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Paper 78
Date: August 29, 2023

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CELLTRION, INC.,
Petitioner,

v.

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

IPR2022-00578
Patent 8,580,264 B2

Before JOHN G. NEW, GEORGIANNA W. BRADEN, and TINA E. HULSE, *Administrative Patent Judges.*

HULSE, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
Dismissing Petitioner's Motion to Exclude
35 U.S.C. § 318(a)

I. INTRODUCTION

Celltrion, Inc. ("Petitioner") filed a Petition requesting *inter partes* review of claims 1–12 of U.S. Patent No. 8,580,264 B2 (Ex. 1001, "the '264 Patent"), owned by Chugai Seiyaku Kabushiki Kaisha, Genentech, Inc., and Hoffmann-La Roche Inc. (collectively, "Patent Owner"). Paper 2 ("Pet."). Upon considering the Petition,[1] we instituted an *inter partes* review of the challenged claims of the '264 Patent. Paper 10 ("Dec. Inst." or "Institution Decision").

After institution, Petitioner filed a Motion to Submit Supplemental Information to file the Second Declaration of Professor Maarten Boers. Paper 13. We granted Petitioner's Motion (Paper 22), and Petitioner filed the Second Boers Declaration as Exhibit 1119. Patent Owner then filed a Response to the Petition (Paper 28, "PO Resp."), Petitioner filed a Reply (Paper 45, "Pet. Reply"), and Patent Owner filed a Sur-reply (Paper 64, "PO Sur-reply").

Petitioner also filed a Motion to Exclude Evidence (Paper 65), to which Patent Owner filed an Opposition (Paper 67), and Petitioner filed a Reply (Paper 72).

An oral hearing was held on May 31, 2023.[2] A transcript of the hearing has been entered in the record. Paper 77 ("Tr.").

We have authority under 35 U.S.C. § 6. We issue this Final Written Decision under 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons

[1] Patent Owner waived the filing of a Preliminary Response. Paper 9.

[2] Oral argument was simultaneously heard in this *inter partes* review and in, *Celltrion, Inc., v. Chugai Seiyaku Kabushiki Kaisha*, IPR2022-00579, which was conducted in parallel, but not consolidated, with the present proceeding.

that follow, we determine Petitioner has shown by a preponderance of the evidence that claims 1–12 of the '264 Patent are unpatentable.

A. Real Parties-in-Interest

Petitioner identifies itself along with Celltrion Healthcare Co. Ltd. and Celltrion Healthcare U.S.A., Inc. as real parties-in-interest. Pet. 32. Patent Owner identifies Chugai Seiyaku Kabushiki Kaisha (also called Chugai Pharmaceutical Co., Ltd.), Genentech, Inc., and Hoffmann-La Roche Inc. as real parties-in-interest. Paper 4, 1.

B. Related Proceedings

The parties state that claims of the '264 Patent were challenged in two *inter partes* review proceedings, both of which were terminated after institution due to settlement: *Fresenius Kabi USA, LLC v. Chugai Seiyaku Kabushiki Kaisha*, IPR2021-01288 ("IPR1288"), Paper 74 (PTAB Oct. 17, 2022) (termination) and *Fresenius Kabi USA, LLC v. Chugai Seiyaku Kabushiki Kaisha*, IPR2021-01542 ("IPR1542"), Paper 72 (PTAB Oct. 17, 2022) (termination). Pet. 32; Paper 4, 1.

Petitioner also filed concurrently with the Petition in this proceeding a petition for *inter partes* review of related U.S. Patent No. 10,874,677 B2 ("the '677 Patent") in IPR2022-00579. Pet. 32; Paper 4, 3. The '677 Patent was also the subject of IPR2021-01336, which was terminated after institution due to settlement. Pet. 32–33; Paper 4, 3; IPR2021-01336, Paper 69 (PTAB Oct. 17, 2022) (termination).

Patent Owner also identifies a list of U.S. patent applications and issued patents that relate to the '264 Patent, including U.S. Patent No. 9,750,752, which was the subject of IPR2022-00201 and was terminated after institution due to settlement. Paper 4, 1–3; IPR2022-00201, Paper 42 (PTAB Oct. 17, 2022) (termination).

C. The '264 Patent

The '264 Patent, entitled "Subcutaneously Administered Anti-IL-6 Receptor Antibody" was filed on November 7, 2011, and claims the benefit of several provisional applications, the earliest of which was filed on November 8, 2010. Ex. 1001, code (54), 1:4–9.

The '264 Patent states rheumatoid arthritis ("RA") is a progressive, systemic autoimmune disease that damages the joints and is accompanied by fatigue, anemia, and osteopenia. Ex. 1001, 1:29–32. According to the Specification, the cause of RA is unknown. *Id.* at 1:37–38. Disease-modifying anti-rheumatic drugs ("DMARDs"), such as methotrexate and tumor necrosis factor ("TNF") inhibitors, are the "cornerstone of RA treatment throughout all stages of the disease." *Id.* at 1:42–44, 14:22–27.

Interleukin-6 ("IL-6") is a proinflammatory cytokine that has been implicated in the pathogenesis of autoimmune diseases, including RA. *Id.* at 1:54–2:11. Antibodies have been developed to bind to the IL-6 receptor ("IL-6R") and prevent IL-6 from binding to the receptor. *See id.* at 3:48–4:29, 8:35–38. These antibodies are referred to as anti-IL-6R antibodies. *See id.* Tocilizumab ("TCZ") is an example of a known immunoglobulin G1-kappa ("IgG1κ") anti-IL-6R antibody. *Id.* at 8:39–46. TCZ is characterized by a light chain amino acid sequence of SEQ ID NO. 1 and a heavy chain amino acid sequence of SEQ ID NO. 2. *Id.*

The Specification states that clinical efficacy and safety studies of intravenous TCZ have been completed. *Id.* at 2:12–18. For example, TCZ has been approved for treating RA by intravenous ("IV") administration (4 mg/kg and 8 mg/kg). *Id.* at 2:19–24. The Specification also describes clinical studies for administering a fixed dose of 162 mg TCZ subcutaneously every week ("SC QW") in RA patients. *See id.* at 28:56–

35:5. A fixed dose is a dosage of a drug "administered without regard to the patient's weight or body surface area (BSA), i.e., it is not administered as either a mg/kg or mg/m^2 dose." *Id.* at 14:64–67. The studies show that disease activity "appears to decrease from baseline more rapidly and to a greater magnitude with the 162 mg SC QW as compared to the other SC dose regimens tested." *Id.* at 30:48–51.

D. Illustrative Claim

Petitioner challenges claims 1–12 of the '264 Patent, of which claims 1, 10, and 12 are independent. Claim 1 is illustrative and reproduced below:

> 1. A method of treating rheumatoid arthritis (RA) in a patient comprising subcutaneously administering an anti-IL-6 receptor (IL-6R) antibody to the patient, wherein the anti-IL-6R antibody is administered as a fixed [dose][3] of 162 mg per dose every week or every [two][4] weeks, and 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. 1001, Certificate of Correction, claim 1. Independent claim 10 differs from claim 1 in that it recites administering tocilizumab instead of an anti-IL-6-recepter antibody, and it does not recite the SEQ ID amino acid sequences. *Id.*, Certificate of Correction, claim 10. Independent claim 12 differs from claim 1 in that it recites "a method of inhibiting the progression

[3] Petitioner notes that original claim 1 included the word "dose," but the Certificate of Correction that issued on August 17, 2021, omits the term from claim 1. Ex. 1001. Because the parties have treated claim 1 as including the term "dose," we do the same for purposes of this Decision.

[4] Petitioner notes that original claim 1 included the word "two," but the Certificate of Correction that issued on August 17, 2021, omits the term from claim 1. Ex. 1001. Because the parties have treated claim 1 as including the term "two," we do the same for purposes of this Decision.

of structural joint damage" in an RA patient, "wherein structural joint damage at week 24 or week 48 is found to be inhibited." *Id.*, Certificate of Correction, claim 12.

E. The Asserted Grounds to Patentability

Petitioner asserts that claims 1–12 of the '264 Patent are unpatentable based on the following grounds:

Claim(s) Challenged	35 U.S.C. §[5]	Reference(s)/Basis
1–3, 6–12	102	NCT '653[6]
1–3, 6–11	103	NCT '653, Morichika[7]
4	103	NCT '653, Morichika, Emery[8]
5	103	NCT '653, Morichika, Maini[9]

[5] Because the claims at issue have an effective filing date before March 16, 2013, the effective date of the applicable provisions of the Leahy Smith America Invents Act, Pub. L. No. 112–29, 125 Stat. 284 (2011) ("AIA"), we apply the pre-AIA versions of 35 U.S.C. §§ 102 and 103(a) in this Decision. Our Decision, however, would not change regardless of which version of the Patent Act applies.

[6] U.S. National Library of Medicine, *Study NCT00965653, A Study of Subcutaneously Administered Tocilizumab in Patients with Rheumatoid Arthritis* (August 21, 2009), *available at* https://clinicaltrials.gov/ct2/history/NCT00965653?V_1. Ex. 1004 ("NCT '653").

[7] Morichika et al., WO 2009/084659 A1, published July 9, 2009 (certified English translation). Ex. 1110 ("Morichika").

[8] P. Emery et al., *IL-6 receptor inhibition with tocilizumab improves treatment outcomes in patients with rheumatoid arthritis refractory to anti-tumour necrosis factor biologicals: results from a 24-week multicenter randomised placebo-controlled trial*, 67 ANN. RHEUM. DIS. 1516–23 (2008). Ex. 1043 ("Emery").

[9] R. N. 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*, 54 ARTHRITIS & RHEUMATISM 2817–29 (2006). Ex. 1040 ("Maini").

Claim(s) Challenged	35 U.S.C. §[5]	Reference(s)/Basis
12	103	NCT '653, Morichika, Kremer 2009[10]
1–11	103	NCT '653, Morichika, Ng,[11] Nishimoto,[12] FDA Review,[13] SC PK Prior Art[14]
4	103	NCT '653, Morichika, Ng, Emery, Nishimoto, FDA Review, SC PK Prior Art
5	103	NCT '653, Morichika, Ng, Maini, Nishimoto, FDA Review, SC PK Prior Art
1–11	103	NCT '653, Morichika, Ng, Nishimoto, EMA Report,[15]

[10] J. Kremer et al., *LITHE: Tocilizumab Inhibits Radiographic Progression and Improves Physical Function in Rheumatoid Arthritis (RA) Patients (Pts) at 2 Yrs with Increasing Clinical Efficacy Over Time*, AM. COLLEGE OF RHEUMATOLOGY ABSTR. SUPPL. (2009). Ex. 1029 ("Kremer 2009").

[11] C. M. Ng et al., *Pharmacokinetic-Pharmacodynamic-Efficacy Analysis of Efalizumab in Patients with Moderate to Severe Psoriasis*, 22 PHARMA. RES. 1088–1100 (2005). Ex. 1007 ("Ng").

[12] N. Nishimoto et al., *Mechanisms and pathological significances in increase in serum interleukin-6 (IL-6) and soluble IL-6 receptor after administration of an anti-IL-6 receptor antibody, tocilizumab, in patients with rheumatoid arthritis and Castleman disease*, 112 BLOOD 3959–64 (2008). Ex. 1008 ("Nishimoto").

[13] Food and Drug Administration, *Clinical Pharmacology and Biopharmaceutics Review(s) for IV Actemra Application No. 125276*, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/125276s000ClinPharmR.pdf. Ex. 1010 ("FDA Review").

[14] Petitioner's citation of "SC PK Prior Art" refers to several references for teaching bioavailability and rate of absorption values for various IgG1-κ-subtype antibodies. *See* Pet. 61–62 (citing Ex. 1007, 1012–1016, 1018–1022).

[15] Europe Medicines Agency, *Assessment Report for RoActemra*, Doc. Ref.: EMEA/26276/2009 (2009). Ex. 1006, Ex. B ("EMA Report").

Claim(s) Challenged	35 U.S.C. §[5]	Reference(s)/Basis
		Chernajovsky,[16] SC PK Prior Art
4	103	NCT '653, Morichika, Ng, Emery, Nishimoto, EMA Report, Chernajovsky, SC PK Prior Art
5	103	NCT '653, Morichika, Ng, Maini, Nishimoto, EMA Report, Chernajovsky, SC PK Prior Art
12	103	NCT '653, Morichika, Ng, Kremer 2009, Nishimoto, FDA Review, SC PK Prior Art
12	103	NCT '653, Morichika, Ng, Kremer 2009, Nishimoto, EMA Report, Chernajovsky, SC PK Prior Art

Petitioner also relies upon the Declarations of Dr. Dhaval K. Shah (Exs. 1032, 1138), Dr. Maarten Boers (Exs. 1034, 1119, 1139), Prescott M. Lassman, Esq. (Exs. 1035, 1137), and Dr. Paul A. Dalby (Exs. 1036, 1140). Patent Owner relies on the Declarations of Dr. Steven R. Little (Ex. 2005), Dr. Emil Samara (Ex. 2006), and Dr. Gregg J. Silverman, M.D. (Ex. 2009). We have reviewed the credentials of Petitioner's and Patent Owner's declarants and consider them each to be qualified to provide the opinions for which their testimony has been submitted. *See Kyocera Senco Indus. Tools Inc. v. Int'l Trade Comm'n*, 22 F.4th 1369, 1376–77 (Fed. Cir. 2022) ("To offer expert testimony from the perspective of a skilled artisan in a patent

[16] N. Nishimoto et al., *Humanized Antihuman IL-6 Receptor Antibody, Tocilizumab*, *in Therapeutic Antibodies* 151–60 (Y. Chernajovsky & A. Nissim eds., 2008). Ex. 1009 ("Chernajovsky").

case—like for claim construction, validity, or infringement—a witness must at least have ordinary skill in the art.").

II. ANALYSIS

Petitioner bears the burden of proving unpatentability of the challenged claims, and that burden of persuasion never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). To prevail, Petitioner must prove unpatentability by a preponderance of the evidence.[17] *See* 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d) (2019).

A. Person of Ordinary Skill in the Art

In determining the level of ordinary skill in the art, we consider the type of problems encountered in the art, the prior art solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the educational level of active workers in the field. *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986).

Petitioner asserts that a person of ordinary skill in the art ("POSA") at the time of the invention "would in fact have been a team of individuals possessing the different skill sets typically employed on such a project." Pet. 27. Petitioner asserts that the "team would have included individuals skilled in the relevant area(s) of clinical medicine (e.g., rheumatologists), pharmacokineticists, formulators and project leads" working together as needed. *Id.* (citing Ex. 1034 ¶ 48; Ex. 1032 ¶ 27; Ex. 1036 ¶¶ 25–26).

[17] Although we find certain of Patent Owner's arguments not persuasive, this should never be taken as an indication that we have assigned Patent Owner the burden of proof on patentability.

In our Institution Decision, we noted that defining a POSA as a "team of individuals" is not conventional. Dec. Inst. 8. We therefore found a POSA "would have 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." *Id.* We also clarified that such a POSA "may alternatively (or also) have a Ph.D. and would have access to individuals skilled in clinical medicine, pharmacokinetics and formulation." *Id.*

Patent Owner agrees with Petitioner's definition and notes that a POSA according to our definition from the Institution Decision "would be unable to develop [the claimed inventions] without assistance from other individuals." PO Resp. 7–8 (citing *Daiichi Sankyo Co. v. Apotex, Inc.*, 501 F.3d 1254, 1256–57 (Fed. Cir. 2007). Patent Owner, however, fails to consider the full scope of our definition. Specifically, Patent Owner does not account for the clarification that a POSA "would have access to individuals skilled in clinical medicine, pharmacokinetics and formulation." Dec. Inst. 8. When considering our complete definition, we do not discern a substantive difference between our definition and the parties' definition of a POSA. Petitioner appears to agree. Pet. Reply. 1 n.1 ("The challenged claims are unpatentable no matter which definition of a POSA is used.").

We remain not persuaded that a person of ordinary skill in the art could be thought of as a "team of individuals." We find no support in *Sankyo* for Patent Owner's contention that "a person of ordinary skill in the art can have the knowledge and experience of multiple individuals working across different arts." *See* PO Resp. 8. Rather, in *Sankyo*, the Federal

Circuit looked to the qualifications of the inventors of the patent-at-issue, all of whom were specialists in drug and ear treatments and noted that others working in the same field as the inventors were of the same skill level. *Sankyo*, 501 F.3d at 1257. Finding that such specialty training was a requisite for ordinary skill in the art, the court defined the level of ordinary skill in the art in that case as "a person engaged in developing pharmaceutical formulations and treatment methods for the ear or a specialist in ear treatments such as an otologist, otolaryngologist, or otorhinolaryngologist who also has training in pharmaceutical formulations." *Id.*

We conclude that there is, as Petitioner acknowledges, little substantial difference between the qualifications of the "team" proposed by the parties, and those of the individual skilled artisan defined in our Decision to Institute. Such an individual would have had not only several years of experience researching treatments for autoimmune disorders, including rheumatoid arthritis, but would additionally have access to individuals skilled in clinical medicine, pharmacokinetics and formulation. *See* Dec. Inst. 8. Indeed, Petitioner's expert, Dr. Shah, acknowledges that an individual person of skill in the art "would have had access to individuals skilled in clinical medicine, pharmacokinetics and formulation." Ex. 1032 ¶ 27. This is consistent with our prior definition. We consequently adopt for this Decision the definition of a person of ordinary skill in the art as defined in our Decision to Institute and quoted above. *See* Dec. Inst. 8.

B. Claim Construction

In an *inter partes* review, 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) (2021). 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). "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). Extrinsic evidence is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" *Phillips*, 415 F.3d at 1317.

1. "fixed dose of 162 mg per dose every week or every two weeks"

Independent claims 1 and 10 recite administering "a fixed dose of 162 mg per dose every week or every two weeks." Ex. 1001, Certificate of Correction, claims 1 and 10. Patent Owner asserts that a POSA would have understood the claim phrase to mean "delivering that amount of tocilizumab in a single injection." PO Resp. 9 (citing Ex. 2009 ¶¶ 51, 52). Petitioner disagrees, asserting that Patent Owner's construction improperly imports a "single injection" limitation into the claims that is not consistent with the plain meaning of "a fixed dose of 162 mg per dose." Pet. Reply 3. Having considered the arguments and evidence presented at trial, we agree with Petitioner.

Beginning with the language of the claims, we note the claims do not expressly recite administration of tocilizumab in a single injection. *See* Ex. 1001, Certificate of Correction, claims 1 and 10. Patent Owner relies on the claim term "per dose" to supply that limitation, arguing that "per dose" would be redundant if it meant something besides "per injection." PO

Resp. 9. According to Patent Owner, if the claimed method could be practiced by administering 162 mg tocilizumab over multiple injections, "a fixed dose of 162 mg" would have sufficed and would render the term "per dose" superfluous. *Id.* at 9–10 (citing *Apple, Inc. v. Ameranth, Inc.*, 842 F.3d 1229, 1237 (Fed. Cir. 2016); *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005)).

Petitioner disagrees that "per dose" is superfluous if construed to encompass multiple injections. Petitioner asserts that a "dose" of drug is "the amount administered to a patient at a given interval," which is often given in more than one tablet or injectable drug. Pet. Reply 3 (citing Ex. 1139 ¶¶ 11–14; Ex. 2032, 2; Ex. 2020, 5). Moreover, Petitioner asserts the term "fixed dose" modifies the term "162 mg per dose," and therefore no part of the phrase is redundant. *Id.*

First, we note that both the *Apple* and *Merck* cases cited by Patent Owner are inapposite. In those cases, the Federal Circuit declined to construe the claim term to include features that were already expressly recited in the claims. *See Apple*, 842 F.3d at 1237 ("Construing a claim term to include features of that term already recited in the claims would make those expressly recited features redundant."); *Merck*, 395 F.3d at 1372 (rejecting construction of "about" to include "on an alendronic acid basis" because that phrase was already recited in the claims). Here, the term "per injection" is not recited in any of the claims. *See* Ex. 1001, Certificate of Correction.

Nevertheless, even if, as Petitioner's expert Dr. Boers testified, a POSA would understand the dose of claim 1 and claim 12 "to mean the same thing" despite the absence of "per dose" in claim 12 (*see* Ex. 2080, 62:1–63:4), that is not the end of the analysis. We also must look to the

Specification to construe the term. *See Intel Corp. v. Qualcomm Inc.*, 21 F.4th 801, 810 (Fed. Cir. 2021) (finding proposed construction would render a claim term superfluous, but noting that that does not "inevitably disqualify[] a construction in every patent" and that "conclusions from the claim language advance the claim-construction inquiry only so far").

Here, the Specification reveals that "per dose" does not mean "per injection." Indeed, the Specification treats those terms differently. For example, in describing "the invention," the Specification repeatedly follows "per dose" with an exemplary parenthetical or clause specifying the frequency of administration. For example, the Specification states that "the invention concerns a method of treating an IL-6-mediated disorder . . . wherein the anti-IL-6R antibody is administered as a fixed dose of 162 mg *per dose (e.g. administered every week or every two weeks)*." *See* Ex. 1001, 4:33–38 (emphasis added); *see also id.* at 5:4–8 (stating "[t]he invention also concerns a method of treating an IL-6-mediated disorder . . . wherein the anti-IL-6R antibody is administered as a fixed dose of 324 mg per dose or 648 mg *per dose (e.g. every four weeks or once every month)*") (emphasis added); 24:54–59 (stating "the invention provides a method of treating an IL-6 mediated disorder . . . wherein the anti-IL-6R antibody is administered as a fixed dose of 162 mg *per dose (e.g. every week, every two weeks, or every ten days)*") (emphasis added). Thus, the Specification repeatedly interprets the term "per dose" to describe the frequency of the dose, and not the number of injections to administer the dose.

In contrast, when specifying a single injection, the Specification uses the terms "per injection" or a "single dose." For example, the Specification states, "[a]vailable subcutaneous formulation is in a 1 mL prefilled syringe delivering 0.9 mL 162 mg TCZ *per injection*." *Id.* at 49:55–56 (emphasis

added); *see also id.* at 43:33–34 ("TCZ (180 mg/mL) SC formulation *single dose* of 0.9 mL corresponding to a dose of TCZ 162 mg TCZ") (emphasis added). Thus, although the Specification makes clear when a single injection is used by stating "per injection" or "single dose," the '264 Patent does not use either of those terms in the claims.

As further evidence against Patent Owner's interpretation of "per dose," the Specification shows that administering tocilizumab in a single injection is merely a preferred embodiment of the invention. Indeed, the portions of the Specification cited by Patent Owner suggest a single injection is preferred, but not required. For example, Patent Owner argues that the Specification describes various issues with "higher concentration[s] of tocilizumab" to "develop subcutaneous formulations capable of delivering the amount of tocilizumab in a single injection." PO Resp. 10 (citing Ex. 1001, 39:1–11). But the Specification states that high concentrations of antibody are only found "[i]n one embodiment." *See* Ex. 1001, 22:40–45 (stating "[i]n one embodiment, the anti-IL-6R antibody-containing liquid formulation according to the present invention contains a high concentration of the anti-IL-6R antibody").

Similarly, Patent Owner argues that the Specification describes a "subcutaneous administration device" that "delivers to a patient a fixed dose of an anti-IL-6 receptor (IL-6R) antibody, wherein the fixed dose is . . . 162 mg." PO Resp. 10 (quoting Ex. 1001, 28:21–25). But the Specification then states that "*[p]referably*, the concentration of the antibody in the device is from 150 to 200 mg/mL, for example 180 mg/mL." *See* Ex. 1001, 28:26–28 (emphasis added). Thus, consistent with the preferred embodiment described above, the Specification does not necessarily require the

subcutaneous administration device to contain high concentrations of anti-IL-6R antibody to deliver the drug in a single injection.

Patent Owner also cites the various Examples in the Specification that describe administration of highly concentrated tocilizumab ("162 mg/0.9 mL") in a single "SC injection." PO Sur-reply 3 (citing Ex. 1001, Examples 1–5). But the Examples in the Specification describing the use of single subcutaneous injections are just that—examples. *See id.* at 28:55–47:14 (Examples 1–5). When determining the meaning of "per dose," we consider the statements in the Summary of the Invention describing "the invention" as administering the 162 mg TCZ "per dose (e.g. administered every week or every two weeks)" to carry more weight. *See* Ex. 1001, 4:33–38. We therefore agree with Petitioner that a "dose" of drug is "the amount administered to a patient at a given interval." *See* Pet. Reply 3 (citing Ex. 1139 ¶¶ 11–14; Ex. 2032, 2; Ex. 2020, 5). Thus, we are not persuaded that the Specification supports limiting the construction of the term "per dose" to mean "per injection."

Having considered the arguments and evidence presented at trial, we determine the claim phrase "a fixed dose of 162 mg per dose every week or every two weeks" to mean "a dose of 162 mg administered without regard to the patient's weight or body surface area and administered every week or every two weeks."

2. "[a] method of treating rheumatoid arthritis in a patient"

Independent claims 1 and 10 of the '264 Patent each recite as their preamble "[a] method of treating rheumatoid arthritis in a patient." Ex. 1001, claims 1 and 5. Petitioner asserts that the preamble should not be construed as limiting because it "does not alter how the actual steps of the method are to be performed." Pet. 36 (citing Ex. 1034 ¶ 118; *Bristol-Myers*

Squibb Co. v. Ben Venue Labs, Inc., 246 F.3d at 1375–76 (Fed. Cir. 2001)). Alternatively, if the preamble is construed to be limiting, Petitioner asserts that the limitation "would merely require administering the dose with an intent to treat RA without any particular degree of efficacy." *Id.* (citing Ex. 1034 ¶¶ 121, 122). According to the Petition, the plain meaning of "treating" is "to give a treatment and is not limited by whether that treatment ultimately ends up being effective." *Id.* at 36–37 (citing Ex. 1034 ¶ 119–121; Ex. 1062, 2434–35 (defining "treat" as to "give medical treatment to"; "to seek cure or relief of (as a disease)"); Ex. 1062, 838).

Patent Owner disagrees, arguing that the preamble is limiting and that the Specification defines "treatment" to mean "therapeutic treatment" in a patient diagnosed with RA. PO Resp. 15–16, 11 (citing Ex. 1001, 13:59–14:12, 15:1–2). According to Patent Owner, "therapeutic" means "having a good effect on the body or mind," particularly "relating to the healing of a disease." *Id.* (citing Ex. 2036, 3; Ex. 2037, 3). Patent Owner's expert Dr. Silverman states that "[f]or a rheumatologist, 'treatment' of a patient suggests achieving, rather than *just trying* to achieve, a therapeutic benefit." Ex. 2009 ¶ 53. Patent Owner also asserts that the experts agree that treatment requires consideration of safety and efficacy when administering a drug to patients. *Id.* at 13 (quoting Ex. 2010, 120:10–22; Ex. 2009 ¶¶ 53, 54). Thus, Patent Owner concludes that "[t]herapeutic treatment . . . requires administering a drug that is expected to be safe and effective, which necessarily includes safety and efficacy in treating 'a patient' diagnosed with rheumatoid arthritis." *Id.* at 11 (citing Ex. 2009 ¶¶ 53, 54).

To start, we agree with Patent Owner that the preamble is limiting. "Whether to treat a preamble as a claim limitation is determined on the facts of each case in light of the claim as a whole and the invention described in

the patent." *Storage Tech. Corp. v. Cisco Sys., Inc.*, 329 F.3d 823, 831 (Fed. Cir. 2003). The Federal Circuit "has not hesitated to hold preambles limiting when they state an intended purpose for methods of using a compound." *Eli Lilly & Co. v. Teva Pharms. Int'l GmbH*, 8 F.4th 1331, 1342 (Fed. Cir. 2021). Where, as here, the claims are directed to methods of using a composition for a specific purpose (i.e., treating rheumatoid arthritis), and the method comprises a single step of administering that composition, the Federal Circuit "has generally construed statements of intended purpose in such method claims as limiting." *Id.* at 1340.

Moreover, as Patent Owner notes, the preamble provides antecedent basis for terms in the body of the claims. That is, the preamble recites "treating rheumatoid arthritis (RA) in a patient" and the claims recite "administering to *the* patient" (claims 1 and 10), "*the* RA patient" (claims 3–5), and "administering to *the* RA patient one or more additional drug which treats *the* RA" (claim 6). Thus, considering the claims as a whole and the invention described in the patent, we determine the preamble of the claims to be limiting. *See Eli Lilly*, 8 F.4th at 1343 (finding preamble limiting where it provides antecedent basis for terms in the body of the claims).

We disagree with Patent Owner, however, that the preamble limits "treatment" to require therapeutic benefit that is shown to be safe and effective. *See* PO Resp. 11–15. The problem with Patent Owner's proposed construction is that it is premised on an incomplete quote from the Specification. Patent Owner argues that the Specification "defines 'treatment' as 'therapeutic treatment,'" and, citing Dr. Silverman, that "therapeutic treatment . . . requires administering a drug that is expected to be safe and effective." PO Resp. 11 (citing Ex. 1001, 15:1–2; Ex. 2009 ¶¶ 53–54). Dr. Silverman states that for a rheumatologist, "'treatment' of a

patient suggests achieving, rather than *just trying* to achieve, a therapeutic benefit." Ex. 2009 ¶ 54. Patent Owner and Dr. Silverman, however, ignore the other half of the Specification's definition of "treatment," which states: "'Treatment' of a subject herein refers to *both* therapeutic treatment and prophylactic or preventative measures." *See* Ex. 1001, 15:1–2 (emphasis added). Thus, limiting the definition of "treatment" to mean only "therapeutic treatment," as Patent Owner asserts, is inconsistent with the express definition in the Specification and, therefore, incorrect on its face. *See Phillips*, 415 F.3d at 1316 (stating "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs.").

Moreover, the Specification defines the term "effective amount" as "an amount of the antibody that is effective for treating the IL-6 disorder." *Id.* at 15:3–4. If "treatment" of the IL-6 disorder required efficacy, it would not be necessary for the Specification to define an "effective amount" for treating the disorder separately, as efficacy would be implicit in the term "treatment." Consistent with this, the Specification defines certain subjects as "inadequate responder[s]" to various medications because they have experienced "an inadequate response to previous or current *treatment* . . . because of toxicity or inadequate efficacy." *Id.* at 14:46–61 (emphasis added). Thus, the Specification uses the term "treatment" to encompass treating a patient with a certain medication, regardless of safety or efficacy.

The Federal Circuit recently addressed the construction of a "method of treatment" claim in *United Therapeutics Corp. v. Liquidia Technologies, Inc.*, 74 F.4th. 1360 (2023). There, the claims were directed to a "method of treating pulmonary hypertension" comprising administering a

"therapeutically effective single event dose" of a drug. *Id.* at 1364. The district court construed the claims to not require safety and efficacy beyond the already recited "therapeutically effective" dose. *Id.* at 1368. Liquidia appealed that construction, arguing that a POSA would have understood the plain and ordinary meaning of "treating pulmonary hypertension" to encompass a method that accomplishes that goal safely and effectively. *Id.* Liquidia asserted that a POSA would have concerns about using the drug on certain pulmonary hypertension patients and would not expect the drug to work. *Id.* The Federal Circuit affirmed the district court's construction, stating that "[r]ead in context, the claim language [of the preamble] does not import any additional efficacy limitations or any safety limitations." *Id.* at 1369. The Federal Circuit rejected Liquidia's safety and efficacy arguments, stating "[q]uestions of safety and efficacy in patent law have long fallen under the purview of the FDA." *Id.* The court concluded, stating "[w]e decline to insert FDA responsibilities into claims by importing requirements where they do not recite such limitations." *Id.*

We similarly decline to limit the phrase "method of treating" to require safety and efficacy where the claims do not recite such limitations. This is consistent with the absence of an "effective amount" limitation in the claims and the Specification's definition of "treatment" to include "prophylactic or preventative measures" and to encompass "inadequate responders." *See* Ex. 1001, 15:1–2, 14:46–63; *see also Eli Lilly*, 8 F.4th at 1342 (noting that because the claims encompass prophylactic uses, the claims "encompass a clinical result, [but] they do not *require* such a result"). Thus, like the Federal Circuit in *Eli Lilly*, we find that the preambles of the claims are "statements of the intentional purpose for which the methods must be performed." *See* 8 F.4th at 1342.

We therefore construe the preamble "a method of treating rheumatoid arthritis" to require that the method be performed with an intentional purpose of treating rheumatoid arthritis, regardless of safety and efficacy.

3. *"is found to be inhibited"*

Independent claim 12 recites "wherein structural joint damage at week 24 or week 48 is found to be inhibited." Ex. 1001, Certificate of Correction, claim 12. In our Institution Decision, we did not construe this term expressly, but preliminarily found that the claim requires "making [assessments of structural joint damage] at 24 or 48 weeks." Dec. Inst. 14.

Patent Owner agrees with our preliminary interpretation, asserting that the Specification "makes clear that inhibition of joint damage is 'found' based on assessment." PO Resp. 16. Patent Owner notes that the Specification states, "[a]ccording to this method, structural joint damage can be assessed at week 24 (or 6 months) and/or week 48 (or 1 year) and found to be inhibited (e.g. relative to a patient not treated with an anti-IL-6R antibody)." *Id.* at 16–17 (quoting Ex. 1001, 25:56–59). Patent Owner's expert, Dr. Silverman, testifies that a POSA would understand that "inhibition of joint damage can only be 'found' if inhibition is actually verified using one of the techniques known in the art." *Id.* at 17 (citing Ex. 2009 ¶¶ 55, 56). And Patent Owner notes that Petitioner's expert Dr. Boers "conceded in his deposition that 'found to be' in the patent means 'measurement,' and requires 'drawing a conclusion from data.'" *Id.* (quoting Ex. 2010, 146:12, 147:1–10).

Petitioner argues that claim 12 does not require assessment at week 24 or 48. It simply requires that an assessment at any time is sufficient, as long as that assessment is sufficient to verify that inhibition occurred at week 24 or 48. Pet. Reply 6. Moreover, Petitioner notes that the claim covers a

method that produces "*any* amount of inhibition in *any* patient, at any time that is sufficient to verify the inhibition occurred at week 24 or 48." *Id.* (citing Ex. 1119 ¶¶ 7–12; Ex. 1139 ¶¶ 21–26).

As an initial matter, we note that Patent Owner does not appear to dispute that the claim encompasses a method that produces any amount of inhibition in any patient, as Petitioner proposes. *See generally* PO Resp. 16–17; PO Sur-reply 5. Moreover, the parties' experts agree that the plain meaning of "found to be" requires some form of actual assessment. That is, both Dr. Silverman and Dr. Boers testify that "found to be" suggests an actual measurement (Ex. 2009 ¶ 56) and drawing a conclusion from data (Ex. 2010, 147:6–10). The parties disagree, however, as to when the measurement must occur. Patent Owner argues the measurement must occur at week 24 or week 48 (PO Sur-reply 5), whereas Petitioner argues the measurement can be made at any time as long as the assessment is sufficient to verify inhibition of structural joint damage at week 24 or week 48 (Pet. Reply 6).

We find that the claim language "wherein structural joint damage at week 24 or week 48 is found to be inhibited" is ambiguous as to when the measurement is actually made and can reasonably be interpreted either way. We therefore look to the Specification for guidance. In doing so, we note that the Specification distinguishes between "assess[ing]" structural joint damage and whether it is "found to be inhibited." That is, the Specification states that "[t]he invention" concerns a method where "structural joint damage can be assessed at week 24 (or 6 months) and/or week 48 (or 1 year) and found to be inhibited." Ex. 1001, 25:56–59. The Specification thus equates assessing at 6 months with 24 weeks, and assessing at 1 year with 48 weeks. In other words, the Specification does not require assessment at

precisely week 24 or 48 for structural joint damage to be "found to be inhibited." *See id.* This is consistent with Dr. Silverman's testimony that "there is no substantial difference between Week 48 and Week 52 or plus or minus a couple of weeks." Ex. 1136, 75:17–19. That said, we do not find—and Petitioner does not cite—any intrinsic evidence to support its assertion that the assessment can be made "at any time." Pet. Reply 6. Regardless, we need not reach that issue for purposes of this Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed to the extent necessary to resolve the controversy." (internal quotes omitted)).

We, therefore, determine that "wherein structural joint damage at week 24 or week 48 is found to be inhibited" encompasses a method where any degree of structural joint damage inhibition is found through actual assessment of structural joint damage at approximately week 24 (e.g., 6 months) or approximately week 48 (e.g., 1 year).

C. Ground 1: Alleged Anticipation by NCT '653

Petitioner argues that NCT '653 anticipates claims 1–3 and 6–12. Pet. 40–50. Patent Owner opposes. PO Resp. 17–25. Having considered the arguments and evidence presented at trial, we determine that Petitioner has established by a preponderance of the evidence that NCT '653 anticipates claims 1–3 and 6–11, but not claim 12.

1. NCT '653 (Ex. 1004)

NCT '653 describes a Phase 1 clinical study entitled "A Study of Subcutaneously Administered Tocilizumab in Patients with Rheumatoid Arthritis." Ex. 1004, 1, 6. The summary states "[t]his open-label randomized 2arm 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." *Id.* at 6. 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." *Id.* NCT '653 states that "[a]ssessments will be made at regular intervals during treatment and on the 3 weeks of follow-up." *Id.*

Petitioner asserts NCT '653 is a printed publication that was available on ClinicalTrials.gov before November 2009 and is therefore prior art under 35 U.S.C. § 102(b). Pet. 40. Petitioner explains that the posting renders NCT '653 publicly available because "the very purpose of ClinicalTrials.gov is to make such trials as widely and promptly available to the public as possible." *Id.* (citing Ex. 1035 ¶¶ 13–19, 23).

2. Analysis

"A claim is anticipated if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference." *Arbutus Biopharma Corp. v. ModernaTX, Inc.*, 65 F.4th 656, 662 (Fed. Cir. 2023). The Federal Circuit explains that "[a]nticipation by inherent disclosure is appropriate only when the reference discloses prior art that must *necessarily* include the unstated limitation." *Monsanto Tech. LLC v. I.E. DuPont de Nemours & Co.*, 878 F.3d 1336, 1343 (Fed. Cir. 2018). Inherent anticipation requires "merely that the disclosure of the prior art is sufficient to show that the natural result flowing from the operation as taught in the prior art would result in the claimed product." *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343–44 (Fed. Cir. 2005) (internal quotes omitted). Moreover, "[n]ewly discovered results of known processes directed to the same purpose are not patentable because such results are

inherent." *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001).

a) NCT '653 Was Publicly Available

As an initial matter, Patent Owner argues that Petitioner has failed to show that NCT '653 is prior art because it was not publicly available as of the effective filing date of the '264 Patent. PO Resp. 17–21. Patent Owner asserts that the Declaration of Mr. Lassman (the "Lassman Declaration"), upon which Petitioner relies to prove public accessibility of NCT '653, is deficient in several respects. *Id.* at 17. Specifically, Patent Owner contends that: (1) Mr. Lassman is unqualified; (2) the Lassman Declaration never identifies the specific search parameters a person of skill in the art would have used to locate NCT '653 on the ClinicalTrials.gov website; and (3) other clinical trial registries existed in addition to ClinicalTrials.gov. *Id.* at 18–21.

Regarding Mr. Lassman's qualifications, Patent Owner notes that Mr. Lassman is a regulatory lawyer who has never been employed by NIH, the National Library of Medicine, FDA, nor any other entity responsible for managing the ClinicalTrials.gov database. *Id.* at 18. Patent Owner asserts that Mr. Lassman possesses none of the skills relevant to those of skill in the art and, in forming his opinion, did not consult anyone possessing those skills to discern how an ordinarily skilled artisan would have searched for NCT '653. *Id.* at 18 (citing Ex. 2012, 41:9–42:12, 44:4–45:4, 66:2–6).

Regarding Mr. Lassman's Declaration, Patent Owner argues that Mr. Lassman attests that he was able to "locate[] the record for clinical study number NCT00965653," but never explains how he did so or how many results he had to review to find this particular study. PO Resp. 18–19 (citing Ex. 1035 ¶ 29). Patent Owner asserts that, rather than locate NCT '653

through the type of search a person of ordinary skill in the art might have conducted, e.g., by searching for keywords such as "tocilizumab" or "rheumatoid arthritis," Mr. Lassman located the study by searching for its number, NCT00965653. *Id.* at 19 (citing Ex. 2012, 63:2–9, 66:17–21).

Patent Owner adds that the existence of a search function on ClinicalTrials.gov does not cure this alleged deficiency. *Id.* According to Patent Owner, keyword searches on sites such as ClinicalTrials.gov were "not always reliable because of lack of standardisation of drug names and health conditions," which directly "contributed to the difficulty of using [those] websites." *Id.* (quoting Ex. 2035, 3). Patent Owner states that searching for synonyms in ClinicalTrials.gov sometimes returned inconsistent results or none at all. *Id.* (citing Ex. 2009 ¶ 62; Ex. 2010, 136:5–19).

Finally, Patent Owner notes that Mr. Lassman testified that as of 2009, "a lot of companies had their own registries" hosted on independent websites or "source[s] other than ClinicalTrials.gov," and that other jurisdictions, such as Europe, also had their own registries. *Id.* at 20–21 (citing Ex. 2012, 27:2–16, 29:21–30:9). Patent Owner argues that it is therefore uncertain that an ordinarily skilled artisan, searching for clinical trials, would have necessarily looked to ClinicalTrials.gov as opposed to one of the many other registries available at the time. *Id.* at 21.

Petitioner replies that, based on his testimony, it is indisputable that Mr. Lassman has personal knowledge of how the ClinicalTrials.gov website functioned in 2010. Pet. Reply 6. Petitioner also argues that Mr. Lassman described in detail how ClinicalTrials.gov facilitated public access to clinical trial records and proffered a wealth of evidence establishing that NCT '653 was published on ClinicalTrials.gov more than one year before the filing

date of the '264 Patent. *Id.* at 6–7 (citing Ex. 1035, Sections IV.A, V.A; Ex. 1137 ¶¶ 9–12).

Petitioner asserts that Patent Owner's argument that searching on ClinicalTrials.gov could be unreliable "because of a lack of standardization of drug names" is irrelevant, because the name Actemra had already been approved, and its non-proprietary name of "tocilizumab" had already been standardized internationally by the applicable regulatory authorities. *Id.* at 7 (citing Ex. 1010, 2; Ex. 1024, 1; Ex. 1006, 24). Petitioner notes that its expert Dr. Boers testified that a person of ordinary skill in the art would have "adjust[ed] the keywords" and "play[ed] around with the specifics of the search machine to get what you want" but "after a while" would "come up with satisfactory conclusions." *Id.* at 7–8 (citing Ex. 2010, 136:11–19).

Having considered the evidence and argument presented at trial, we find that NCT '653 was publicly accessible as of the earliest effective filing date of the '264 Patent. We find that Mr. Lassman credibly testifies that he is extensively familiar with the ClinicalTrials.gov website, and additionally, worked on drafting the statute that expanded and governed Clinicaltrials.gov. *See* Ex. 1035 ¶¶ 6, 9. Mr. Lassman testifies that "Clinicaltrials.gov is a site designed to be used by members of the public, not by experts. The site is designed to require less skill in searching clinical trial records than a POSA would have had." Ex. 1137 ¶ 4 (emphasis omitted). More to the point:

> On February 29, 2000, Clinicaltrials.gov was launched by NIH in fulfillment of the above-described statutory requirement for a clinical trials registry. When it was launched, the site was described by NIH as "a consumer-friendly database … with information on more than 4,000 federal and private medical studies involving patients and others at more than 47,000 locations nationwide." NIH confirmed that the site was intended

> to "provide[] patients, families and members of the public easy access to information about the location of clinical trials, their design and purpose, criteria for participation, and, in many cases, further information about the disease and treatment under study."

Ex. 1035 ¶ 14 (quoting Ex. 1063, internal citation omitted) (alteration in original).

Patent Owner's argument that Mr. Lassman is not qualified to opine with respect to this subject matter is not persuasive, given Mr. Lassman's intimate knowledge of, and experience with, the ClinicalTrials.gov website. *See* Ex. 1035 ¶ 6. Moreover, the NIH press release, quoted in the passage above, expressly states that the website provides easy access to information concerning clinical trials to "patients, families and members of the public." *See* Ex. 1063. We thus find persuasive Mr. Lassman's testimony that NCT '653 was publicly accessible on the ClinicalTrials.gov website as of the priority date of the '264 Patent.

b) Alleged Anticipation of Claims 1–3 and 6–12 by NCT '653

Claims 1–3 and 6–11

Petitioner provides a detailed explanation of how NCT '653 discloses each limitation of independent claims 1 and 10. Pet. 42–47. Patent Owner disagrees with Petitioner's analysis. PO Resp. 21–23. Having considered the arguments and evidence presented at trial, we find that Petitioner has shown by a preponderance of the evidence that NCT '653 discloses each limitation of those claims.

We address each limitation of claims 1 and 10 below.

(1) "A method of treating rheumatoid arthritis (RA) in a patient comprising"

We find NCT '653 discloses the preamble because it describes a study to "investigate the pharmacokinetics, pharmacodynamics, efficacy and

safety of subcutaneously administered tocilizumab in patients with rheumatoid arthritis." Ex. 1004, 6; Ex. 1034 ¶ 127. As Petitioner notes, NCT '653 states that "assessments will be made at regular intervals during ***treatment*** and on the 3 weeks follow-up." Pet. 42–43 (quoting Ex. 1004, 6); *see also* Ex. 1004, 8 (describing sampling at various intervals during and throughout "treatment"). We credit the testimony of Dr. Boers, who explains that the because the study protocol requires assessing the treatment's efficacy at certain intervals, a POSA would understand that the tocilizumab was administered to the patients in NCT '653 with the intent to treat RA. Ex. 1034 ¶ 127.

(2) "subcutaneously administering [an anti-IL-6 receptor (IL-6R) antibody (claim 1)]/[tocilizumab (claim 10)] to the patient"

We find NCT '653 discloses this limitation because it discloses a study of "subcutaneously administer[ing] tocilizumab in patients" with rheumatoid arthritis. Ex. 1004, 6; Ex. 1034 ¶ 129. Regarding claim 10, we find that Petitioner has shown that a POSA would have understood that tocilizumab is "an anti-IL-6R antibody." *See* Pet. 42 (citing Ex. 1032 ¶ 187; Ex. 1034 ¶¶ 52, 129); Ex. 1001, 5:9–10 ("The invention also concerns subcutaneously administering an anti-IL-6R antibody (e.g. tocilizumab)").

(3) "wherein the [anti-IL-6R antibody (claim 1)]/[tocilizumab (claim 10)] is administered as a fixed dose of 162 mg per dose every week or every two weeks"

We find NCT '653 discloses this limitation because it discloses that patients received subcutaneously162 mg tocilizumab either every week or every other week, regardless of body weight or body surface area (i.e., a fixed dose). *See* Ex. 1004, 6 (stating "[p]atients will be randomized to receive tocilizumab 162 mg sc either weekly or every other week");

Ex. 1034 ¶ 130 ("The 162 mg dose is 'fixed' because it does not vary with body weight, body surface area or other criteria.").

(4) "wherein the anti-IL-6R antibody comprises the light chain and heavy chain amino acid sequences of SEQ ID Nos. 1 and 2, respectively" (claim 1)

We find NCT '653 discloses this limitation of claim 1. As Dr. Boers explains, and Patent Owner does not dispute, a POSA would have understood that the light and heavy chains of tocilizumab have the amino acid sequences of SEQ ID Nos. 1 and 2, respectively. *See* Ex. 1034 ¶¶ 132–138; *see also* Ex. 1001, 6:60–62 ("FIGS. 7A and 7B depict the amino acid sequences of the light chain (FIG. 7A; SEQ ID NO:1) and heavy chain (FIG. 7B; SEQ ID NO:2) of Tocilizumab.").

Regarding claims 2, 3, and 6–9, which depend directly or indirectly from claim 1, and claim 11, which depends from claim 10, Petitioner asserts that NCT '653 discloses the additional limitations of those claims. Pet. 47–48. We have considered the arguments and evidence presented by the Petition and find Petitioner has shown by a preponderance of the evidence that NCT '653 discloses each limitation of those claims, as well, for the reasons stated in the Petition, which we adopt as our own. *See id.* (citing Ex. 1004, 6, 7, 9; Ex. 1001, 14:22–33; Ex. 1034 ¶¶ 139–42). Patent Owner does not argue separately the patentability of those dependent claims. *See* PO Resp. 21–23.

Rather, Patent Owner argues that NCT '653 does not anticipate any of the challenged claims because it does not disclose, either expressly or inherently, the subcutaneous administration of the claimed amount of tocilizumab "in a single injection." PO Resp. 21–22. As explained above, however, the claims are not limited to administering tocilizumab in a single

injection. *See supra* Section II.B.1 (declining to construe "per dose" to require a single injection). Patent Owner's argument, therefore, fails on its face.

Patent Owner also argues that NCT '653 does not contain "any statement or suggestion on the efficacy of the subcutaneous dosing regimen." PO Resp. 22–23. But, as explained above, the claims do not require efficacy; they simply require performing the method with an intent to treat rheumatoid arthritis. *See supra* Section II.B.2 (construing "method of treating rheumatoid arthritis" to require that the method be performed with an intentional purpose of treating rheumatoid arthritis, regardless of actual safety or efficacy). We find that NCT '653 expressly discloses that intentional purpose of treating rheumatoid arthritis when it repeatedly refers to making assessments "during treatment." *See, e.g.*, Ex. 1004, 6 (stating "[a]ssessments will be made at regular intervals during treatment"); *id.* at 8 (describing assessing various outcome measures at certain intervals "during treatment"); *see also* Ex. 1034 ¶ 127 (opining that in light of the assessments described in NCT '653, "tocilizumab was administered to the patients in *NCT '653* with the intent to treat RA").

We therefore conclude that Petitioner has shown by a preponderance of the evidence that NCT '653 discloses each limitation of claims 1–3 and 6–11.

Claim 12

Regarding independent claim 12, which recites a "method of inhibiting progression of structural joint damage in a rheumatoid arthritis patient" and "wherein structural joint damage at week 24 or week 48 is found to be inhibited," Petitioner asserts that a POSA would have understood that the method of treating rheumatoid arthritis in NCT '653

encompasses treating the symptoms of RA, including structural joint damage, and therefore anticipates claim 12. Pet. 48–50. And, to the extent the claim requires the step of actually finding inhibition, Petitioner asserts that NCT '653 discloses examining patients at regular intervals to determine efficacy. *Id.* at 49 (citing Ex. 1004, 6). Moreover, Petitioner notes that although NCT '653 does not expressly identify structural joint damage as a symptom to be measured as a secondary outcome, it does teach assessing plasma levels of TCZ and other factors that would indicate inhibition of joint damage. *Id.* at 49–50 (citing Ex. 1004, 8; Ex. 1034 ¶ 146).

In our Institution Decision, we were not persuaded that Petitioner had shown sufficiently that there is a reasonable likelihood that it would prevail in showing that NCT '653 anticipates claim 12. Dec. Inst. 13–14. Because Petitioner admitted that NCT '653 does not expressly measure structural joint damage (Pet. 49), we found Petitioner had not shown sufficiently that NCT '653 inherently discloses the limitation that "structural joint damage at week 24 or week 48 is found to be inhibited." Dec. Inst. 14. Specifically, we noted that it appears the study described in NCT '653 extends for only 15 weeks (i.e., 12 weeks of treatment and 3 weeks of follow-up), and not the requisite 24 or 48 weeks. *Id.* (citing Ex. 1004, 6 (stating patients will "receive tocilizumab 162 mg sc either weekly or every other week . . . for 12 weeks. Assessments will be made at regular intervals during treatment and on the 3 weeks of follow-up")).

Petitioner and its expert Dr. Boers now argue that although NCT '653 only tested the regimen for 12 weeks, a POSA would have understood that the regimen being tested was "designed for *chronic use*, well past 24 or 48 weeks." *See* Ex. 1139 ¶ 36 (citing Ex. 1004, 7); Pet. Reply 9. Petitioner also cites Example 3 of the '264 Patent, which states that radiographic

assessment "will be explored" at weeks 24 and 48, suggesting that the inventors expected inhibition of the progression of structural joint damage at week 24 and 48 without actually performing the analysis. *Id.* at 10.

We do not find Petitioner's argument persuasive. Inherent anticipation requires that NCT '653 "must *necessarily* include the unstated limitation." *See Monsanto*, 878 F.3d at 1343 (emphasis added). Petitioner, however, cites to insufficient evidence to establish that NCT '653 necessarily discloses the step of finding structural joint damage inhibition at week 24 or week 48. *See* Pet. Reply 9–10 (citing Ex. 1139 ¶ 36; Ex. 1034 ¶ 144; Ex. 1139 ¶¶ 22, 23, 68; Ex. 1128; Ex. 1154; Ex. 1046, 15–16; Ex. 1127). That the '264 Patent states assessments "will be explored" at weeks 24 and 48 is irrelevant as to what NCT '653 necessarily discloses. At best, Petitioner's argument amounts to what a POSA *could* do, not what it necessarily *would do* based on the disclosure of NCT '653. That is insufficient as a matter of law. *See HTC Corp. v. Cellular Comm'cns Equip., LLC*, 877 F.3d 1361, 1369 (Fed. Cir. 2017) ("Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.") (citations omitted).

We therefore find Petitioner has not shown by a preponderance of the evidence that NCT '653 inherently anticipates claim 12.

Conclusion

Accordingly, having considered the arguments and evidence presented at trial, we determine that Petitioner has demonstrated by a preponderance of the evidence that NCT '653 anticipates claims 1–3 and 6–11, but does not anticipate claim 12.

D. Ground 2: Alleged Obviousness of Claims 1–3 and 6–11 over NCT '653 and Morichika

Petitioner argues claims 1–3 and 6–11 of the '264 Patent are unpatentable as obvious over the combination of NCT '653 and Morichika. Pet. 50–52. Patent Owner opposes. PO Resp. 25–30.

Based on the record presented at trial, we determine Petitioner has shown by a preponderance of the evidence that the challenged claims would have been unpatentable as obvious over NCT '653 and Morichika.

We incorporate here our earlier findings and discussion regarding NCT '653.

1. Morichika (Ex. 1110)

Morichika is a certified English translation of an international patent application from a group of Chugai scientists published on July 9, 2009, thereby making it prior art to the challenged claims. Ex. 1001, 1, 3; PO Resp. 25. Patent Owner does not argue otherwise. *See generally* PO Resp.; PO Sur-reply.

Morichika relates to highly concentrated antibody-containing formulations suitable for subcutaneous administration. Ex. 1001, Abstract, ¶ 1. Morichika explains that most known antibody formulations are used for intravenous injection, but there is "growing demand" for antibody-containing formulations that can be self-injected subcutaneously. *Id.* ¶ 2. Morichika further explains that for antibody-containing formulations for subcutaneous injection, "it is necessary to increase the concentration of antibody in the injection solution because the amount of antibody administered per dose is large (about 100-200 mg), which the amount of injection solution is generally limited." *Id.* ¶ 3. Morichika notes that highly concentrated antibody solutions "tend to form highly viscous solutions" and

"are prone to aggregate formation" and "loss of bioactivity due to deamidation of amino acid residues. *Id.* ¶ 4. Accordingly, Morichika states that the purpose of its invention is to "provide a stable, highly concentrated antibody-containing formulation suitable for subcutaneous administration, in which dimer formation and deamidation are suppressed during longer-term storage." *Id.* ¶ 7. Morichika then states that "[a]s a result of intensive research . . . , the inventors found that adding arginine or its salt . . . as a stabilizer could produce a stable antibody-containing solution formulation at a high concentration." *Id.* ¶ 8.

Morichika states that its highly concentrated antibody-containing liquid formulations are "especially suited for subcutaneous injection." *Id.* ¶ 53. Morichika also states that "the antibody concentration of the highly concentrated antibody solution formulation of the present invention is preferably 50–300 mg/mL, . . . especially 150–200 mg/mL." *Id.* ¶ 15. Moreover, "[h]umanized anti-IL-6 receptor antibody is particularly preferred as a humanized antibody for use in the present invention." *Id.* ¶ 29. Morichika then describes specific examples of highly concentrated solutions using an anti-IL-6R antibody referred to as "MRA" (i.e., tocilizumab[18]). *Id.* ¶¶ 9, 61. In each sample prepared of the MRA formulation, Morichika uses a concentration of 180 mg/mL MRA. *Id.* ¶¶ 64 (Table 1-1), 73 (Tale 2-1), 82 (Table 3-1).

2. Analysis

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

[18] According to Dr. Boers, tocilizumab was previously referred to as MRA. Ex. 1034 ¶ 78; *see also* Ex. 1040, 2817 ("tocilizumab (previously known as MRA)").

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). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

In analyzing the obviousness of a combination of prior art elements, it can be important to identify a reason that would have prompted one of skill in the art "to combine . . . known elements in the fashion claimed by the patent at issue." *KSR*, 550 U.S. at 418. A precise teaching directed to the specific subject matter of a challenged claim is not necessary to establish obviousness. *Id.* Rather, "any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *Id.* at 420. Accordingly, Petitioner must show 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." *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016) (quotations and citations omitted).

Petitioner argues that a person of ordinary skill in the art would have combined NCT '653 with Morichika, because Morichika's subcutaneous formulation would have been suitable for use in NCT '653's clinical trial. Pet. 50–51 (citing Ex. 1034 ¶ 149). Petitioner argues that a person of ordinary skill would have been motivated to do so due to the well-known advantages of subcutaneous administration over the intravenous route. *Id.*

(citing Ex. 1034 ¶¶ 62–65, 149; Ex. 1110 ¶ 53). For example, subcutaneous administration takes less time and does not require a visit to the clinic, improves patient compliance because it is self-administered, and avoids spikes and troughs in serum plasma concentrations that can cause adverse effects. Ex. 1034 ¶ 62.

Petitioner further argues that a person of ordinary skill would have had a reasonable expectation of success in making the combination because using Morichika's formulations in the NCT '653 protocol "would have involved only routine skill." *Id.* at 51 (citing Ex. 1034 ¶ 150; Ex. 1036 ¶ 37). Moreover, Petitioner argues that a POSA would have had a reasonable expectation of efficacy in at least some patients because "162 mg of tocilizumab administered SC QW or Q2W would produce roughly similar antibody exposure as the 4 mg/kg [IV] monthly dose that was known to be effective." *Id.* at 52 (citing Ex. 1034 ¶¶ 153–157). Petitioner also notes that Roche sponsored NCT '653, had announced that subcutaneous Actemra was "in development," and stated that the "preferred" form of administering tocilizumab was "thought to be subcutaneous formulation." *Id.* at 51 (citing Ex. 1071, 4; Ex. 1072 slide 12; Ex. 1030, 4; Ex. 1034 ¶¶ 69, 154–157).

As explained above, we find Petitioner has shown by a preponderance of the evidence that NCT '653 anticipates claims 1–3 and 6–11 of the '264 Patent. Thus, for the same reasons we find NCT '653 anticipates claims 1–3 and 6–11, we find Petitioner has shown that the combination of NCT '653 and Morichika renders those claims obvious. *See Realtime Data, LLC v. Iancu*, 912 F.3d 1368, 1373 (Fed. Cir. 2019) ("[I]t is well settled that a disclosure that anticipates under § 102 also renders the claim invalid under § 103, for anticipation is the epitome of obviousness.") (internal quotations and citations omitted).

That said, even if the claims were construed to be limited to administering tocilizumab subcutaneously in a single injection, as Patent Owner asserts, we find the claims would still be unpatentable as having been obvious at the critical time.

Petitioner asserts that a POSA would have been motivated to modify NCT '653 in view of Morichika's disclosure of highly concentrated tocilizumab formulations and administer subcutaneously a fixed dose of 162 mg tocilizumab in a single injection with a reasonable expectation of success. Pet. 50–51 (citing Ex. 1034 ¶¶ 149–150). Dr. Boers explains the clinical benefits of administering a single injection, testifying that a POSA would have been motivated to minimize the number of injections given to a patient "for purposes of patient compliance and comfort, including ease of administration and less pain, and to reduce needle-stick injuries to the healthcare workers administering the injections." Ex. 1139 ¶ 51. Dr. Boers further explains that Morichika's statements that the formulation of tocilizumab was stable and highly concentrated would have motivated the POSA to use that formulation, which would have enabled the POSA to give the 162 mg dose in a single injection subcutaneously. *Id.*; *see* Ex. 1110 ¶¶ 14–15, 33.

Patent Owner disagrees, arguing that "nothing in *Morichika* suggests that any of the formulations it contains were ever administered to humans," and that a POSA would not have reasonably expected success. PO Resp. 26 (citing Ex. 2005 ¶ 49; Ex. 2009 ¶¶ 77–80); *see also* PO Sur-reply 11–13. Patent Owner's expert Dr. Little explains that Morichika does not disclose the formulation actually used to administer subcutaneous tocilizumab and criticizes Patent Owner's expert Dr. Dalby because he never explains why a POSA would have picked the one formulation that was "essentially the

same" as the one the FDA eventually approved as safe and effective. PO Resp. 26 (citing Ex. 2005 ¶¶ 50–52). Moreover, Patent Owner argues there would not have been a reasonable expectation of success given the many issues with highly concentrated antibody formulations, like increased viscosity, aggregation, and what kind of device would be used to administer the drug. *Id.* at 26–30 (citing Ex. 2013, 8–14; Ex. 2005 ¶¶ 17–19).

Having considered the parties' respective arguments, we find Petitioner has the better position. We find Patent Owner applies an improperly heightened standard to its reasonable expectation of success argument. Although it is true that Morichika does not expressly state that any of the formulations were actually administered to humans, the law does not require it to. Morichika "is prior art for all that it teaches." *See Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551 (Fed. Cir. 1989). And Morichika teaches a highly concentrated antibody-containing formulation "suitable for subcutaneous administration." Ex. 1110 ¶ 7. Moreover, as the Federal Circuit has said, "our case law makes clear that a showing of reasonable expectation of success in a method of treatment claim need not rely on clinical data . . . nor must it include a demonstration of certainty that the treatment would be successful in every instance." *Eli Lilly*, 8 F.4th at 1346. This is particularly true where, as here, the claims do not recite an "effective amount" or "efficacy" limitation. *Cf. OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1385 (Fed. Cir. 2019) (finding no reasonable expectation of success where claims recited administering a "therapeutically effective amount" of drug to treat non-small cell lung cancer [NSCLC] and prior art references "contain no data or other promising information regarding [the drug's] efficacy in treating NSCLC"). All that the claims require is that the method be performed with an

intentional purpose of treating rheumatoid arthritis, regardless of safety and efficacy. *See supra* Section II.B.2.

Viewing the evidence as a whole, we find a POSA would have had a reason to administer tocilizumab according to the dosing regimen of NCT '653 in a single subcutaneous injection in view of Morichika's high-concentration tocilizumab formulations with a reasonable expectation of success. Unlike those cases where the prior art provided no information, direction or suggestion that would have led to a reasonable expectation of success (*see, e.g.*, *Eli Lilly*, 8 F.4th at 1346–47), we find Morichika and the state of the art provide ample information and direction to provide a POSA with a reasonable expectation of success in achieving the claimed invention.

As an initial matter, we credit the testimony of Dr. Dalby that a POSA would look to Morichika because it was published by Patent Owner Chugai, the innovator of tocilizumab. Ex. 1140 ¶ 16. That is, a POSA who was attempting to formulate a 162 mg subcutaneous dosage form of tocilizumab would have started with a formulation published by the innovator, who would reasonably be expected to have the most up-to-date information regarding how that drug should be formulated. *Id.*

With that as background, a POSA would understand that Morichika describes various tocilizumab formulations that are "especially suited for subcutaneous injection." Ex. 1110 ¶ 53. Morichika also states that "there have been no examples of commercial use of antibody-containing solution formulations of 120 mg/mL or higher, preferably 150 mg/mL or higher, and [that] the formula of the present invention enabled the commercial use of such highly concentrated antibody-containing solution formulations for the first time." *Id.* ¶ 14. Importantly, Morichika addresses the various concerns raised by Patent Owner relating to high-concentration antibody formulations,

such as deamidation, aggregation, and viscosity (*see* PO Resp. 26–27), and includes examples with recipes of formulations of high-concentration tocilizumab that address those concerns. *See* Ex. 1110 ¶¶ 33, 61–83 (describing results of study showing synergistic effect of the combined use of arginine and methionine as a stabilizer to make a stable tocilizumab formulation with less dimerization and prevention of deamidation); *see also id.* ¶¶ 9, 55, claim 13 (describing preferable viscosity of formulation); Ex. 1140 ¶¶ 19–28 (explaining Morichika's formulations and the studies evaluating their stability). Because Morichika found formulation A8/A26 to be one of the two most stable formulations, we credit the testimony of Dr. Dalby that "[t]here is no reason why a POSA trying to formulate a 162 mg fixed dose of tocilizumab would not have tried to formulate using one of these stable formulations (A8 or A9, identical to A26 or A27)." *See* Ex. 1140 ¶¶ 18–25 (explaining why, based on the data presented in Morichika, a POSA would have chosen the two most stable formulations, A8/A26 or A9/A27, which are similar to the formulation described in the '264 Patent).

Patent Owner argues that Dr. Dalby "concedes that the formulation actually used to administer subcutaneous tocilizumab is not among those listed in *Morichika*." PO Resp. 26; *see also* Ex. 2005 ¶ 51 ("[N]otably absent from the number of formulations disclosed in *Morichika* is the actual formulation disclosed in Table 2 of the '264 . . . Patent[]."). Patent Owner and its expert Dr. Little also assert that even minor differences in formulations can change their pharmacokinetic characteristics when administered to patients. PO Resp. 26; Ex. 2005 ¶¶ 49, 53. The problem with Patent Owner's argument, however, is that the claims do not require a specific formulation. That Morichika does not disclose "the formulation actually used" is inapposite. *See* PO Resp. 26. Rather, "[t]he reasonable

expectation of success requirement refers to the likelihood of success in combining references to meet the limitations of the *claimed invention*." *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016) (emphasis added).

Because Morichika—and the innovators of tocilizumab—describe various highly concentrated formulations of tocilizumab that are "suitable for subcutaneous administration," we find that a POSA would have had a reasonable expectation of success that the tocilizumab dosing regimen of NCT '653 could be administered in a single injection to treat rheumatoid arthritis in view of Morichika's disclosure of its high-concentration tocilizumab formulations.

Thus, having considered the arguments and evidence presented at trial, we find that the combination of NCT '653 and Morichika teaches or suggests each limitation of claims 1–3 and 6–11 and that a POSA would have had a reason to combine the references with a reasonable expectation of success in reaching the claimed invention.

Before considering Patent Owner's objective evidence of nonobviousness, we address the remaining grounds challenging claims 4, 5, and 12 as having been obvious at the critical time.

E. Grounds 3–4: Alleged Obviousness of Claims 4 and 5

Petitioner asserts that claim 4 would have been obvious over NCT '653, Morichika, and Emery. Pet. 53–54. Petitioner also asserts that claim 5 would have been obvious over NCT '653, Morichika, and Maini. *Id.* at 55. Patent Owner opposes. PO Resp. 30–34.

Based on the record presented at trial, we determine Petitioner has shown by a preponderance of the evidence that claims 4 and 5 are

unpatentable as obvious over the cited art. We incorporate here our earlier findings and discussion regarding NCT '653 and Morichika.

1. Emery (Ex. 1043)

Emery is a journal article that appears to have been published in 2008, thereby making it prior art to the challenged claims. Ex. 1043. Patent Owner does not assert otherwise. *See generally* PO Resp. Emery describes a clinical trial study relating to IL-6 receptor inhibition in RA patients who failed to respond or did not tolerate one or more tumor necrosis factor ("TNF") antagonists (i.e., the patients were refractory to TNF). Ex. 1043, 1516. Specifically, Emery discloses that "[t]ocilizumab plus methotrexate is effective in achieving rapid and sustained improvements in signs and symptoms of RA in patients with inadequate response to TNF antagonists and has a manageable safety profile." *Id.*

2. Maini (Ex. 1040)

Maini is a journal article that appears to have been published in 2006, thereby making it prior art to the challenged claims. Ex. 1040. Patent Owner does not assert otherwise. *See generally* PO Resp. Maini describes a clinical trial study relating to the efficacy of "tocilizumab (previously known as MRA), a humanized anti-interleukin-6 (IL-6) receptor antibody, alone and in combination with methotrexate (MTX), for the treatment of rheumatoid arthritis (RA)." Ex. 1040, 2817. Maini states that TCZ "was used either as monotherapy (by discontinuation of MTX) or concomitantly with MTX therapy." *Id.* at 2818. Maini discloses that a "20% response (improvement) according to the American College of Rheumatology criteria (ACR20 response) was achieved by 61% and 63% of patients receiving 4 mg/kg and 8 mg/kg of tocilizumab as monotherapy, respectively, and by 63% and 74% of patients receiving those doses of tocilizumab plus MTX." *Id.* Maini

states that "[t]he results of this study clearly show that infusions of tocilizumab every 4 weeks, with or without background MTX therapy, can produce marked and dose-related improvement in RA disease activity." *Id.* at 2826.

3. Analysis

Claim 4 depends from claim 1 and further recites that the patient be a "TNF-inhibitor-inadequate responder." Ex. 1001, Certificate of Correction, claim 4. Petitioner asserts that Emery teaches that the combination of TCZ and MTX was effective in treating RA in TNF-non-responders. Pet. 53–54 (citing Ex. 1043, 1522; Ex. 1034 ¶¶ 61, 159–160). Petitioner argues that the known efficacy of TCZ and MTX in TNF inhibitor-inadequate responders, as well as the commercial approval of its use, "would have motivated a POSA to treat such patients with the fixed-dose SC regimen" of NCT '653. *Id.* at 54 (citing Ex. 1006, 55; Ex. 1034 ¶ 161). Petitioner adds that a person of ordinary skill in the art would have been further motivated by the known advantages of subcutaneous formulations over IV formulations. *Id.* (citing Ex. 1034 ¶ 161).

Claim 5 depends from claim 1 and further recites that the patient be "methotrexate (MTX) naïve or has discontinued MTX." Ex. 1001, Certificate of Correction, claim 5. Petitioner asserts that Maini describes the results of a study in which TCZ was used as monotherapy "by discontinuation of MTX" or together with MTX, and reports that both treatments were safe and efficacious. Pet. 55 (citing Ex. 1040, 2818, 2821; Ex. 1034 ¶¶ 61, 166–167). Petitioner argues that in light of this known efficacy, and for the same reasons asserted for claim 4, claim 5 would have been obvious. *Id.*

In response, Patent Owner argues that neither Emery nor Maini supports Petitioner's argument that a POSA would have been motivated to use the claimed method of treatment in the patient populations of claims 4 and 5. PO Resp. 31. Specifically, Patent Owner argues that a POSA would have understood that the high-concentration required for subcutaneous administration could increase the risk of an immunogenic reaction, tissue damage, and formation of neutralizing anti-drug antibodies. *Id.* (citing Ex. 2009 ¶¶ 85–88; Ex. 2030, 3, 5; Ex. 2020, 9; Ex. 2022, 2; Ex. 2031, 5). Patent Owner also asserts that TNF-α and MTX inadequate responders ("TNF-IR" and "MTX-IR," respectively) like the patients in claims 4 and 5 can have poor overall prognosis and various other issues that complicate their treatment, which was known to be due in part to immunogenic reactions. *Id.* at 32 (citing Ex. 2009 ¶¶ 84–88). According to Patent Owner, because the prior art taught away from subcutaneous dosing of tocilizumab, a POSA would not have been motivated to administer NCT '653's subcutaneous dosing regimen to the TNF-IR and MTX-IR patients in Emery and Maini. *Id.* at 33 (citing Ex. 2030,[19] 6).

We do not agree with Patent Owner's arguments. As Patent Owner's expert, Dr. Silverman notes, a POSA would have understood from Emery and Maini that tocilizumab was effective in TNF-inhibitor-inadequate responders and MTX naiive or discontinued patients. Ex. 2009 ¶¶ 82, 83. Moreover, we credit the testimony of Dr. Boers that any acute immunogenic events caused by subcutaneous administration would be within the high

[19] Braun et al., *Protein Aggregates Seem to Play a Key Role Among the Parameters Influencing the Antigenicity of Interferon Alpha (IFN-a) in Normal and Transgenic Mice*, 14 Pharm. Res. 1472–78 (1997) (Ex. 2030, "Braun").

level of skill in the art and manageable by a POSA. *See* Ex. 1139 ¶¶ 43–45; Ex. 1142; Ex. 1143 (showing co-administration of methotrexate with adalimumab and infliximab effectively reduced immunogenicity). Moreover, as Petitioner notes, Patent Owner's reliance on Braun as teaching away is not persuasive, particularly given that it does not specifically concern tocilizumab and was published ten years before NCT '653. Pet. Reply 16 (citing Ex. 1139 ¶¶ 38, 39, 56). To the extent Patent Owner repeats its arguments regarding the lack of reasonable expectation of success, we have addressed those arguments above.

Accordingly, based on the arguments and evidence presented at trial, we find that (1) the combination of NCT '653, Morichika, and Emery teaches or suggests each limitation of claim 4, (2) the combination of NCT '653, Morichika, and Maini teaches or suggests each limitation of claim 5, and (3) a POSA would have had a reason to combine the references with a reasonable expectation of success in reaching the claimed invention.

We address Patent Owner's objective evidence of nonobviousness below. But first, we turn to Petitioner's obviousness challenge to claim 12.

F. Ground 5: Alleged Obviousness of Claim 12

Petitioner asserts that claim 12 would have been obvious over NCT '653, Morichika, and Kremer 2009. Pet. 55–56. Patent Owner opposes. PO Resp. 34–39.

Based on the record presented at trial, we determine Petitioner has shown by a preponderance of the evidence that claim 12 is unpatentable as obvious over the cited art. We incorporate here our earlier findings and discussion regarding NCT '653 and Morichika.

1. Kremer 2009 (Ex. 1029)

Kremer 2009 discloses an abstract entitled "LITHE: Tocilizumab Inhibits Radiographic Progression and Improves Physical Function in Rheumatoid Arthritis (RA) Patients (Pts) at 2 Yrs with Increasing Clinical Efficacy Over Time." Ex. 1029, 516. Kremer 2009 appears to have been published in October 2009 from the 73rd Annual Scientific Meeting of the American College of Rheumatology (October 16–21, 2009), thereby making it prior art to the challenged claims. Ex. 1029. Patent Owner does not assert otherwise. *See generally* PO Resp.

Kremer 2009 "report[s] the results of a 2-yr planned analysis of a double-blind, randomized controlled, phase 3 trial of TCZ in [patients] with moderate to severe RA who remained on MTX despite inadequate response," also referred to as the LITHE study. Ex. 1029, 516; Ex. 1119 ¶ 4. Kremer 2009 discloses that patients in the clinical trial received "TCZ + MTX (4 mg/kg [TCZ4] or 8 mg/kg [TCZ8]) or placebo + MTX (control [CON]) every 4 wks." Ex. 1029, 516. "At wk 52, all pts were required to initiate open-label TCZ8 for yr 2, unless they had achieved ≥ 70% improvement in SJC and TJC, allowing them to continue the blinded therapy they were receiving at the end of yr 1 to wk 104." *Id.* Moreover, the "[p]rimary 2-yr end points were change from baseline in Genant-modified Total Sharp Score (GmTSS) and physical function." *Id.*

Kremer 2009 discloses that "clinically significant improvements in SJC [swollen joint count] occurred [] that were maintained through [week] 104" in patients treated with TCZ. *Id.* Additionally, Kremer 2009 discloses "significantly less radiographic progression (81% inhibition)" in the TCZ8 group. *Id.* Kremer 2009 explains that "TCZ + MTX continues to inhibit radiographic progression and improve physical function with a clinical

effect, as evidenced by improving DAS28 [disease activity score] remission, LDAS [low disease activity state], and SJC at 2 yrs and with a manageable safety profile." *Id.*

2. Analysis

Petitioner asserts that the prior art disclosed that tocilizumab "was effective in inhibiting structural joint damage." Pet. 55 (citing Ex. 1034 ¶¶ 169–170). Petitioner's expert Dr. Boers explained that Kremer 2008[20] reported the results after 12 months from the same LITHE clinical trial as Kremer 2009. Ex. 1034 ¶ 169. Dr. Boers explained that the results of Kremer 2008 established that tocilizumab "significantly inhibited the progression of structural joint damage" and that "the percentage of patients showing no progression of joint erosion, joint space narrowing or progression in Genant-modified total Sharp score (GnTSS) were essentially the same for the 4 mg/kg and 8 mg/kg groups." *Id.* (citing Kremer 2008 at Table).

Petitioner asserts that Kremer 2009 teaches administering 4 mg/kg or 8 mg/kg IV TCZ every four weeks for 12 months and found that patients receiving 4 mg/kg had almost the same inhibition of structural joint damage as those receiving 8 mg/kg IV TCZ, showing similar percentages of "no GmTSS progression." Pet. 55–56 (citing Ex. 1029, Table A; Ex. 1028). Petitioner also asserts that an assessment near the 52-week mark, including 48 weeks, would have been obvious, as doctors typically assess

[20] Kremer et al., *Tocilizumab Inhibits Structural Joint Damage in Rheumatoid Arthritis Patients with an Inadequate Response to Methotrexate: The LITHE Study*, 58 ARTHRITIS & RHEUMATISM 4031 (2008) (Ex. 1028, "Kremer 2008").

joint damage "around" the one-year mark. Pet. Reply 22 (citing Ex. 1136, 75:21–76:10; Ex. 1119 ¶¶ 9–15, 28)

In response, Patent Owner argues that neither NCT '653 nor Morichika describe any parameters necessary for assessing progression of joint damage. PO Resp. 34. Moreover, Kremer 2009 only discloses assessments of structural joint damage at baseline and week 104, not week 24 or 48, as recited in claim 12. *Id.* at 35. According to Patent Owner's expert Dr. Silverman, a POSA would not necessarily expect inhibition of joint damage at weeks 24 and 48 in light of results at week 104 because clinical improvements like inhibition of joint damage do not necessarily occur linearly. *Id.* Patent Owner also argues that Kremer 2009 does not test tocilizumab as a monotherapy, as required by claim 12, and does not distinguish between patients who received 4 mg/kg for the entire 104 weeks and those who received 8 mg/kg tocilizumab at some point during trial. *Id.* at 35–36. Moreover, Patent Owner asserts that Kremer 2009 would teach a POSA that "the 4 mg/kg dose (equivalent to 162 mg subcutaneous tocilizumab every other week) would not be effective at inhibiting joint damage and that the higher 8 mg/kg dosage (equivalent to 162 mg every week) should be used instead." *Id.* at 36; *see also* PO Sur-reply 22–24 (arguing a POSA would have doubted that 4 mg/kg Q2W IV would inhibit progression of structural joint damage).

Having now considered the complete record presented at trial, we find Petitioner has the better position. Although Kremer 2009 discloses the GmTSS scores of the patients after 104 weeks, that data shows that a number of patients receiving TCZ4 and TCZ8 had no progression of structural joint damage. *See* Ex. 1029, Table A. We credit the testimony of Dr. Boers that if structural joint damage has not progressed after 104 weeks,

then it would not have progressed after 24 or 48 weeks. *See* Ex. 1119 ¶¶ 14–15. Dr. Boers explains that because "joint damage can only progress," a POSA would have understood that those patients whose GmTSS scores did not increase from baseline for the entire 104-week period would have had the same baseline GmTSS scores at weeks 24 and 48. *Id.*

Although Patent Owner's expert Dr. Silverman disagrees, we find Dr. Boers's explanation to be more credible than Dr. Silverman's. Both experts offer analogies to explain the Kremer 2009 data. Dr. Boers compares the LITHE study to a study of whether fluoridated water prevents cavities in children over a two-year period. Ex. 1119 ¶ 16. According to Dr. Boers, if the study finds that 75% of children consuming fluoridated water had no cavities over the two-year period, at least those same children would also have had no cavities at 24 and 48 weeks. *Id.* As Dr. Boers explains, "[t]he cavities—like joint damage—are a one-way street: once they are detected in a study patient, that patient permanently falls out of the group that got no cavities during the study." *Id.*

Dr. Silverman disagrees, stating that clinical improvements like inhibition of joint damage do not necessarily occur linearly. Ex. 2009 ¶ 91. To support his opinion, Dr. Silverman analogizes inhibition of joint damage to treating a fever with a course of antibiotics. According to Dr. Silverman, if a patient has a fever and other symptoms and is prescribed medication on day 1, the patient may no longer have the fever and symptoms by day 10. *Id.* Dr. Silverman states, however, that "it does not follow that at day 2 and day 5, the patient also had no fever or symptoms" without specifically measuring on day 2 and day 5. *Id.*

We agree with Petitioner that Dr. Silverman's analogy is insufficiently supported by the record. As explained by Dr. Boers, joint damage is not like

a transient fever that comes and goes. *See* Ex. 1139 ¶ 59. Rheumatoid arthritis is a progressive disease and joint erosion—like a tooth cavity—"is essentially a one-way street." *Id.*

Furthermore, Dr. Boers's explanation is confirmed by the results of Kremer 2008, showing joint erosion was assessed after 52 weeks and certain patients receiving TCZ4 and TCZ8 had "[n]o progression" in GmTSS after 52 weeks.[21] *See* Ex. 1028, Table. Kremer 2008 therefore concluded that "TCZ therapy significantly inhibited the progression of structural joint damage." *Id.*, 4031. We thus find that a POSA, in view of the one-way progression of joint erosion and the disclosure of Kremer 2008, would have understood Kremer 2009 to have measured the GmTSS score at 52 weeks and found inhibition of structural joint damage at that time. As explained above, because the claims encompass assessing joint damage at 52 weeks to find inhibition of joint damage (*see supra* Section II.B.3), we find Petitioner has shown that Kremer 2009 teaches or suggests this limitation of claim 12.

As for Patent Owner's arguments that Kremer 2009 (1) does not teach treating with tocilizumab as a monotherapy, (2) does not distinguish between patients who receive 4 mg/kg and 8 mg/kg, and (3) does not suggest administering 4 mg/kg over 8 mg/kg, we find those arguments to be

[21] Patent Owner objects to Petitioner's reliance on Kremer 2008 as not included in any petitioned Ground. PO Sur-reply 21. But Petitioner cites Kremer 2008 in the Petition and in Dr. Boers's First Declaration. *See* Pet. 55–56; Ex. 1034 ¶¶ 169–170; *see also* Tr. 22:1–7 (Petitioner's counsel stating "it is our view that Kremer 2008 informs Kremer 2009"). We therefore do not consider Petitioner's use of Kremer 2008 to be improper. Regardless, even without Kremer 2008, our conclusion would be the same as we find it would have been obvious for a POSA to evaluate joint damage at 52 weeks, which the parties' experts agree is standard practice for rheumatologists. *See* Ex. 1139 ¶ 60; Ex. 1136, 75:21–76:10.

inapposite. Notwithstanding Patent Owner's assertion to the contrary, claim 12 does not preclude the use of methotrexate together with tocilizumab. *See* Ex. 1001, Certificate of Correction, claim 12 (using transition term "comprising"); Ex. 1139 ¶ 62. Moreover, as Dr. Boers explains, because the control arm of the LITHE study was methotrexate alone, a POSA would have attributed the increased efficacy to tocilizumab. Ex. 1139 ¶ 63.

We also credit the testimony of Dr. Boers that a POSA would have understood from Kremer 2009 (as informed by Kremer 2008) that at least some TCZ4 patients would have experienced inhibition of structural joint damage at 52 weeks, even without the data that mixes the two groups together. *See* Ex. 1119 ¶¶ 5–6, 25–26; Ex. 1139 ¶¶ 65–66. Whether Kremer 2009 suggests that TCZ8 was also effective does not take away from the teaching that TCZ4 inhibited structural joint damage, as well.

Thus, having considered the arguments and evidence presented at trial, we find the combination of NCT '653, Morichika, and Kremer 2009 teaches or suggests each limitation of claim 12 and that a POSA would have had a reason to combine the references with a reasonable expectation of success in reaching the claimed invention.

Before reaching our conclusion on obviousness, we now consider Patent Owner's objective evidence of nonobviousness.

3. Objective Evidence of Nonobviousness

"Objective indicia of nonobviousness can serve as an important check against hindsight bias and 'must always when present be considered.'" *Merck & Cie v. Gnosis S.P.A.*, 808 F.3d 829, 837 (Fed. Cir. 2015). Patent Owner argues that evidence of unexpected results supports the nonobviousness of the claims. PO Resp. 50–52.

"To be particularly probative, evidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art, and that the difference would not have been expected by one of ordinary skill in the art at the time of the invention." *Bristol-Myers Squibb Co. v. Teva Pharms USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014). According to Patent Owner and its experts Drs. Samara and Silverman, a POSA would have considered Maini and Nishimoto to be the closest prior art. Patent Owner asserts that both references teach that 8 mg/kg IV tocilizumab showed superior efficacy compared to doses of 4 mg/kg and 2 mg/kg. PO Resp. 50–51 (citing Ex. 2006 ¶¶ 68–73; Ex. 2009 ¶¶ 105–108). In light of these results, Patent Owner argues that a POSA would not have expected 162 mg tocilizumab administered every other week would be effective because such a regimen would provide patients with far less tocilizumab than they would receive using the 8 mg/kg IV treatment regimen. *Id.* at 51 (citing Ex. 2006 ¶¶ 68–73; Ex. 2009 ¶¶ 107–108).

In response, Petitioner argues that because Patent Owner's main argument for nonobviousness is that Morichika does not provide a formulation that would be safe and effective to practice the claimed invention, the alleged unexpected results are not commensurate in scope with the claims, which do not recite any specific formulation. Pet. Reply 27 (citing PO Resp. 25–27; Ex. 1140 ¶¶ 7–9). Petitioner also argues that administering 162 mg tocilizumab every other week was known to be effective, as that dosing regimen inhibited bone damage in at least some rheumatoid arthritis patients. *Id.* at 27–28 (citing Ex. 1139 ¶¶ 71–73). Thus, Petitioner's expert Dr. Boers opines that "[t]o the extent that the claimed regimens produced somewhat better results than expected, this is a difference of degree only and does not negate the motivation that the

expected efficacy would have given a POSA to try the claimed regimen." Ex. 1139 ¶ 72.

Having considered the evidence of unexpected results presented by Patent Owner, we do not agree that it outweighs the strong evidence of obviousness, particularly for claims 1–3 and 6–11, which we found to be obvious based on anticipation. *See Newell Cos. v. Kenney Mfg. Co.*, 864 F.2d 757, 769 (Fed. Cir. 1988), *cert. denied*, 493 U.S. 814 (1989) (holding that although the record may establish evidence of secondary considerations which are indicia of nonobviousness, the record may also establish such a strong case of obviousness that the objective evidence of nonobviousness is not sufficient to outweigh the evidence of obviousness). Moreover, as explained above with respect to claim 12, we find a POSA would have had a reasonable expectation that administering 162 mg subcutaneously every other week would be effective at inhibiting structural joint damage given the positive results from Kremer 2009 studying the effects of 4 mg/kg IV tocilizumab. *See supra* Section II.F.2. To the extent there may have been some level of surprise at the results of administering 162 mg TCZ every other week, we find that to be a difference in degree and not kind, as it is a "predictable result but to an unexpected extent." *See UCB, Inc. v. Actavis Labs. UT, Inc.*, 65 F4th 679, 693 (Fed. Cir. 2023) (stating "[a] difference of degree is not as persuasive as a difference in kind—i.e., if the range produces a new property dissimilar to the known property, rather than producing a predictable result but to an unexpected extent.").

4. Conclusion on Obviousness of Claims 1–12

Having considered the arguments and evidence presented at trial, we find Petitioner has shown by a preponderance of the evidence that claims 1–12 are unpatentable as obvious over the cited references.

G. Remaining Grounds

In the remaining grounds of the Petition, Petitioner asserts claims 1–12 of the '264 Patent would have been unpatentable as obvious over the same combinations of art as the previous grounds (i.e., NCT '653 and Morichika alone (claims 1–3, 6–11) or in combination with Emery (claim 4), Maini (claim 5), or Kremer 2009 (claim 12)), but adds references to bolster its argument that a person of ordinary skill in the art would have had a reasonable expectation that a 162 mg SC fixed dose of TCZ weekly or twice weekly would have been effective against RA. Pet. 56–73. Specifically, Petitioner adds Ng, Nishimoto, FDA Review, and SC PK Prior Art in one set of grounds (identified as Grounds 6 and 8 in the Petition) and Ng, Nishimoto, EMA Report, Chernajovsky, and SC PK Prior Art in another set of grounds (identified as Grounds 7 and 9 in the Petition).

Because we have determined claims 1–12 of the '264 Patent are unpatentable as anticipated and/or obvious over NCT '653 alone or in combination with other cited references, and therefore dispositive as to all challenged claims, we need not reach the remaining grounds for purposes of our Decision. *See SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1359 (2018) (holding that a petitioner "is entitled to a final written decision addressing all of the claims it has challenged"); *Bos. Sci. Scimed, Inc. v. Cook Grp. Inc.*, 809 F. App'x 984, 990 (Fed. Cir. 2020) (non-precedential) (recognizing that the "Board need not address issues that are not necessary to the resolution of the proceeding" and, thus, agreeing that the Board has "discretion to decline to decide additional instituted grounds once the petitioner has prevailed on all its challenged claims").

III. PETITIONER'S MOTION TO EXCLUDE

The party moving to exclude evidence bears the burden of proving that it is entitled to the relief requested—namely, that the material sought to be excluded is inadmissible under the Federal Rules of Evidence ("FRE"). *See* 37 C.F.R. §§ 42.20(c), 42.62(a).

Petitioner filed a Motion to Exclude Exhibits 2005, 2006, 2009, 2034, 2065, 2080, 2081, and 2083. Paper 65. Patent Owner opposes Petitioner's Motion. Paper 67. Because we determine claims 1–12 of the '264 Patent are unpatentable by a preponderance of the evidence, we need not reach Petitioner's Motion to Exclude and we dismiss Petitioner's Motion as moot.

IV. CONCLUSION[22]

For the foregoing reasons, we determine that Petitioner has established by a preponderance of the evidence that claims 1–12 of the '264 Patent are unpatentable.

In summary:

Claim(s)	35 U.S.C. §	Reference(s)/Basis	Claim(s) Shown Unpatentable	Claim(s) Not shown Unpatentable
1–3, 6–12	102	NCT '653	1–3, 6–11	12
1–3, 6–11	103	NCT '653, Morichika	1–3, 6–11	

[22] Should Patent Owner wish to pursue amendment of the challenged claims in a reissue or reexamination proceeding subsequent to the issuance of this decision, we draw Patent Owner's attention to the April 2019 *Notice Regarding Options for Amendments by Patent Owner Through Reissue or Reexamination During a Pending AIA Trial Proceeding*. *See* 84 Fed. Reg. 16,654 (Apr. 22, 2019). If Patent Owner chooses to file a reissue application or a request for reexamination of the challenged patent, we remind Patent Owner of its continuing obligation to notify the Board of any such related matters in updated mandatory notices. *See* 37 C.F.R. § 42.8(a)(3), (b)(2).

4	103	NCT ’653, Morichika, Emery	4	
5	103	NCT ’653, Morichika, Maini	5	
12	103	NCT ’653, Morichika, Kremer 2009	12	
1–11	103	NCT ’653, Morichika, Ng, Nishimoto, FDA Review, SC PK Prior Art[23]		
4	103	NCT ’653, Morichika, Ng, Emery, Nishimoto, FDA Review, SC PK Prior Art[24]		
5	103	NCT ’653, Morichika, Ng, Maini, Nishimoto, FDA Review, SC PK Prior Art[25]		
1–11	103	NCT ’653, Morichika, Ng, Nishimoto, EMA Report,		

[23] As explained above, we need not reach this ground because the grounds over NCT ’653; NCT ’653 and Morichika; NCT ’653, Morichika and Emery; and NCT ’653, Morichika and Maini are dispositive of challenged claims 1–11.

[24] As explained above, we need not reach this ground because the ground over NCT ’653, Morichika and Emery is dispositive of challenged claim 4.

[25] As explained above, we need not reach this ground because the ground over NCT ’53, Morichika and Maini is dispositive of challenged claim 5.

		Chernajovsky, SC PK Prior Art[26]		
4	103	NCT ’653, Morichika, Ng, Emery, Nishimoto, EMA Report, Chernajovsky, SC PK Prior Art[27]		
5	103	NCT ’653, Morichika, Ng, Maini, Nishimoto, EMA Report, Chernajovsky, SC PK Prior Art[28]		
12	103	NCT ’653, Morichika, Ng, Kremer, Nishimoto, FDA Review, SC PK Prior Art[29]		
12	103	NCT ’653, Morichika, Ng, Kremer, Nishimoto, EMA Report,		

[26] As explained above, we need not reach this ground because the grounds over NCT ’653; NCT ’653 and Morichika; NCT ’653, Morichika and Emery; and NCT ’653, Morichika and Maini are dispositive of challenged claims 1–11.

[27] As explained above, we need not reach this ground because the ground over NCT ’653, Morichika and Emery is dispositive of challenged claim 4.

[28] As explained above, we need not reach this ground because the ground over NCT ’53, Morichika and Maini is dispositive of challenged claim 5.

[29] As explained above, we need not reach this ground because the ground over NCT ’653, Morichika, and Kremer 2009 is dispositive of challenged claim 12.

		Chernajovsky, SC PK Prior Art[30]		
Overall Outcome			1–12	

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1–12 of U.S. Patent No. 8,580,264 B2 are held unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude is *dismissed as moot*; and

FURTHER ORDERED that, because this is a Final Written Decision, the parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirement of 37 C.F.R. § 90.2.

[30] As explained above, we need not reach this ground because the ground over NCT '653, Morichika, and Kremer 2009 is dispositive of challenged claim 12.

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