the Declaration of Robert Paarlberg (Ex. 1004) to support contentions regarding the prior art status of NCT00965653. Patent Owners rely on the Declarations of Kimio Terao (Ex. 2005), Masayuki Nishiyama (Ex. 2006), and Amy Zhang (Ex. 2007) to support contentions regarding reduction to practice.

II. ANALYSIS

A. Person of Ordinary Skill in the Art

The level of skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1323 (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)).

Petitioners assert that a person of ordinary skill in the art at the time of the invention (also referred to as "POSA") "would have had been an individual with an M.D. specializing in the treatment of autoimmune disorders and having several years of experience treating patients with such disorders, including rheumatoid arthritis, or having several years of experience researching treatments for autoimmune disorders, including rheumatoid arthritis." Pet. 19 (citing Ex. 1002 ¶ 34). At this stage in the proceeding, Patent Owners do not dispute Petitioners' definition of the person of ordinary skill in the art. Prelim. Resp. 16 n.4.

Because Petitioners' uncontested definition of one of ordinary skill in the art is reasonable and consistent with the '677 patent and the cited art, we adopt Petitioners' definition for purposes of this Decision.

B. Claim Construction

The Board applies the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 100(b) (2019). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). "In determining the meaning of the disputed claim limitation, we look principally to the intrinsic evidence of record, examining the claim language itself, the written description, and the prosecution history, if in evidence." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 469 F.3d 1005, 1014 (Fed. Cir. 2006) (citing *Phillips*, 415 F.3d at 1312–17).

Petitioners propose constructions for two claim terms. *See* Pet. 20–21. In the following discussion, we address those proposed constructions, along with Patent Owners' proposed construction for an additional claim term. *See* Prelim. Resp. 16–17.

1. "fixed dose"

Petitioners address the term "fixed dose" by asserting that the term is defined in the Specification as "a dosage of a drug, such as an anti-IL-6R antibody which is administered without regard to the patient's weight or body surface area (BSE), i.e., it is not administered as either a mg/kg or mg/m2 dose." Pet. 20 (quoting Ex. 1006, 15:15–18). Patent Owners assert that it agrees with Petitioners' proposed construction for the term. Prelim. Resp. 16. Because the term "fixed dose" is defined by the Specification and is not disputed by the parties, we determine, based on the current record, that the term requires no further construction.

2. "subcutaneous administration device"

Petitioners address the term "subcutaneous administration device" by asserting that the term is defined in the Specification as "a device, such as syringe, injection device, infusion pump, injector pen, needleness device, patch delivery system, etc, which is adapted or designed to administer a drug or pharmaceutical formulation by the subcutaneous route." Pet. 20 (quoting Ex. 1006, 20:7–11). Patent Owners assert that it agrees with Petitioners' proposed construction for the term. Prelim. Resp. 16. Because the term "subcutaneous administration device" is defined by the Specification and is not disputed by the parties, we determine, based on the current record, that the term requires no further construction.

3. "patient"

Patent Owners assert that the claim term "patient" should be construed to mean "a patient with an IL-6 mediated disorder." Prelim. Resp. 16. In support of that proposed construction, Patent Owners cite to the Specification references to patients with IL-6 mediated disorders. *Id.* at 16–17 (citing Ex. 1006, 1:35–38; 14:30–32; 25:21–26; 25:27–57; 29:19–34).

Petitioners assert that Patent Owners misconstrue the term "patient." Pet. Reply 10. Petitioners contend that because the claims are directed to a device and not a method of treatment, the recitation that the device "delivers to a patient" is merely an intended use. *Id.* at 9. According to Petitioners, "the claims cover a device that contains the recited dose of the drug, regardless of whether used for delivering the drug to a 'patient.'" *Id.* at 10. Further, Petitioners assert that the Specification makes clear that the term "patient" is not limited to one with an IL-6 mediated disorder, as the Specification refers also to prophylactic treatment, i.e., for patients that do not have an IL-6 mediated disorder. *Id.* (citing Ex. 1006, 15:19–20).

Patent Owners disagree with Petitioners by asserting that "[u]nless the claimed article of manufacture is used to deliver a 162 mg fixed dose of tocilizumab to a patient—that is, a patient with an IL-6 mediated disorder—creation of the device would be 'merely an academic exercise[]." PO Sur-reply 9 (quoting *Griffin v. Bertina*, 285 F.3d 1029, 1033 (Fed. Cir. 2002). Further, Patent Owners assert that the Specification uses the term "a subject" instead of "a patient" when referring to "therapeutic treatment" and "prophylactic or preventative measures." *Id.* at 9–10 (citing Ex. 1006, 15:19–20). Patent Owners reiterate its contention that when discussing the treatment of "a patient," the Specification "ties that term to therapeutic treatment of an individual suffering form an IL-6 mediated disorder." *Id.* at 10 (citing Prelim. Resp. 16–17).

Based on our review of the Specification and consideration of the arguments and the evidence, we find that Petitioners have the better position. As Petitioners assert, the claims are directed to a device and not to a method of treatment. The claim recitation that the device contains and delivers to a patient the recited fixed dosage of tocilizumab is achieved by the structure of the device, and not by the patient status of the individual for whom the device is intended.

Additionally, we do not find that Patent Owners have demonstrated that the Specification limits the term "patient" to individuals with IL-6 mediated disorders. Rather, the references to "patient" in the Specification, cited by Patent Owners, demonstrate that the term is used broadly and then modified in some instances to refer to a specific type of patient, e.g., "[a] patient with 'active rheumatoid arthritis'" (Ex. 1006, 14:30) or "an IL-6-mediated disorder in a patient" (*id.* at 25:22). The challenged claims,

however, do not include any such modifying phrases to limit the scope of the term "patient." Nor do the claims recite an IL-6 mediated disorder.

Further, we find that the Specification uses the term "patient" and "subject" interchangeably. For example, the Specification refers to "[t]he *subject* who is a 'TNF inhibitor inadequate responder' has experienced an inadequate response to previous or current treatment with one or more TNF inhibitors," and thereafter immediately refers to that subject by explaining that "such patient has received, for example, etanercept." Ex. 1006, 15:1–5. Thus, we do not find that the Specification supports Patent Owners' assertion that the Specification only uses the term "patient" when it discusses treatment. *See* PO Sur-reply 9–10.

Accordingly, at this stage in the proceeding, we preliminarily construe "patient" to include any individual for whom delivery of the recited 162 mg fixed dose of tocilizumab by the subcutaneous administration device is intended.

C. Anticipation by NCT0965653

Petitioners assert that claims 1 and 5 are anticipated by NCT00965653. Pet. 21–30. Patent Owners disagree. Prelim. Resp. 17–32.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Schering Corp. v. Geneva Pharms*, 339 F.3d 1373, 1379 (Fed. Cir. 2003) (quoting *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987)).

1. NCT00965653

NCT00965653 is a clinic trial study, entitled "A Study of Subcutaneously Administered Tocilizumab in Patients with Rheumatoid Arthritis." Ex. 1028, 1; Ex. 1038, 1. The summary states, "This open-label

randomized [2 arm] study will investigate the pharmacokinetics, pharmacodynamics, efficacy and safety of subcutaneously administered tocilizumab in patients with rheumatoid arthritis who have shown an inadequate response to methotrexate." Ex. 1028, 2; Ex. 1038, 3–4. The summary explains further that "[p]atients will be randomized to receive tocilizumab 162 mg sc [subcutaneously] either weekly or every other week, in combination with methotrexate, for 12 weeks." Ex. 1028, 2; Ex. 1038, 4.

2. Discussion

Petitioners identify the disclosures in NCT00965653 that Petitioners assert disclose each limitation of claims 1 and 5. Pet. 26–30. Specifically, Petitioners relies on the NCT00965653 protocol which involves administering to a patient 162 mg of tocilizumab subcutaneously. *Id.* According to Petitioners, a POSA would have understood that NCT00965653 implicitly discloses a device for administering the subcutaneous dose, as one must necessarily use a "subcutaneous administration device" to administer tocilizumab subcutaneously. *Id.* at 26 (citing *In re Baxter Traven Labs*, 952 F.2d 388, 390 (Fed. Cir. 1991).

Additionally, Petitioners assert that the Specification describes tocilizumab as an anti-IL-6 receptor antibody and contend that it inherently comprises the recited light chain and heavy chain amino acid sequences of SEQ ID. Nos. 1 and 2, respectively, as further required for claim 5. *Id.* at 27–30.

Based upon our review and consideration of the current record, we determine that Petitioners have demonstrated a reasonable likelihood of prevailing in showing that each and every limitation in claims 1 and 5 is disclosed expressly or inherently by protocol set forth in NCT00965653.

In reaching our determination that Petitioners have demonstrated a reasonable likelihood of prevailing in it challenge of claims 1 and 5, we considered Patent Owners' arguments, which we address in the following discussion.

Patent Owners argue that NCT00965653 does not anticipate the challenged claims for two alleged reasons: (a) NCT00965653 is not prior art, Prelim. Resp. 17–25; and (b) NCT00965653 does not enable the POSA to make the claimed article of manufacture, *id.* at 25–32. We address each of those contentions in the following discussion and explain why we find them unsupported based on the current record.

a) Prior Art Status of NCT00965653

Petitioner has the burden to prove NCT00965653 qualifies as prior art under 35 U.S.C. § 102. *See In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1376 (Fed. Cir. 2016). "[A]t the institution stage, the petition must identify, with particularity, evidence sufficient to establish a reasonable likelihood that the reference was publicly accessible before the critical date of the challenged patent and therefore that there is a reasonable likelihood that it qualifies as a printed publication." *Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29 ("*Hulu*") at 13 (PTAB Dec. 20, 2019) (precedential).

"Public accessibility" is considered to be "the touchstone in determining whether a reference constitutes a 'printed publication' bar under 35 U.S.C. §102(b)." *In re Hall*, 781 F.2d 897, 899 (Fed. Cir. 1986). "A given reference is 'publicly accessible' upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it." *SRI Int'l, Inc. v. Internet*

Sec. Sys., Inc., 511 F.3d 1186, 1194 (Fed. Cir. 2008) (quoting *Bruckelmyer v. Ground Heaters, Inc.*, 445 F.3d 1374, 1378 (Fed. Cir. 2006)).

A determination whether a particular reference qualifies as a printed publication "is a legal determination based on underlying fact issues, and therefore must be approached on a case-by-case basis." *Hall*, 781 F.2d at 899. In a proceeding before the Board, there is no presumption in favor of finding that a reference is a printed publication. *Hulu*, 16.

Petitioners assert that NCT00965653 is a prior art printed publication, which was "publicly available on ClinicalTrials.gov prior to November 2009, or more than one year before the earliest claimed priority date of the '677 patent." Pet. 21, 23. To support that contention, Petitioners rely on the declaration of Mr. Paarlberg[8] to assert background information regarding the ClinicalTrials.gov website. According to Petitioners and Mr. Paarlberg, pursuant to the FDA Modernization Act, The National Library of Medicine, under the National Institutes of Health ("NIH"), launched ClinicalTrials.gov in February 2000 to provide the public with access to information on clinical studies conducted in the United States for drugs for serious or life-threatening diseases and conditions. *Id.* at 23–24 (citing Ex. 1004 ¶¶ 12–13). Petitioners quote a press release from the NIH explaining that the database published on ClinicalTrials.gov "is intended to provide 'patients, families and members of the public ***easy access to information***.'" *Id.* at 24 (quoting Ex. 1029, 1) (emphasis added by Petitioners).

Petitioners assert also that "[t]he FDA Amendments Act of 2007 later expanded the database by requiring additional submission information,

[8] Mr. Paarlberg is the founder of and a principal at "a consultancy specializing in regulatory policy, regulatory intelligence, and global clinical trial disclosure strategy and operations." Ex. 1004 ¶ 3.

mandating searchable categories in the database, and imposing a fine for failure to submit information within 21 days of first patient enrollment" in a trial. *Id.* (citing Ex. 1004 ¶¶ 15–16). Referring to the ClinicalTrials.gov "Glossary," Petitioners assert that the NIH explains that the "First Posted" date identified for a particular study is "[t]he date on which the study record was first available on ClinicalTrials.gov." *Id.* (quoting Ex. 1030, 7). Petitioners additionally assert that NIH tracks all subsequent versions of the study and identifies those versions for the public in a "History of Changes" feature on the website. *Id.* (citing Ex. 1004 ¶ 23).

Regarding NCT00965653, Petitioners assert that study record was "First Posted" on ClinicalTrials.gov on August 25, 2009, and therefore available to the public on that date. *Id.* (citing Ex. 1028, 1; Ex. 1004 ¶ 28). Petitioners assert that the History of Changes indicates each of the subsequent updates to the study record. *Id.* at 25 (citing Ex. 1004 ¶¶ 29–33); Ex. 1037 ("History of Changes" showing all updates to the original NCT00965653 study record through November 1, 2016). According to Petitioners, ClinicalTrials.gov confirms that those changes have not involved changes to the protocol itself, which has remained the same since it was published in the "First Posted" version. *Id.*; Ex. 1004 ¶¶ 34–38; Ex. 1038 ("History of Changes" showing original version NCT00965653 study record). Based on the foregoing, Petitioners assert that "[t]he totality of the evidence, including the indicia on the face of [the relied upon] documents and the testimony of Mr. Paarlberg, establishes that NCT00965653 (Ex. 1028) was publicly accessible more than one year before the earliest claimed priority date." *Id.*

Patent Owners assert that the particular document submitted as Exhibit 1028 was published on November 2, 2016, which is the date

identified as the "last update[d]" on the document. Prelim. Resp. 18. Patent Owners assert that because that publication date was several years after the '677 patent's priority date, Exhibit 1028 is not prior art. *Id.* Additionally, Patent Owners assert that Exhibit 1028 contains information not disclosed until after the priority date, as "[s]everal different 'versions' of the webpage have been published on Clinicaltrials.gov between August 2009 and November 2016," wherein each version is updated with new information. *Id.* (citing Ex. 1037).

Patent Owners acknowledge that Petitioners also "cite to Exhibit 1038, which purportedly corresponds to the original version of the webpage published in August 2009." *Id.* at 19–20. However, Patent Owners assert that Petitioners do not make that exhibit the basis of its grounds relying on the NCT00965653 study. *Id.* at 20. According to Patent Owners, institution cannot proceed on a different basis that adds to or replaces the Ex. 1028 reference specified in the Petition" for those grounds. *Id.* at 21 (citing *Sirona Dental Sys. GmbH v. Institut Straumann AG*, 892 F.3d 1349, 1356 (Fed. Cir. 2018) (explaining that it would be improper for the Board to "deviate from the grounds in the petition and raised its own obviousness theory" because "[a]n inter partes review must proceed 'in accordance with or in conformance to the petition'") (quoting *SAS Inst., Inc. v. Iancu*, 138 SCt. 1348, 1356 (2018)).

Further, Patent Owners assert that Petitioners fail to prove that an interested artisan could have located NCT00965653 in November 2009 with reasonable diligence. *Id.* at 23. In particular, Patent Owners allege that Mr. Paarlberg's testimony is insufficient because he does not explain "how clinical trials were indexed or what search allegedly would have allowed a reasonably diligent POSA to pick *NCT00965653* out of the thousands of

available clinical trial records." *Id.* According to Patent Owners, "Mr. Paarlberg simply speculates that NCT00965653 'would have been readily accessible,'" without attesting to any personal knowledge that the record was available on the Clinicaltrials.gov website. *Id.* at 24 (citing Ex. 1004, 22; *Coal. for Affordable Drugs IV LLC v. Pharmacyclics, Inc.*, IPR2015-01076, Paper 33 ("*Coal. for Affordable Drugs*"), 7 (PTAB Oct. 19, 2015) (giving little to no weight to declarant's unsupported assertions that that a clinical trial document was publicly available on Clinicaltrials.gov on a certain date sufficient to establish it as a prior art printed publication).

In the Reply, Petitioners assert that "Mr. Paarlberg identified precisely what information was included in the prior art version of NCT00965653" and "[i]t is that printed publication—i.e., the disclosure of NCT00965653 as it existed more than one year before the claimed priority date—upon which Petitioners' invalidity challenges are based." Pet. Reply 5 (citing Pet. 25). Petitioners assert that "[w]hile Ex. 1028 itself may not have been published until 2016, as explained by Mr. Paarlberg, it, along with the various history of change documents, evidences the information that was include in the prior art version of NCT00965653 that forms the basis of Petitioners' challenge." *Id.* at 6. Petitioners contend that, although they do not have access to the original version of the NCT00965653 study, they have established that the original version was a printed publication, publicly available more than one year prior to the earliest claimed priority date. *Id.* at 6–7.

Petitioners respond to Patent Owners' assertion that they have not shown that an interested artisan could have located NCT00965653 by November 2009 by reiterating Mr. Paarlberg's testimony that Congress mandated the ClinicalTrials.gov website to "contain searchable categories, allowing the public to search for trials by the disease or condition, name of

the intervention, location, age group, study phase, sponsor, recruitment status, or identification number." *Id.* at 8 (citing Ex. 1004 ¶¶ 16, 32). Additionally, Petitioners note that their declarant, Dr. Zizic, also offers testimony that "a POSA would routinely access ClinicalTrials.gov for up-to-date information on clinical trials." *Id.* at 8–9 (quoting Ex. 1002 ¶ 68).

Regarding Patent Owners' reliance on *Coal. for Affordable Drugs*, Petitioners assert that, contrary to the record here, petitioner in that case did not submit any evidence of the website's publishing practices or offer an explanation or evidence of what the dates on the face of the document represent. *Id.* at 9.

In the Sur-reply, Patent Owners assert that "[t]he 'prior art version of NCT00965653' [Petitioners] now assert as the basis for their grounds is pieced together through several non-prior-art documents and other extrinsic evidence." According to Patent Owners, that patchwork of circumstantial evidence was not necessary because Petitioner had access to what they purport to be the "original version" of NCT which they have submitted as Exhibit 1038. PO Sur-reply 3.

Further, Patent Owners argue that Exhibit 1028 is not analogous to a version of the original document that would be available through the Internet Archive, i.e., the Wayback Machine[9], as alleged, because that archive provides snapshots captured before the priority date and no changes or additions are made to the contents of the captured webpage itself. *Id.* (citing Pet. Reply 6–7).

As for public accessibility, Patent Owners reiterate their argument that Petitioners have not provided testimony from someone who had accessed the

[9] *See* https://archive.org/web/

reference before the priority date, or established that the website was searchable such that a POSA could have found the reference with reasonable diligence. *Id.* (citing *Celltrion, LLC v. Biogen, Inc.*, IPR2017-01230, Paper 10 ("*Celltrion*"), 11–14 (PTAB Oct. 12, 2017)).

Having considered the arguments and the evidence, we determine that, for purposes of institution, and based on the totality of the evidence currently in the record, Petitioners have established a reasonable likelihood that NCT00965653 is a printed publication that was publicly accessible before the critical date of the challenged patent, and therefore, qualifies as prior art.

To begin, we recognize and accept Petitioners' clarification that it relies on the "First Posted" version of NCT00965653, that is referenced in Exhibit 1028, and is best represented in the History of Changes document submitted as Exhibit 1038. Both exhibits were submitted with the Petition (*see* Pet. viii–ix, List of Exhibits) and described by Mr. Paarlberg's testimony regarding the publication of the study on ClinicalTrials.gov (*see* Ex. 1004 ¶¶ 24–38).

In reaching our determination, we have considered Mr. Paarlberg's currently unrebutted testimony that "ClinicalTrials.gov displays the most recent version of the study record," and that "a history of changes is available on the ClinicalTrials.gov archive site." Ex. 1004 ¶ 23 (citing Ex. 1051, 2. Indeed. Mr. Paarlberg's testimony appears be a direct quote from the ClinicalTrials.gov "How to Edit Your Study Record" webpage. *See* Ex. 1051, 2 (explaining that "[t]he most recent version of a study record is displayed on ClinicalTrials.gov. A history of changes made to a study record is available on the ClinicalTrials.gov archive site").

It is our understanding, based on the current record, that the first

posted version of the study, along with all versions of the study record posted prior to the most recent version are no longer available on the website in the original form that they were posted. In other words, it is only the most recent version of the study record that is available on the website in the original form that it was posted. Thus, it is understandable that it is this most recent version that Petitioners referenced for its grounds and submitted as Exhibit 1028, as they do not have current access to the original form of the first posted document on the ClinicalTrials.gov website.

However, Petitioners did not rely on Exhibit 1028 alone. As the website explains, ClinicialTrials.gov includes its own "archive site" which makes available a history of changes that lists the first posted version of the study record, and each update to the study record, organized by its submission date and noting changes involved. *Id.*, *see e.g.*, Ex. 1037; Ex. 1004 ¶ 33. That archive site also allows a user to compare versions of the study records to view changes between those records. Additionally, a user may access details of the "First Posted" version of the study record by comparing that record with itself, as Mr. Paarlberg explained and performed. Ex. 1004 ¶ 36. Petitioners have relied upon that comparative record also, which they have submitted as Exhibit 1038. Petitioners and Mr. Paarlberg refer to that exhibit as "NCT00965653 August 21, 2009 Study Record." *Id.*

Further, Petitioners rely on Exhibit 1053, which Mr. Paarlberg testifies is a merged comparison of the August 21, 2009 version of the study record and the November 1, 2016 current version of the study record, that he testifies may be readily accomplished on ClinicalTrials.gov in the "History of Changes" webpage. *Id.* ¶ 33. He explains that "[t]he merged comparison [in Exhibit 1053] identifies all of the changes that were made to the NCT00965653 record between the original and final postings." *Id.* ¶ 33 (citing Ex. 1053).

Additionally, Mr. Paarlberg demonstrates credibly, on the current record, that such changes did not alter the dosing regimen originally disclosed in the first posted version of the study record, i.e., 162 mg tocilizumab administered subcutaneously either weekly or every other week, in combination with 7.5–25 mg methotrexate administered weekly, or the same goal of the study to determine the efficacy and safety of the regimens in patients with rheumatoid arthritis who had inadequate responses to methotrexate. *Id.* ¶ 35 (citing Ex. 1053, 4).

Taken together, we find that the evidence relied on in the Petition, i.e., Exhibits 1028, 1038, 1053, and Mr. Paarlberg's currently unrebutted testimony, provides strong indicia that the first posted version of the NCT00965653 study record, as best represented on the current record by Exhibit 1038, is a printed publication that was published on the ClinicalTrials.gov website prior to the '677 patent's priority date.

Contrary to Patent Owners' contention, our recognition of Petitioners' reliance on Exhibit 1038 does not deviate from the grounds in the Petition. *See* Prelim. Resp. 21 (citing *Sirona Dental*, 892 F.3d at 1356). Although citing to Exhibit 1028, Petitioners have clearly relied upon the first posted version of the NCT00965653 study record as the basis for their first two

grounds. Indeed, Petitioners have explicitly identified the disclosures published in that first posted version of the study record that they allege to recite or render obvious the challenged claims. *Id.* at 21–36. Further, Petitioners explicitly confirm that intention in their Reply brief. Pet. Reply 5–6. That we consider the Exhibit 1038 version of that study record as the best representation of the relied upon version of the NCT00965653 study record, rather than Exhibit 1028, amounts only to a different, more accurate citation for the study version relied upon in the Petition and not some improper revision of the grounds for the challenges based on that study discussed in *Sirona Dental* and *SAS*.

Further, we do not find that the current record supports Patent Owners' contention that Petitioners have not shown sufficient for institution that NCT00965653 was publicly accessible as of the critical date. See Prelim. Resp. 22–25. According to Patent Owners, Mr. Paarlberg's testimony merely amounts to speculation that NCT00965653 would have been readily accessible prior to the critical date of the '677 patent because he does not attest to having personal knowledge that the record was available on the Clinicaltrials.gov website. *See* Prelim. Resp. 24 (citing *Coal. for Affordable Drugs*, 7. We disagree.

The issue in *Coalition for Affordable Drugs* was not merely that the declarant did not attest to any personal knowledge of the public accessibility or dissemination of the clinical trial record. *Coal. for Affordable Drugs*, 7. Rather, the issue was that the declarant's testimony provided nothing more than a conclusory opinion that the clinical trial record constitutes prior art without disclosing any underlying facts or data supporting that testimony. *Id.* Further, the Board determined in that case that the petitioner failed to explain or provide evidence regarding what the date on the clinical trial

record represented and also failed to offer any evidence of the website's publishing practices. *Id.* Based on those collective deficiencies, the Board determined that the petitioner had not made a threshold showing that the clinical trial record was a prior art printed publication.

Petitioners' showing here does not suffer the deficiencies involved in *Coalition for Affordable Drugs*. Instead, Mr. Paarlberg has provided what is currently unrebutted testimony, that we determine, based on the current record, is credibly supported by disclosures on the ClinicalTrials.gov website. For example, Mr. Paarlberg explains how the records on ClinicalTrials.gov are managed and supports that testimony by referring to the webpage on that site that describes those practices. *See, e.g.*, Ex. 1004 ¶¶ 17, 20–23. He also refers to the relevant provisions of the FDA Amendments Act of 2007 to support his testimony that the website was designed to "contain searchable categories, allowing the public to search for trials by the disease or condition, name of the intervention, location, age group, study phase, sponsor, recruitment status, or identification number." *Id.* ¶ 16. Further, as discussed above, he demonstrates how an individual may readily access current and archived records on the website, including records submitted by Petitioners as Exhibits 1028, 1038, and 1053. *See, e.g.*, *id.* at ¶¶ 24–36. Regarding the date relied upon in those exhibits to address the prior art status of the printed publication, Mr. Paarlberg provides the meaning of the "First Posted" date by quoting the definition for the term set forth in the ClinicalTrials.gov Glossary. *Id.* ¶ 26 (quoting Ex. 1030, 7).

Based on the foregoing testimony by Mr. Paarlberg, and the evidence that he cites, we determine on the current record that Petitioners have established sufficiently for institution that the "First Posted" NCT00965653 study record was sufficiently accessible to the public interested in the art and

searchable on the ClinicalTrials.gov website such that a POSA could have found it with reasonable diligence.

Accordingly, at this stage in the proceeding, we consider NCT00965653 as prior art.

b) Enablement of NCT00965653

Patent Owners argue that NCT00965653 does not enable the claimed article of manufacture. Prelim. Resp. 25–32. Specifically, Patent Owners assert that NCT00965653 "neither discloses nor otherwise provides the POSA with any guidance whatsoever on how to make the subcutaneous, 162 mg fixed-dose tocilizumab formulation 'contain[ed]' within the claimed subcutaneous administration device or the device itself." *Id.* at 26. Patent Owners' contentions are largely centered on its assertion that antibodies must be stabilized in a suitable formulation before administration to patients and arriving at such a formulation may be challenging because of the unpredictable solution behavior for various antibodies. *Id.* at 27. Patent Owners allege also that experimentation and guidance to minimize antibody aggregation is required to avoid potentially serious health consequences of immunogenic antibody aggregates. *Id.* at 29.

Petitioners assert in the Reply that "[p]rior art publications are presumed enabled, and at this stage, Petitioners are entitled to rely upon that presumption to establish invalidity." Pet. Reply 3 (citing *Apple Inc. v. Corephotonics, Ltd.*, 861 Fed. App'x 443, 450 (Fed. Cir. 2021). Petitioners assert also that Patent Owners have not satisfied its burden to prove nonenablement by demonstrating that developing a tocilizumab formulation would have required undue experimentation. *Id.* (citing *Invitrogen Corp. v. Clonetech Labs., Inc.*, 429 F.3d 1052, 1068 (Fed. Cir. 2005). Further, Petitioners contend that Patent Owners' allegations are directed to unclaimed

subject matter, as the challenged claims do not require any particular formulation of the recited drug and do not require it to be shelf-stable, commercially viable formulation. *Id.* at 4 (citing *In re Antor Media Corp.*, 689 F.3d 1282, 1290-91 (Fed. Cir. 2012) ("[A] prior art reference need not enable its full disclosure; it only needs to enable the portions of its disclosure alleged to anticipate the claimed invention.").

Patent Owners appear to suggest that Petitioners are not entitled to a presumption that prior art publications like NCT0096563 are enabled, because such a presumption is only recognized for prior art patents and for prior art publications during patent prosecution. PO Sur-reply 5–6. Patent Owners dismiss Petitioners reliance on *Apple v. Corephotonics* as a non-precedential Federal Circuit decision. *Id.* at 6. Patent Owners assert that, in any event, it has presented evidence and arguments sufficient to rebut that presumption. *Id.* at 6–8.

Based on our consideration of the arguments and evidence, we find Petitioners have the better position. To begin, as Petitioners correctly assert, we recognize the same presumption of enablement for prior art printed publications in AIA trial proceedings as would be applied during patent examination and in district court litigation. *See, e.g., Antor*, 689 F.3d at 1287; *Apple Inc. v. Corephotonics*, 861 Fed. App'x at 450. As a result, the burden of production shifts to Patent Owners to present evidence demonstrating that NCT0096563 is not enabling.

Having reviewed Patent Owners' argument, we do not find that Patent Owners have sufficiently addressed the *Wands* factors or produced persuasive evidence to demonstrate that NCT0096563 is not enabling. *See* Prelim. Resp. 25–32; *see also In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Thus, based on the current record, we do not find that Patent Owner

has rebutted that presumption that NCT0096563 is enabling so as to shift the burden of production back to Petitioners at this stage in the proceeding.

c) Conclusion for Anticipation by NCT00965653

Based on the foregoing and the information presented at this stage of the proceeding, we determine that Petitioners have demonstrated a reasonable likelihood that they would prevail in showing claims 1 and 5 are anticipated by NCT00965653.

D. Obviousness over NCT00965653 and Kivitz

Petitioners assert that claims 1–8 would have been obvious over the combined teachings of NCT00965653 and Kivitz. Pet. 30–36. Patent Owners disagree. Prelim. Resp. 41–49.

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). "An obviousness determination requires finding both 'that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.'" *CRFD Research, Inc. v. Matal*, 876 F.3d 1330, 1340 (Fed. Cir. 2017) (quoting *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367–1368 (Fed. Cir. 2016)).

Notwithstanding what the teachings of the prior art would have suggested to one with ordinary skill in the art at the time of the patent's invention, the totality of the evidence submitted, including objective evidence of nonobviousness, may lead to a conclusion that the challenged

claims would not have been obvious to one with ordinary skill in the art. *In re Piasecki*, 745 F.2d 1468, 1471–72 (Fed. Cir. 1984); *see also Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Leapfrog Enters., Inc. v. Fisher–Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007).[10]

We incorporate our description and discussion of NCT00965653 in Section II.C. here.

1. Kivitz

Kivitz discusses the Humira® adalimumab pen, which is described as "a novel, integrated, disposable autoinjection deliver system for the subcutaneous injection of adalimumab." Ex. 1070, 1 (Absract). Kivitz explains that self-administered injectables offer several advantages over intravenous injections (i.e., portability, convenience and flexible scheduling)." *Id.* Kivitz further explains that "patients with chronic, debilitating diseases may need a self-administered medication available in an easy-to-use and convenient delivery device that minimizes pain and facilitates adherence to therapy." *Id.* Kivitz states that, "[b]ased on the positive response from patients to the adalimumab pen, it is quite possible that biological therapies delivered by autoinjector pens may rapidly become the preferred treatment in RA and related diseases." *Id.* at 6.

2. Discussion

Petitioners assert here again that claims 1 and 5 are obvious over NCT00965653 for the same reasons they have asserted that the claims are anticipated by the reference, i.e., because it discloses subcutaneous administration of a fixed dose of 162 mg of tocilizumab and implicitly

[10] At this stage of the proceeding, Patent Owner does not assert evidence of objective indicia supporting nonobviousness of the challenged claim. *See* Prelim. Resp. 41–57.

discloses a subcutaneous administration device, as required by the claims. Pet. 30. Petitioners combine Kivitz with NCT00965653 to reach the additional limitations in dependent claims 2–4 and 6–8 requiring the use of specific types of subcutaneous administration devices. Claims 2 and 6 recite that the device is "selected from the group consisting of a syringe, an injection device, an infusion pump, an injector pen, a needleless device, an autoinjector, and a subcutaneous patch delivery system." Ex. 1006, 63:47–51, 64:48–52. Claims 3 and 7 recite that the device is "a syringe, including a pre-filled syringe." *Id.* at 63:52–54, 64:52–54. Claims 4 and 8 recited that the device is "an autoinjector." *Id.* at 63:55–56; 64:55–56.

According to Petitioners, all of the challenged claims would have been obvious over NCT00965653 in view of Kivitz, which discloses the successful use of a pre-filled syringe and an autoinjector for an antibody used to treat RA. *Id.* at 31. In particular, Petitioners assert that NCT00965653 alone provides motivation for a POSA to use a subcutaneous administration device to contain and deliver to a patient the disclosed subcutaneous 162 mg fixed dose of tocilizumab. *Id.* at 32. Additionally, Petitioners assert that a POSA would have been motivated to use either a syringe or autoinjector, as recited in the dependent claims, to deliver such dose in view of Kivitz. *Id.* at 32. In support of that assertion, Petitioners rely on Kivitz disclosure of several advantages provided by self-administered injectables over intravenous injections, including portability, convenience, ease of use, and minimization pain that facilitates adherence to therapy. *Id.* at 31 (citing Ex. 1070, 1). Petitioners note also that Kivitz discloses three monoclonal antibody drugs that were available to patients in either an autoinjector pen or pre-filled syringe for administration of a subcutaneous dose. *Id.* at 32 (citing Ex. 1070, 3). Petitioners additionally

point to the statement in Kivitz that "[b]iological therapies delivered by autoinjector pens may quickly become the treatment of choice in RA and related diseases." *Id.* (citing Ex. 1070, 7).

Among other rationale offered, Petitioners assert that a POSA would have had a reasonable expectation that "the 162 mg fixed dose of tocilizumab disclosed in NCT00965653 could be successfully contained and delivered to a patient in a 'subcutaneous administration device,'" as the reference discloses administering the drug subcutaneously, which would have necessarily required using such a device. *Id.* at 36. Petitioners assert that a POSA would have also reasonably expected that a syringe or autoinjector could be used as that device, as Kivitz discloses the successful use of such devices for other monoclonal antibody drugs. *Id.*

Patent Owners assert that a POSA would not have had a reasonable expectation of success combining the tocilizumab formulation in NCT00965653 with the administration devices in Kivitz. Prelim. Resp. 41. In particular, Patent Owners' challenge centers on what they characterize as Petitioners' "pharmacokinetic arguments" which involve reliance on alleged efficacy, pharmacokinetic and pharmacodynamic properties, and safety data for the tocilizumab formulation disclosed in NCT00965653. Prelim. Resp. 41–49. Patent Owners raise those same arguments regarding the combination of Maini 2006, Kivitz, Bonilla and Wang, discussed below in Section II.E.4. We address the positions of both parties on that issue in that section and explain why we find Petitioners' have the better position, based on the current record.

Here, it is sufficient, for institution purposes, for us to rely on Petitioners' separate, additional rationale why a POSA would have had a reasonable expectation of success in combining the teachings of

NCT00965653 and Kivitz to provide the claimed articles of manufacture. This rationale persuasively rests upon the understanding that NCT00965653 necessarily used a subcutaneous administration device to administer its subcutaneous 162 mg fixed dose of tocilizumab, while Kivitz discloses the specific subcutaneous administration devices recited by the challenged dependent claims and explains that those devices have been used to deliver monoclonal antibody formulations with success. *See* Pet. 36 (citing Ex. 1004 ¶¶ 123–124). Based on the current record, we find that rationale to be sufficient for purposes of determining whether to institute trial.

Our determination is unchanged, at this stage of the proceeding, based on Patent Owners' assertion that Kivitz teaches away from the claimed administration device. Prelim. Resp. 48. According to Patent Owners, Kivitz suggested a "concentration limit" of only 40 mg of adalimumab in a volume of 0.8 mL for its disclosed subcutaneous administration device. *Id.* Based on that assertion, Patent Owners contend that "[i]f the POSA had uses the same concentration limit suggested by *Kivitz*, the POSA would have concluded that it was necessary to administer a 162 mg dose of tocilizumab using at least four separate subcutaneous administration devices (three devices containing 50 mg doses and one device containing a 12 mg dose)." *Id.* According to Patent Owners, "*Kivitz* therefore would have taught the POSA not to use a single administration device that contains and delivers 162 mg of subcutaneous tocilizumab as claimed in the '677 patent." *Id.* at 48–49.

Based on the current record, Patent Owners' contention that Kivitz teaches away is merely attorney argument that is inadequately supported to demonstrate that a POSA would have viewed Kivitz as suggesting a "concentration limit" for drugs contained in an autoinjector pen or pre-filled

syringe. Indeed, Patent Owners have not referred us to any such suggested "concentration limit" in Kivitz. *See* Prelim. Resp. 48 (providing no citation to Kivitz). In any event, we find that Kivitz explains that, "[l]ike its precursor, the pre-filled syringe, the adalimumab Pen contains adalimumab 40 mg in 0.8-ml solution." Ex. 1070, 2. Kivitz also discloses an autoinjector that contains etanercept dosage of 50 mg/ml. *Id.* at 6. What we do not see, and what Patent Owners has not identified in the reference is any characterization that those dosages represent any "concentration limit" for the subcutaneous devices disclosed. Without more, it is reasonable to consider that Kivitz discloses those doses simply because they were the standard doses for treating patients with those medications.

Thus, having considered the parties' arguments and evidence, at this stage in the proceeding, we conclude that Petitioners have shown sufficiently for institution that, in view of and Kivitz, a POSA would have had a reason to use one of its disclosed subcutaneous administration devices to contain and deliver the tocilizumab subcutaneous dose disclosed in NCT00965653, with a reasonable expectation of success. Accordingly, based on the information presented at this stage of the proceeding, we determine that Petitioners have shown sufficiently that there is a reasonable likelihood that it would prevail in showing that claims 1–8 are rendered obvious by the combination of NCT00965653 and Kivitz.

E. Obviousness over Maini 2006, Kivitz, Bonilla, and Wang

Petitioners assert that claims 1–8 would have been obvious over Maini 2006, Kivitz, Bonilla and Wang. Pet. 40–51. Patent Owners disagree. Prelim. Resp. 51–57.

We incorporate our description and discussion of Kivitz in Section II.D. here.

1. Maini 2006

Maini 2006 reports a double-blind randomized controlled clinical trial of tocilizumab. Ex. 1025, 2. There, patients with "an inadequate response to [methotrexate] or a disease flare while receiving [methotrexate] (at a dosage of 10–25 mg weekly) during a minimum of 6 months of therapy" were recruited for the study. *Id.* at 3–4. In that trial, all patients received a total of four IV infusions of tocilizumab or tocilizumab placebo every four weeks, together with 10–25 mg methotrexate or methotrexate placebo each week. *Id.* at 3–4. Tocilizumab was administered at a dose of 2 mg/kg, 4 mg/kg, or 8 mg/kg. *Id.* at 3.

Maini 2006 shows that IV infusions of tocilizumab every four weeks, with or without methotrexate therapy, were safe and effective for treating RA. *Id.* at 11–13. According to Maini 2006, tocilizumab monotherapy at the dose of 4 mg/kg or 8 mg/kg generated the highest responses, and "those doses are proposed for use in future clinical studies." *Id.* at 12.

2. Bonilla

Bonilla compares administering polyclonal human immunoglobulin (Ig) via the IV and the SC routes. Ex. 1021, 4. According to Bonilla, "IVIG is usually administered every 3 to 4 weeks," whereas "SCIG is usually given weekly," and "a 2-week interval is also practical." *Id.* at 15, 18. Despite the different frequencies of the IV and SC administrations, Bonilla teaches "the amount of IgG administered over time is generally equivalent." *Id.* at 15.

Bonilla states that, when administering Ig via the SC route, because "[t]he dose is absorbed slowly and redistributed slowly," and because the amount administered each time is smaller and the interval is shorter, "the fluctuations in IgG level that are characteristic of IVIG dosing are expected to be much smaller." *Id.*; *see also id.* at 18 ("SCIG leads to more

physiologic IgG levels because the peaks and nadirs between infusions are blunted by slow absorption and maintenance of closer equilibrium between intra- and extravascular compartments.").

3. Wang

Wang states that "without clear scientific rationale, body size-based dosing is often used for administering monoclonal antibodies (mAbs)." Ex. 1022, 7. After comparing fixed dosing versus body size-based dosing of monoclonal antibodies in adult clinical trials, Wang concludes that the two dosing approaches "perform similarly across the mAbs investigated." *Id.* Based on this finding, Wang "recommend[s] fixed dosing as the preferred approach because it offers advantages in ease of dose preparation, reduced cost, and reduced chance of dosing errors." *Id.* at 7, 18 (emphasis omitted); *see also id.* at 18 ("[W]hen there is no advantage of one dosing approach over another from a PK and PD perspective, fixed dosing is the approach of choice.").

4. Discussion

Petitioners argue that "[t]he only difference between claims 1–8 of the '677 patent and Maini 2006 is that the claims recite a device for delivery of subcutaneous fixed dose of 162 mg for tocilizumab, whereas Maini 2006 discloses an intravenous dose of tocilizumab of 4 mg/kg to 8 mg/kg." Pet. 40–41. Petitioners rely on Wang for its contention that "a fixed dose would be preferable to a weight-based dose in the absence of a reason to the contrary." *Id.* at 44 (citing Ex. 1022, 18; Ex. 1002 ¶¶ 151–154). Petitioners rely on Bonilla for its teaching that immunoglobulins are "preferably administered by subcutaneous injection of an equivalent amount every other week instead of every four weeks by IV because it leads to more stable serum concentration levels." *Id.* at 44 (citing Ex. 1021, 8, 15–18).

Petitioners assert that "a POSA would have looked to Bonilla to determine an equivalent subcutaneous fixed dose of the 4 mg/kg every four week intravenous regimen." *Id.* at 45 (citing Ex. 1002 ¶ 152–154). Further, Petitioners assert that a POSA would have known from Kivitz that subcutaneous delivery offered several advantages over intravenous injections (i.e., portability, convenience, flexible scheduling), and that several biologics were available to in a pre-filled syringe and an autoinjector. *Id.* at 47 (citing Ex. 1070, 3).

According to Petitioners, a POSA artisan would have been motivated to combine Maini 2006 with Kivitz, Bonilla and Wang to arrive at the claimed devices with a reasonable expectation of success. *Id.* at 41–49.

Patent Owners counter that Petitioners have not established a motivation to create a subcutaneous fixed dose of tocilizumab, and have not explained how a POSA would have arrived at the claimed 162 mg dose. Prelim. Resp. 51. For the reasons explained below, based on the current record, we find Petitioners have made a sufficient showing on these issues for institution. In our analysis, we address the claims together, in a similar manner as the parties.

a) Reason for Subcutaneous Administration

Petitioners point out that before the priority date of the '677 patent, Patent Owners publicly disclosed the development of a subcutaneous form of tocilizumab for treating RA. Pet. 43; Ex. 1045, 12 (Subcutaneous dose form in development); Ex. 1046, 4 ("Started phase I / II study for subcutaneous injection formulation for rheumatoid arthritis in Japan and overseas"). In addition, Chugai also disclosed that, for tocilizumab, "[i]ts preferred form of administration in chronic autoimmune diseases is thought

to be subcutaneous formulation." Ex. 1011,[11] 4. Petitioners assert that these disclosures, together with advantages of administering Ig subcutaneously every other week over intravenously every four weeks, as Bonilla teaches, would have motivated a POSA to administer tocilizumab via the subcutaneous route "every other week in an amount equivalent to the 4 mg/kg every four week dose disclosed by Maini 2006." Pet. 43–44.

Citing Haller,[12] Patent Owners argue that Petitioners' argument "ignores 'several well-known *disadvantages* associated with SC injections." Prelim. Resp. 51 (quoting Ex. 2032, 2). Patent Owners are correct that Haller discusses certain issues of subcutaneous administration; Patent Owners, however, fails to mention that Haller also points out solutions to those problems. *See* Ex. 2032, 2.

More importantly, Haller touts the advantages of subcutaneous injections. *Id.* According to Haller, "[f]rom many perspectives, including reduced pain, improved patient quality of life, reduced cost of patient care, and reduced risk of infection, SC represents a preferred route for administering a drug by self-injection." *Id.* Despite the disadvantages associated with subcutaneous injections that Patent Owners emphasize, Haller reports that in a survey of oncology practices across the country, "there is a conscious shift to SC administration." *Id.* "Compared with IV drugs, the majority of participants in the survey considered SC drugs clinically safer and more cost-effective, resulting in higher patient satisfaction." *Id.*

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[11] WO2009/041621 A1, published April 2, 2009 (Ex. 1011).
[12] Haller, Converting Intravenous Dosing to Subcutaneous Dosing with Recombinant Human Hyaluronidase, 31 Pharm. Tech. 118–32 (2007) ("Haller").

Perhaps more relevant to our case here, Haller also discusses "the relative desirability of subcutaneous versus IV administration" using "anti-TNF-alpha treatments for rheumatoid arthritis" as examples. *Id.* Two of those examples, infliximab and adalimumab, both monoclonal antibodies against TNF-α, were approved for treating RA before 2002. Prelim. Resp. 2; *see also* Ex. 1006, 14:56–62 (listing infliximab and adalimumab as examples of TNF inhibitor). Haller explains that infliximab is administered intravenously, whereas adalimumab is given subcutaneously. Ex. 2032, 2. According to Haller, efficacy differences between the two drugs when administered with methotrexate are "considered minimal." *Id.* Interestingly, Haller points out that

> A broad indicator, such as revenues . . . shows that IV- and SC-delivered agents were essentially equal in 2001, and both have been growing at healthy rates. The relative growth rate of the SC agent, however, is approximately 50% higher than that of the IV drug (a 33% compound annual growth rate for IV versus 50% for SC), translating into 2006 revenues for the SC agent that are almost double that of the IV agent. This increase occurred despite reimbursement dynamics for SC injectables that were unfavorable until recently.

Id.

Although these revenue numbers may be not be of concern to a POSA, they appear to reflect the patients' preference for subcutaneous over intravenous administration, which seemingly would be at least a part of the consideration for developing RA treatments. Thus, Haller does not support Patent Owners' argument that the reason to shift from intravenous to subcutaneous administration is "pure hindsight." *See* Prelim. Resp. 58–59.

Accordingly, based on this record, Petitioners have shown sufficiently, for purposes of institution, that a POSA would have been motivated to administer tocilizumab via the subcutaneous route.

b) Reason for Fixed Dose

Patent Owners also challenge Petitioners' reliance on Wang for teaching the fixed dose. Prelim. Resp. 54. According to Patent Owners, Wang advises that "[a] full population PK and PD analysis should be conducted, including covariate analysis," and if "body size is identified as a covariate of PK or PD parameters, population and individual performances of both dosing approaches should be evaluated." *Id.* (quoting Ex. 1022, 18). Patent Owners argue that because data on the pharmacokinetics ("PK") or pharmacodynamics ("PD") of subcutaneously administered tocilizumab in humans was not publicly available before the priority date of the '677 patent, Wang would not have motivated a POSA to pursue fixed dosing for tocilizumab. *Id.* at 54–55.

Again, Patent Owners' characterization of Wang is not incorrect, but it is incomplete. We agree that Wang suggests determining dosing route based on PK and PD analyses, but only for phase 3 studies. Ex. 1022 at 18. Patent Owners omit to mention Wang's teaching that

> When an mAb is first tested in humans, the effect of body size on PK and/or PD parameters in humans is unknown. Because no obvious advantage has been identified for one approach over the other in terms of reducing variability in PK/PD measurements, either dosing approach may be used in FIH [first-in-human] and other early stage trials before the effect of body size on PK and PD in humans can be evaluated. However, we recommend using fixed dosing approach because it offers advantages in ease of preparation, reduced cost, and reduced chance of dosing errors.

Id.

Moreover, as Petitioners points out, "several IgG antibodies and other proteins" including etanercept, adalimumab, certolizumab, and golimumab, "were approved in the prior art that were used in a subcutaneous fixed dose." Pet. 49; *see also id.* at 13–14 (listing approval date, dosage, and indications). Among them, adalimumab and golimumab, are monoclonal antibodies approved for treating RA before the priority date. Prelim. Resp. 5–6. Each is administered subcutaneously with a fixed dose, every other week for adalimumab, and once a month for golimumab. Ex. 1023, 14; Ex. 1084, 4.

Thus, on this record and for purposes of institution, Petitioners have shown sufficiently that, at the relevant time, when the PK and PD data for tocilizumab allegedly were not publicly available, a POSA would have been motivated to administer tocilizumab using a fixed dose.

c) 162 mg Per Dose

Petitioners argue that a POSA "would have looked to Bonilla to determine an equivalent subcutaneous fixed dose of the 4 mg/kg every four week intravenous regimen." Pet. 45 (citing Ex. 1002 ¶¶ 152–154). According to Petitioners, the equivalent amount of an antibody administered via subcutaneous "may be as low as the amount administered intravenously and as high as the amount necessary to account for the potential impact of reduced bioavailability of the subcutaneous mode of administration." *Id.* (citing Ex. 1021, 16–17). Petitioners assert that the reported bioavailability of tocilizumab administered subcutaneously was 72%, "which means that as much as 139% of the IV dose may be required if administered subcutaneously." *Id.* (citing Ex. 1019,[13] 18; Ex. 1002 ¶¶ 152–153).

[13] European Medicines Agency, Assessment Report for Ro-Actemra (2009) (Ex. 1019, "EMA Assessment Report").

Petitioners argue that, starting from the 4 mg/kg every four week intravenous dose, as Maini 2006 teaches, and assuming the body weight of a typical patient is 70 kg, 140 mg tocilizumab would be administered subcutaneously every other week.[14] *Id.* at 46 (citing Ex. 1002 ¶ 153). According to Petitioners, "[a]ccounting for the potential 39% increase, a POSA would have understood that an equivalent subcutaneous every other week regimen would require administering a fixed dose of between 140 mg and 195 mg." *Id.* at 46 (citing Ex. 1002 ¶ 153). Thus, Petitioners conclude that a POSA "would have arrived at the claimed 162 mg every other week subcutaneous regimen through routine optimization as 162 mg falls squarely within the range, and there is no evidence that the particular amount is critical." *Id.* at 46–47 (citing Ex. 1002 ¶ 153).

Patent Owners criticize Bonilla as being directed to polyclonal immunoglobulins. Prelim. Resp. 44 (citing Ex. 1021, 4). According to Patent Owners, that is "an entirely different class of molecules," which "bear little resemblance to monoclonal antibodies" like tocilizumab. *Id.* Patent Owners have not produced evidence to show that the differences between a polyclonal antibody and a monoclonal antibody would affect a POSA's understanding of Bonilla's teaching, specifically that, over time, the amount of immunoglobulins administered, whether via intravenous or subcutaneous, is generally equivalent. *See* Ex. 1021, 15, 17. Thus, based on the current record, we accord little weight to this attorney argument.

[14] Petitioners calculate the dose as follows: "70 kg x (4 mg/kg every four weeks) = 280 mg every four weeks, or 140 mg every two weeks, for a 70 kg patient." Pet. 46 n.11.

Patent Owners also note that Bonilla describes "the results of just a single study in which participants were subcutaneously administered a product called Vivaglobin® at between 1.02 and 1.92 times the IV dosage." Prelim. Resp. 44 (citing Ex. 1021, 17). According to Patent Owners, Bonilla "does not state, or even suggest, that the results it describes would be applicable to other immunoglobulins, let alone recombinant monoclonal antibodies" like tocilizumab. *Id.* We disagree, because Bonilla teaches that "any product suitable for IV administration with concentration of 10% or more . . . may be administered SC." *See* Ex. 1021, 17.

Patent Owners further challenge Petitioners' reliance on the 72% relative subcutaneous/IV bioavailability. Prelim. Resp. 45. Patent Owners note that number was from "one study in *monkeys*." *Id.* (citing Ex. 1019, 18). Patent Owners contend that "[i]t was well-known that monoclonal antibodies exhibited marked interspecies variation in subcutaneous bioavailability." *Id.* (citing Ex. 2028, 7). Thus, Patent Owners conclude that a POSA would not have assumed the 72% bioavailability reported in monkeys would remain the same in humans. *Id.*

We recognize, as Patent Owners emphasize, that "interspecies variation makes it challenging to predict human bioavailability from animal data." *Id.* at 46 (citing Ex. 2029, 8; Ex. 2030, 2) (quotation marks and bracket omitted). On the other hand, the EMA Assessment Report, which Petitioners refer to for reporting the 72% bioavailability, states:

> The cynomolgus monkey was chosen as the pharmacologically relevant species because tocilizumab cross-reacts with monkey IL-6R under in vitro and in vivo conditions. In a cynomolgus monkey model of collagen-induced arthritis (CIA), tocilizumab was shown to prevent both the local joint and the systemic inflammatory disease manifestations.

Ex. 1019, 17 (emphasis omitted). Thus, on this record, and for purposes of institution, we find it is reasonable for Petitioners to rely on the bioavailability data from monkeys.

On the dose amount, Patent Owners contend that the range of potential dosing options is "far broader" than Petitioners present. Prelim. Resp. 56. Patent Owners assert that multiple studies had shown that Maini 2006 teaches tocilizumab administered intravenously at both 4 mg/kg and 8 mg/kg is safe and effective. *Id.* Thus, following Petitioners' way of calculation, Patent Owners contend that the potential subcutaneous dosage could range from 70 mg to 389 mg.[15] *Id.*

Based on this record, we agree with Patent Owners that the potential subcutaneous dosage ranges from 70 mg to 389 mg. This, however, does not change the fact the claimed dose of 162 mg still falls within that range. Where, as here, the prior art suggests a range, and the claimed invention falls within that range, there is a presumption of obviousness. *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004). Patent Owners may rebut this presumption by showing unexpected results or criticality of the claimed dosage, that the prior art taught away from the claimed dosage, or other pertinent objective indicia indicating that the claimed invention would not have been obvious in light of the prior art. *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1008 (Fed. Cir. 2018). At this stage, Patent Owners have not presented such evidence.

[15] Patent Owners calculate the dose as follows: 70 kg x (4 mg/kg every four weeks) = 70 mg every week. 70 kg x (8 mg/kg every four weeks) = 560 mg every four weeks, or 280 mg every two weeks. Adjusting 280 mg to account for the alleged 72% relative subcutaneous/intravenous bioavailability, the upper limit would be 389 mg (280/0.72 = 382). Prelim. Resp. 56 n.12.

Patent Owners also criticize Petitioners for relying on the "typical 70 kg" body weight. Prelim. Resp. 47. Patent Owners note that Wang reports results of an experiment assuming 75 kg and 90 kg median body weights.[16] *Id.* (citing Ex. 1022, 16–17). Patent Owners assert that the potential subcutaneous dosing range would be between 150 and 208 mg for 75 kg weight and between 180 and 250 mg for 90 kg weight. *Id.* n.11. "In the latter case," Patent Owners argue, "the lowest recommended dosage would be *above* the 162 mg amount claimed." *Id.* We are not persuaded by Patent Owners' analysis.

As an initial matter, in Wang's simulation, the median body weight is 75.7 kg. Ex. 1022, 9. This number is close to the 70 kg "typical" weight Petitioners use for calculating the dosing amount. Moreover, even with Patent Owners' calculation, the proper range, using Patent Owners' model, would be from 150 to 250 mg. *See* Prelim. Resp. 47 n.11 (presenting the range as between the lowest and highest). Thus, with the claimed 162 mg within the range, there is a presumption of obviousness, which Patent Owners may rebut during trial. *See Iron Grip*, 392 F.3d at 1322.

d) Subcutaneous Administration Device

Based on the teachings of Kivitz, Petitioners have asserted persuasively that a POSA would have known that "subcutaneous delivery offered several advantages over intravenous injections (i.e., portability, convenience and flexible scheduling), and that several biologics were available to RA patients in a pre-filled syringe and an autoinjector." Pet. 47 (citing Ex. 1070, 3). Insofar as Patent Owners assert that Kivitz teaches

[16] Although not statisticians ourselves, we understand "median" and "average" are different measures of central tendency.

away from using a single administration device as recited in the claims, *see* Prelim. Resp 53–54, we disagree for the reasons discussed above in Section II.D.2, i.e., Kivitz does not characterize the dosages that it used for different drugs to represent any "concentration limit" for the subcutaneous devices disclosed. Thus, we find that, based on the current record, Patent Owners' assertions that a POSA would have considered a 162 mg fixed dose of tocilizumab to be too high of a concentration of antibody to be contained and delivered in a single subcutaneous administration device to be inadequately supported.

For purposes of institution, we find that Petitioners have demonstrated sufficiently that a POSA would have been motivated to provide the subcutaneous 162 mg fixed dose of tocilizumab in a subcutaneous administration device, such as a pre-filled syringe and/or an autoinjector. *See* Pet. 47 (citing Ex. 1002 ¶ 154).

e) Reasonable Expectation of Success

Petitioners argue that a POSA would have reasonably expected a 162 mg fixed dose of tocilizumab administered via subcutaneously every other week to be successful because Maini 2006 teaches that 4 mg/kg of tocilizumab administered intravenously every four weeks was safe and effective, and Bonilla teaches that an equivalent subcutaneous dose would provide equivalent results. Pet. 47 (citing Ex. 1002 ¶ 159).

In addition, Petitioners assert that "a POSA would have understood that the efficacy of tocilizumab depended upon maintaining trough concentrations above a minimum threshold." *Id.* at 48 (citing Ex. 1033, 9; Ex. 1002 ¶ 157). In view of Bonilla's teaching that the trough concentrations would be higher for a subcutaneous dose administered every other week than an equivalent intravenous dose administered every four

weeks, Petitioners assert that a POSA would have reasonably expected the trough concentration in the subcutaneous dosing regimen (162 mg fixed dose administered subcutaneously every other week) to be higher than that in the intravenous dosing regimen (4 mg/kg administered intravenously every four weeks). *Id.* (citing Ex. 1002 ¶ 157; Ex. 1021, 17).

Further, Petitioners contend that a POSA would have reasonably expected a fixed dose "to be successful over a wide range of patient weights." *Id.* (citing Ex. 1002 ¶ 157). Petitioners acknowledge that tocilizumab's "clearance was dependent upon body weight, and hence a fixed dose would result in heavier patients having a lower AUC than lighter patients." *Id.* 48 (citing Ex. 1019, 23–24; Ex. 1002 ¶ 158). According to Petitioners, however, AUC was known "to vary significantly" when tocilizumab was administered as a weight-based dose, with "as much as a two-fold increase in AUC as between light and heavy patients." *Id.* at 48–49 (citing Ex. 1019, 23–24). "This doubling of AUC," Petitioners contend, was found to "not affect efficacy or safety in a clinically relevant manner." *Id.* at 49 (citing Ex. 1019, 23–24). Thus, Petitioners conclude that "[a] POSA would therefore have reasonably expected any AUC variation based on different clearance rates due to body weight to similarly not affect the safety or efficacy of the 162 mg dose." *Id.* (citing Ex. 1002 ¶ 159).

Additionally, Petitioners point out that "several IgG antibodies and other proteins" including etanercept, adalimumab, certolizumab, and golimumab, "were approved in the prior art that were used in a subcutaneous fixed dose." *Id.*; *see also id.* at 13–14 (listing approval date, dosage, and indications). Petitioners assert that "[t]hese approvals would have further reinforced to a POSA that a subcutaneous fixed dose of tocilizumab would have reasonably been expected to be successful." *Id.*

Finally, Petitioners assert persuasively that "a POSA would have reasonably expected that a 162 mg fixed dose of tocilizumab could be successfully administered to a patient with a pre-filled syringe or autoinjector" because, by the time of the invention, several other biologic drugs were already available to patients in those dosage forms, as disclosed in Kivitz. *Id.* at 49 (Ex. 1070, 3).

Patent Owners argue "Petitioners' Invocation of 'Routine Optimization' Does Not Satisfy their Burden of Establishing a Reasonable Expectation of Success." Prelim. Resp. 55. Specifically, Patent Owners contend that Bonilla "never actually teaches" the intravenous to subcutaneous dosage calculation. *Id.* We disagree.

Bonilla teaches the amount of immunoglobulin administered over time, whether intravenously or subcutaneously, "is generally equivalent," despite the different frequencies of administrations. Ex. 1021, 15. Bonilla explains, for example, in one study,

> patients were switched from IVIG to SCIG under a protocol that called for dose adjustment of the SC product to give a time-averaged area under the curve that was equivalent to what had been obtained previously with IVIG. This change required administration of an average of 1.37 times (range 1.02–1.92) the IV dose by the SC route.

Id. at 17. Thus, for purposes of institution, we find it is reasonable for Petitioners to rely on Bonilla's teaching to calculate the subcutaneous dosage for tocilizumab.

In addition, Patent Owners assert that the range of potential dosing option is "far broader" than Petitioners' calculation, and should be from 70 mg to 389 mg. Prelim. Resp. 56. As explained above, although we agree with Patent Owners on this point, the claimed dose of 162 mg still falls

within the broader range, and thus, there is a presumption of obviousness. *see supra* Section II.E.4.c.

Accordingly, based on the current record and for purposes of this Decision, we find Petitioners have made a sufficient showing of reasonable expectation of success.

f) Conclusion for Obviousness Over Maini 2006, Kivitz, Bonilla and Wang

Based on the foregoing and the information presented at this stage of the proceeding, we determine that Petitioners have demonstrated a reasonable likelihood that they would prevail on their obviousness challenge of claims 1–8 over the combination of Maini 2006, Kivitz, Bonilla, and Wang.

F. Anticipation and Obviousness Based on Georgy

In these remaining grounds, Petitioners assert that claims 1 and 5 are anticipated by Georgy, Pet. 36–38, and claims 1–8 are obvious over Georgy in view of Kivitz, *id.* at 38–40. Patent Owners disagree. Prelim. Resp. 32–41, 48–50. We find that based on the current record, some of Patent Owners' arguments may have merit. In particular, we find that Patent Owners assert, what appears at this stage of the proceeding, to be a strong showing for its contention that Georgy is not prior art. *See id.* at 32–41.

In any event, we have already determined that Petitioners have demonstrated a reasonable likelihood of prevailing in showing the unpatentability of each challenged claims, based on NCT00965653 alone, NCT00965653 combined with Kivitz, and the combination of Maini 2006, Kivitz, Bonilla, and Wang. In view of those determinations we institute an *inter partes* review of all the challenged claims based upon all grounds raised in the Petition.

G. Discretion to Institute under 35 U.S.C. § 314(a)

Institution of *inter partes* review is discretionary:

> The Director may not authorize an inter partes review to be instituted unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.

35 U.S.C. § 314(a). This language provides the Director with discretion to deny institution of a petition. *See Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 273 (2016) ("[T]he agency's decision to deny a petition is a matter committed to the Patent Office's discretion."); Patent Trial and Appeal Board Consolidated Trial Practice Guide ("CTPG") at 55 (November 2019), *available at* https://www.uspto.gov/TrialPracticeGuideConsolidated. The Director has delegated his authority under § 324(a) to the Board. 37 C.F.R. § 42.4(a) ("The Board institutes the trial on behalf of the Director.").

The Leahy-Smith America Invents Act was "designed to establish a more efficient and streamlined patent system that will improve patent quality and limit unnecessary and counterproductive litigation costs." H.R. Rep. No. 112−98, pt. 1, at 40 (2011), 2011 U.S.C.C.A.N. 67, 69 (reviews were meant to be "quick and cost effective alternatives to litigation"); *see also* S. Rep. No. 110−259, at 20 (2008); CTPG 56. The Board recognized these goals, but also "recognize[d] the potential for abuse of the review process by repeated attacks on patents." *General Plastic Co. v. Canon Kabushiki Kaisha*, IPR2016-01357, Paper 19, 16−17 (PTAB Sept. 6, 2017) (precedential).

In *NHK Spring Co. v. Intri-Plex Technologies, Inc.*, IPR2018-00752, Paper 8 (PTAB Sept. 12, 2018) (precedential), the Board determined that the advanced state of a parallel proceeding is an additional factor weighing in favor of denying institution under 35 U.S.C. § 314(a). *Id.* at 19–20. In *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019 ("*Fintiv*"), Paper 11 (PTAB Mar. 20, 2020) (precedential), the Board articulated a list of factors that we consider in determining whether to exercise discretion to deny institution based on an advanced stage of a parallel proceeding:

> 1. whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted;
>
> 2. proximity of the court's trial date to the Board's projected statutory deadline for a final written decision;
>
> 3. investment in the parallel proceeding by the court and the parties;
>
> 4. overlap between issues raised in the petition and in the parallel proceeding;
>
> 5. whether the petitioner and the defendant in the parallel proceeding are the same party; and
>
> 6. other circumstances that impact the Board's exercise of discretion, including the merits.

Fintiv, Paper 11, 5–6. "These factors relate to whether efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in the parallel proceeding." *Id.* In evaluating these factors, we take "a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review." *Id.* (citing CTPG 58).

Patent Owners assert that we should decline to institute under *NHK Spring/Fintiv*. Prelim. Resp. 57–60. However, as Patent Owners admit, there is no pending litigation between the parties. *Id.* at 58. Nevertheless, Patent Owners urge that we could deny institution under *Fintiv* "because of the near-certainty of parallel, duplicative proceedings." *Id.* at 57. In particular, Patent Owners assert that "[t]he absence of any currently pending litigation between the parties does not mean they do not have a dispute." *Id.* at 58. According to Patent Owners, "[t]he statutory scheme governing biosimilars like Petitioners' copy of Actemra® [Patent Owners' product comprising tocilizumab] all but guarantees patent litigation between Petitioners and Patent Owner[s]." *Id.* Specifically, Patent Owners contend,

> Once Petitioners seek approval from FDA for their copy of Actemra®, the parties' patent disputes are likely to explode into full-blown district court litigation, including, potentially, preliminary injunction proceedings on patents like the '052 patent. By refusing to hold off serving its notice of intent to market until this proceeding concludes, Petitioners virtually guarantee that the trial court and the Board will be addressing the '052 patent in parallel.

Id. at 58–59.

As noted above, the Board's discretionary denial analysis, set forth in *NHK Spring/Fintiv* pertains to matters before us that involve a parallel proceeding—typically an ongoing lawsuit in court. Here, Patent Owners have identified, at best, a hypothetical future district court litigation. Because Patent Owners have not identified an existing parallel proceeding to consider, we decline Patent Owners' invitation for us to consider discretionary denial of the institution under *Fintiv*.

III. CONCLUSION

For the foregoing reasons, we conclude that Petitioners have established a reasonable likelihood of prevailing in its assertion that claims 1–8 of the '677 patent are unpatentable. Accordingly, in light of *SAS*, 138 S. Ct. at 1354, and the Patent Trial and Appeal Board Consolidated Trial Practice Guide, we institute an *inter partes* review of all of the challenged claims on all of the asserted grounds.

Our determination in this Decision is not a final determination on either the patentability of any challenged claims or the construction of any claim.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–8 of the '677 patent on all grounds set forth in the Petition is instituted, commencing on the entry date of this decision; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of review.

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