

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GRÜNENTHAL GMBH,
Petitioner,

v.

ANTECIP BIOVENTURES II LLC,
Patent Owner.

PGR2018-00062
Patent 9,707,245 B2

Before TONI S. SCHEINER, GRACE KARAFFA OBERMANN, and
SHERIDAN K. SNEDDEN, *Administrative Patent Judges*.

OBERMANN, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
35 U.S.C. § 328(a)

I. INTRODUCTION

This is a Final Written Decision in a post-grant review of claims 1–30 of U.S. Patent No. 9,707,245 B2 (Ex. 1001, “the ’245 patent”). The Board has jurisdiction under 35 U.S.C. § 6. We issue this Final Written Decision pursuant to 35 U.S.C. § 328(a).

We instituted review based on all grounds asserted in the Petition (Paper 2, “Pet.”). See Paper 11 (“Dec.”), 21. Thereafter, in timely sequence, Patent Owner filed a Response (Paper 15, “Resp.”), Petitioner filed a Reply (Paper 18), and Patent Owner filed a Sur-Reply (Paper 21). The Board held a final oral hearing on July 31, 2019. Paper 31 (“Tr.”). For reasons that follow, we find unpatentable claims 1–30 of the ’245 patent.

A. Related Proceedings

The Petition identifies three related post grant reviews that do not involve the ’245 patent. Pet. 5 (citing PGR2017-00008 (“PGR008”); PGR2017-00022 (“PGR022”); PGR2018-00001 (“PGR001”)). During the pendency of this proceeding, the Board entered a final written decision in each case. PGR008, Paper 43 (entered June 22, 2018); PGR022, Paper 50 (entered November 14, 2018); PGR001, Paper 48 (entered April 29, 2019).

After we instituted review, Petitioner identified as related five additional post grant reviews that do not involve the ’245 patent. Paper 30, 2 (Petitioner’s Second Updated Mandatory Notices) (citing PGR2018-00092 (“PGR092”); PGR2019-00003 (“PGR003”); PGR2019-00026 (“PGR026”); PGR2019-00027 (“PGR027”); PGR2019-00028 (“PGR028”)). The Board instituted review in each case. PGR092, Paper 7 (entered February 25, 2019); PGR003, Paper 7 (entered May 7, 2019); PGR026, Paper 6 (entered

July 30, 2019); PGR027, Paper 6 (entered July 30, 2019); PGR028, Paper 6 (entered August 20, 2019).

B. The '245 Patent (Ex. 1001)

The '245 patent is titled “Neridronic Acid for Treating Complex Regional Pain Syndrome.” Ex. 1001, code (54). The Specification describes “[o]ral dosage forms of osteoclast inhibitors, such as nitrogen-containing bisphosphonates” for treating or mitigating “pain or related conditions such as complex regional pain syndrome” (“CRPS”). *Id.* at Abstract. The Specification identifies both zoledronic acid and neridronic acid as among the bisphosphonate compounds useful for treating CRPS by the method of the claimed invention. *See* Ex. 1001, Figs. 1–13, 2:44–3:24 (figures and descriptions of figures, all pertaining to a method that employs zoledronic acid); *see also id.* at 3:29, 3:33, 6:62–67, 12:4–15, 63:3–5, 64:40–42, 65:14–15 (identifying zoledronic acid and neridronic acid as suitable bisphosphonate compounds for use in the claimed method).

The Specification also discloses the administration of bisphosphonates for treating “bone fractures or to enhance the healing of bone fractures” as a function separate from mitigating “pain associated with vertebral crush fractures.” Ex. 1001, 7:35–37, 7:65. On that point, Example 3 relates to “[t]he effect of orally administered zoledronic acid” in a “rat tibia fracture model of” CRPS. *Id.* at 43:6–8. Example 3 expressly reports, however, that zoledronic acid mitigates pain associated with CRPS, where the condition is induced in “rats by fracturing the right distal tibias of the animals.” *Id.* at 43:8–9. Example 3 discusses pain assessment methods and pain reduction achieved in the rat tibia fracture model when zoledronic acid is selected as the bisphosphonate. *Id.* at 43:25–44:31. In addition, Example 3 explains,

“[t]his animal model has been shown to replicate the inciting trauma” (for example, a bone “fracture”) that is “observed in human[s].” *Id.* at 43:11–16.

The ’245 patent includes no working example that employs neridronic acid as the bisphosphonate. The general disclosure, however, provides dosing information pertaining to neridronic acid for use in the claimed method. *Id.* at 28:5–11, 28:42–45, 29:59–30:50.

C. The Challenged Claims

Claim 1, the only independent challenged claim, is illustrative and reproduced below:

1. A method of treating pain associated with complex regional pain syndrome (CRPS) comprising administering neridronic acid to a human being *with CRPS, wherein bone fracture was a predisposing event for CRPS*, and wherein the neridronic acid is in a salt or an acid form.

Ex. 1001, 84:59–63 (emphasis added).

The other challenged claims (namely, claims 2–30) depend directly or indirectly from claim 1 and specify additional limitations pertaining to the type of CRPS, the form of neridronic acid, the method of administration, the age of the treated human being, baseline pain intensity, and dosing regimens. *See id.* at 84:64–86:29.

D. The Prosecution History

We provide a brief overview of the prosecution history to supply context for Petitioner’s challenge. In our reproduction of claim 1 above, we emphasize a claim limitation that requires a human being “with CRPS, wherein bone fracture was a predisposing event for CRPS.” *Id.* at 84:61–62. Patent Owner added that limitation by

amendment after the Examiner rejected the claim as obvious over prior art that demonstrated bisphosphonates, prior to the date of the claimed invention, were generally recognized as useful for treating and effectively “relieving symptoms of CRPS.” Ex. 1022, 453, 510.

The Examiner found, “employing any known bisphosphonates, including neridronic acid, in the method of treating CRPS would be reasonably expected to be effective.” Pet. 10 (citing Ex. 1022, 454). In other words, the absence of a working example, specifically directed to the use of neridronic acid, was of little import during patent prosecution, given that “the dosage forms and the herein claimed routes of administration and the dosing regimen are all well-known according to the teachings of the cited prior art.” *Id.*

The Examiner allowed claim 1 to issue, however, only after Patent Owner included claim language that requires “bone fracture” as “a predisposing event for CRPS” (Ex. 1022, 506) and submitted evidence that patients “with fracture as the predisposing factor” exhibited a response to bisphosphonates that “was superior” to the response in patients “with other pre-disposing factors.” *Id.* at 548; *see id.* at 516–518 (data submitted during patent prosecution to show that humans suffering from CRPS were nearly three times as likely to respond favorably to bisphosphonate treatment when bone fracture was a predisposing event), 547 (notice of allowance). That evidence

consisted of results reported in 2017 by Varenna,¹ in a printed publication that Patent Owner asserts here as evidence of unexpected results (Resp. 23–28). Earlier work conducted by Varenna, completed prior to the critical date of the invention,² is the subject of an asserted prior art reference, which, as explained in the next section, we identify simply as “Varenna” (Ex. 1005).

E. Asserted Prior Art

The Petition identifies the following references as prior art in the grounds of unpatentability:

(1) M. Varenna et al., *Treatment of complex regional pain syndrome type I with neridronate: a randomized, double-blind, placebo-controlled study*, RHEUMATOLOGY 52: 534–42 (Nov. 2012) (Ex. 1005, “Varenna”);

(2) S. Bruehl, “How common is complex regional pain syndrome-Type I,” PAIN 129:1–2 (2007) (Ex. 1006, “Bruehl”);

(3) D. Gatti et al., *Neridronic acid for the treatment of bone metabolic diseases*, EXPERT OP. ON DRUG METABOLISM & TOXICOLOGY 5(10): 1305–11 (Sept. 2009) (Ex. 1007, “Gatti”);

(4) G. La Montagna et al., *Successful neridronate therapy in transient osteoporosis of the hip*, CLIN. RHEUMATOL. 24: 67–69 (Aug. 2004) (Ex. 1008, “La Montagna”);

(5) D. Manicourt et al., *Role of alendronate in therapy for posttraumatic complex regional pain syndrome type I of the lower extremity*,

¹ Varenna et al., *Predictors of responsiveness to bisphosphonate treatment in patients with complex regional pain syndrome type I: A retrospective chart analysis*, PAIN MED. 18:1131–38 (2017) (“Varenna 2017”).

² We agree that the “earliest possible priority date” of the ’245 patent “is May 14, 2013,” the date of filing of priority application No. 13/894,274. Pet. 34; see *id.* at 17–22 (for persuasive argument and evidence on point); Ex. 1001, code (63) (identification of asserted priority applications).

ARTHRITIS & RHEUMATISM 50(11): 3690–97 (Nov. 2004) (Ex. 1009, “Manicourt”);

(6) M. Muratore et al., *Il neridronato nel trattamento dell’algodistrofia simpatica riflessa dell’anca: confronto in aperto con il clodronato*, PROGRESSI IN RHEUMATOLOGIA, ABSTRACT BOOK VII CONGRESSO NAZIONALE COLLEGIO DEI REUMATOLOGI OSPEDALIERI 5 (Suppl. 1): 89 (Apr. 16–18, 2004) (certified English translation) (Ex. 1010, “Muratore”); and

(7) Schwarzer & Maier, *Complex regional pain syndrome*, in GUIDE TO PAIN MANAGEMENT IN LOW-RESOURCE SETTINGS 249–54 (Kopf & Patel eds. 2010) (Ex. 1020, “Schwarzer”).

F. Declaration Evidence

Petitioner relies on the Declaration of Lawrence Poree, M.D., Ph.D., in support of factual contentions and opinions regarding the level of ordinary skill and understanding in the art. Ex. 1003. Patent Owner submits no declaration testimony from a witness advanced as qualified to opine about the level of skill or understanding of an ordinarily skilled artisan.

G. The Asserted Patentability Challenges

We instituted review of claims 1–30 of the ’245 patent as follows.

Claim(s) Challenged	Statutory Basis	Reference(s)
1–4, 9, 10, 12, 14, 16–18, 23, 24, 27–29	35 U.S.C. § 102 (a)	Varenn
1–29	35 U.S.C. § 103	Varenn, Bruehl, Gatti, La Montagna, Muratore
5–8, 21, 25	35 U.S.C. § 103	Varenn, Manicourt
30	35 U.S.C. § 103	Varenn, Schwarzer, Bruehl, Gatti, La Montagna, Muratore

Claim(s) Challenged	Statutory Basis	Reference(s)
1–30	35 U.S.C. § 112 (written description)	
1–30	35 U.S.C. § 112 (enablement)	

Pet. 8; Dec. 21.

II. ANALYSIS

Petitioner directs us to persuasive evidence, which is not refuted effectively by Patent Owner, that the earliest possible priority date of the claims of the '245 patent is May 14, 2013. Pet. 17–22 (and evidence cited therein). As an initial matter, based on the arguments and evidence provided by Petitioner (*id.*), we find that the '245 patent is eligible for post-grant review. We first resolve whether Varenna qualifies as prior art. We then turn to the asserted patentability challenges.

A. *The Prior Art Status of Varenna (Ex. 1005)*

The prior art status of Varenna (Ex. 1005) emerged as a central dispute during the course of this review and was a focus of the final hearing. See Resp. 12–15; Reply 3–7; Sur-Reply 2–11 (both parties, devoting significant briefing to that issue); Tr. 9:14–12:15, 31:4–37:25, 51:14–55:17 (devoting oral argument to that issue). Petitioner filed the Declaration of Dr. Philip Robinson in support of Reply arguments pertaining to that issue. Ex. 1031. Patent Owner submits, “this Reply evidence is improper and should be stricken or at least ignored.” Sur-Reply 9.

For reasons set forth in this section, we find that a preponderance of the evidence demonstrates that Varenna qualifies as prior art, even if we set

aside Dr. Robinson’s Declaration. Alternatively, we are not persuaded that Dr. Robinson’s Declaration represents “improper reply evidence” and, further, we determine that his testimony bolsters our conclusion that Varena qualifies as prior art. *Id.* (quoting *Intelligent Bio-Systems, Inc. v. Illumina Cambridge, Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016)).

a) Varena (Ex. 1005) Includes Sufficient Indicia of Reliability

Even if we set aside Dr. Robinson’s Declaration, substantial evidence supports a finding that Varena (Ex. 1005) was “sufficiently accessible to the public interested in the art” and “disseminated or otherwise made available” to the interested public before the critical date. *Blue Calypso, LLC v. Groupon, Inc.*, 815 F.3d 1331, 1348 (Fed. Cir. 2016). That reference was filed with the Petition, includes the legend “Original article,” the notation “Rheumatology 2013; 52:534–42,” and the statement “Advance Access publication 30 November 2012.” Ex. 1005, 534.

An additional indicium joins that cluster of indicia to support the prior art status of Exhibit 1005: A copyright notice appears at the bottom of its first page: “© The Author 2012. Published by Oxford University Press on behalf of the British Society for Rheumatology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.” *Id.* A notation appears in Varena, indicating that the article was downloaded from an academic website on December 6, 2017.³ *Id.* On this record, Exhibit 1005

³ The date included in that notation (namely, December 6, 2017) does not undercut our finding that Exhibit 1005 is what it appears to be—a downloaded copy of a journal article from the journal *Rheumatology* published by Oxford University Press (and, therefore, available to the interested public) on “30 November 2012.” Ex. 1005, 534.

appears on its face to be a downloaded copy of an article by Varenna (listed first, with others) published by the Oxford University Press in the journal *Rheumatology* on November 30, 2012, well before May 14, 2013, the earliest priority date of the '245 patent claims. Ex. 1005, 534; *supra* note 2.

Patent Owner counters, “a reader of *Rheumatology* would not” expect to see the words “original article” or “advance access publication” on an article from that journal. Resp. 13–14 (bridging paragraph). Patent Owner directs us to nothing, beyond bare attorney argument, in support of that contention regarding how “a reader of *Rheumatology*” would interpret those indicia. *Id.* Accordingly, we find Patent Owner’s position lacks merit.

In the alternative, we take notice that *Rheumatology* is a peer-reviewed medical journal that has been published monthly for over half a century by Oxford University Press, the largest university press in the world. *See* Tr. 9:22–10:10, 37:15–19, 54:14–17 (colloquy on whether the Board may take notice of a point not open to meaningful dispute). We agree with Petitioner that what is actually “being questioned here is the veracity of claims about a publication date made by Oxford University Press.” Tr. 54:14–17. This is not a case involving, for example, a thesis, conference paper, or poster bearing none of the ordinary indicators of indexing or public distribution. This case involves a downloaded copy of an article from a medical journal bearing indicia of publication before the critical date.

An additional circumstance informs our finding that Exhibit 1005 was publicly accessible as of November 2012. During patent prosecution, “Patent Owner submitted this reference to the PTO with a filename ‘Varenna2012.pdf.’ and represented that it had a publication date of November 2012.” Reply 7 (citing Ex. 1022, 432, 440); Sur-Reply 2–11

(nowhere disputing that contention). The document identified by Patent Owner as “Varennna2012.pdf” is from the same journal (“Rheumatology”), bears the same page numbering (534–542), and includes the word-for-word identical title as Exhibit 1005 (“Treatment of Complex Regional Pain Syndrome Type I with Neridronate: A Randomized, Double-Blind, Placebo-Controlled Study”). *Compare* Ex. 1005, 534, *with* Ex. 1022, 432.

Patent Owner submits that its identification of Exhibit 1005 during patent prosecution cannot “be taken as an admission that the reference is prior art against the claims.” Resp. 14 n.1.⁴ We do not imply an admission here, however; we simply observe that Patent Owner previously identified to the Office a publication date for Varennna that is consistent with the date of public access disclosed on the face of Exhibit 1005. *Compare* Ex. 1022, 430 (reporting a publication date of November 2012), *with* Ex. 1005 (reporting a publication date of “30 November 2012”). Patent Owner disputes that Varennna (Exhibit 1005) was, in fact, published by November of 2012 – but does not contest that it previously represented the same reference to the Office as having a publication date of November 2012. Resp. 14 n.1

⁴ By way of support, Patent Owner directs us to MPEP § 2129, which relates to disclosures of an “applicant’s own prior patent” during prosecution. MPEP § 2129 (quoting *Riverwood Int’l Corp. v. R.A. Jones & Co.*, 324 F.3d 1345, 1354–55 (Fed. Cir. 2003)). The only other support cited by Patent Owner relates to “materiality,” which is not contested and differs from accessibility. Resp. 14 n.1 (quoting 37 C.F.R. § 1.97(h)).

(nowhere contesting that fact); Reply 6–7 (bridging paragraph, asserting that fact); Sur-Reply 2–11 (nowhere disputing that fact).

Patent Owner further argues that the publication date that appears on the face of Varenna (Ex. 1005) is “inadmissible hearsay.” Resp. 13. We decline to entertain that objection because Patent Owner failed to preserve it within the ten-day window required by our rules, much less file a motion to exclude that would preserve an objection. Reply 4 (citing 37 C.F.R. §§ 42.65(b)(1), (c)); *see* Paper 13 (nowhere objecting to Exhibit 1005). Alternatively, we accept Petitioner’s position that “the publication and copyright dates in Varenna” fall into two hearsay exceptions (namely, the residual exception to hearsay as well as the exception that applies to documents generally relied upon by the public)—a position not refuted by Patent Owner. Reply 5 (citing Fed. R. Evid. 803(17), 807); *see generally* Sur-Reply (nowhere contesting the applicability of those exceptions to the hearsay objection at issue).

Patent Owner submits that Exhibit 1005 is not authentic. Resp. 13–14 (bridging paragraph). At the oral hearing, counsel for Patent Owner reiterated argument attempting to cast doubt on whether Exhibit 1005 represents “the way it looked on the priority date, 2013.” Tr. 34:15–36:12 (but nowhere disputing that Patent Owner submitted the same document to the Office during patent prosecution). Here again, Patent Owner did not preserve that objection within the ten-day window required by our rules or file a motion to exclude as necessary to preserve an objection. Reply 5–6 (citing 37 C.F.R. §§ 42.65(b)(1), (c)); *see* Paper 13 (nowhere objecting to

Exhibit 1005). Alternatively, Patent Owner rests on bare attorney argument that we find insufficient to cast doubt on the authenticity of Exhibit 1005.

For the above reasons, we find that Varena (Ex. 1005) qualifies as prior art against the challenged claims of the '245 patent, even if we set aside Dr. Robinson's Declaration.

b) Additional Support Provided by Dr. Robinson

Petitioner offers Dr. Robinson's Declaration as additional proof that Exhibit 1005 was publicly accessible prior to the critical date. Reply 5. Patent Owner objects to Dr. Robinson's Declaration as untimely because Petitioner filed it with the Reply instead of the Petition. Paper 20, 2. We find that Dr. Robinson's Declaration, however, supports Reply arguments that fairly respond to positions raised for the first time in the Response. *Compare* Reply 3–7, and Ex. 1031, with Resp. 12–15. Further, as a practical matter, we discern no prejudice from the timing of the filing, given that Patent Owner was afforded an opportunity (fully taken) to file a Sur-Reply on issues raised in Dr. Robinson's Declaration. Sur-Reply 2–11.

Dr. Robinson's Declaration confirms the indicia of public accessibility that appear on the face of Varena (Exhibit 1005). Reply 5 (citing Ex. 1031). Specifically, Dr. Robinson attests, under oath, that he “accessed, reviewed, and posted about Varena . . . on the social media site Twitter” before the critical date. Reply 5; Ex. 1031 ¶¶ 4–8. Dr. Robinson backs up his testimony with objective support. Specifically, he identifies an exhibit and attests, this is “my tweet,” which “can still be viewed publicly” and includes a link that “is still active and leads to Varena.” Ex. 1031 ¶ 5, Exhibit A. Patent Owner advances no objective evidence tending to contradict Dr. Robinson's statement that he has “personal knowledge” that

Varennna (Exhibit 1005) “was available and accessible to the public” before the critical date. Ex. 1031 ¶ 3. Instead, Patent Owner rests on conclusory assertions that Dr. Robinson’s sworn testimony “defies belief” and details a feat that would require “a photographic” or “infallible memory.” Sur-Reply 9. We find unpersuasive those bare attorney arguments.

Dr. Robinson’s testimony bolsters our finding that Varennna (Ex. 1005) is what it appears to be – a downloaded copy of an article from a medical journal that was “sufficiently accessible to the public interested in the art” and “disseminated or otherwise made available” to the interested public by November 30, 2012. *Blue Calypso*, 815 F.3d at 1348.

2. Additional Objections to Petitioner’s Evidence

Patent Owner objects to Dr. Poree’s Declaration (Ex. 1003), Dr. Poree’s Curriculum Vitae (Ex. 1004), and the Certificate of Translation filed by Petitioner in connection with Muratore (Ex. 1010), a prior art reference published in Italian. Paper 13. Petitioner, for its part, objects to Patent Owner’s submission of Exhibits 2002, 2003, and 2004, which relate to Orange Book information pertinent to oral dosage forms of neridronic acid. Paper 17. We find that both parties waived their objections by failing to preserve them in a motion to exclude evidence, as required by 37 C.F.R. § 43.64(c). Alternatively, we overrule those objections for reasons set forth in the next two subparts of our analysis.

a) The Declaration of Dr. Poree (Ex. 1003) And the Curriculum Vitae of Dr. Poree (Ex. 1004)

Patent Owner challenges Dr. Poree’s background and experience, disputes his qualifications as a technical expert or even “a lay witness,” and questions his citations to “facts and data from a number of sources,”

submitting that his opinions do not meet the requirements of Federal Rule of Evidence 702. Paper 13, 2–4. Patent Owner further objects to Dr. Poree’s Curriculum Vitae as “inadmissible hearsay under Rule 802” because “it consists of assertions not made while testifying at the current proceeding” and “which are being offered to prove the truth of the matter asserted.” *Id.* at 4–5.

As an initial matter, we overrule the hearsay objection. Without exception, the Board accepts the filing of sworn witness declarations in lieu of live testimony in administrative patent trials. We also routinely accept curricula vitae filed in support of sworn witness declarations. That historical practice is a key feature of our streamlined administrative process. Fairness is ensured by the Board rule that provides an opposing party the opportunity, as of right, to cross-examine declarants under oath in a deposition. 37 C.F.R. § 42.51(b)(ii). When effective, cross-examination testimony – taken under oath to facilitate reliability – may cast doubt on conflicting statements in a declaration or accompanying curriculum vitae.

Patent Owner did not avail itself of the opportunity, provided as of right by our rules, to cross-examine Dr. Poree under oath in this case. Tr. 28:15–16. Instead, Patent Owner advances objections to Exhibit 1003 (Dr. Poree’s Declaration) and Exhibit 1004 (Dr. Poree’s Curriculum Vitae) based on bare argument that Dr. Poree is not qualified to opine about the level of ordinary skill in the art. Paper 13, 2–4.

It is worth providing here an overview of the uncontroverted (and quite extensive) record of Dr. Poree’s education, professional credentials, practical experience, and other qualifications. Dr. Poree holds a Ph.D. in Toxicology/Environmental Health Sciences from the University of

California and an M.D. from Stanford University School of Medicine. Ex. 1004, 1; Ex. 1003 ¶ 7. Dr. Poree “completed a Pain Fellowship at the University of California at San Francisco.” Ex. 1003 ¶ 7. He is currently involved in a research project directed to the management of pain associated with CRPS. Ex. 1004, 1. Dr. Poree is “an author of over 20 publications on the treatment of pain, including several papers on the treatment of CRPS in both animal models and clinical trials.” Ex. 1003 ¶ 10; Ex. 1004, 3–6. He is board certified by the American Academy of Pain Medicine and a member of the American and California Societies of Interventional Pain Physicians. Ex. 1004, 1. Dr. Poree “served on the editorial board for the journal *Pain* from 2009 to 2010.” *Id.*; Ex. 1003 ¶ 10. Dr. Poree has significant practical experience treating pain associated with CRPS. Ex. 1003 ¶ 8. Specifically, he has “over 20 years of experience treating patients with chronic pain and studying treatments for pain disorders including complex regional pain syndrome (‘CRPS’).” *Id.* Currently, Dr. Poree treats “patients at the University of California Pain Management Center, seeing approximately 30 patients per week.” *Id.*

Patent Owner observes that Dr. Poree does not mention “using neridronate or [an]other bisphosphonate” as part of his significant experience treating patients experiencing pain. Paper 13, 2. Patent Owner further observes that Dr. Poree does not mention “treating patients with intravenous or oral bisphosphonates” or “conducting research” specifically “involving intravenous or oral bisphosphonates.” *Id.* at 3. Patent Owner directs us to nothing, however – not even bare attorney argument – tending to show that such specialized experience is necessary to establish

Dr. Poree’s qualifications to opine about the level of ordinary skill in the art or otherwise provide useful information to the Board in this review. *Id.*

Dr. Poree attests under oath that Exhibit 1004 is a copy of his Curriculum Vitae. Ex. 1003 ¶ 5; *see id.* at 45 (oath). Dr. Poree’s testimony on that point stands un rebutted by opposing evidence – such as cross-examination testimony taken under oath in a deposition. We discern no basis, on this record, for doubting the information provided by Dr. Poree in Exhibit 1004. Ex. 1003 ¶ 5.

Accordingly, we overrule Patent Owner’s objections to Dr. Poree’s Declaration (Ex. 1003) and Curriculum Vitae (Ex. 1004). We find that Exhibit 1004 is a true copy of Dr. Poree’s Curriculum Vitae. Taking account of Dr. Poree’s sworn statements regarding his education, experience, and other qualifications, and in view of the level of ordinary skill resolved in our analysis below, we find that Dr. Poree is qualified to opine about the perspective of a person of ordinary skill in the art at the time of the invention. Further, we determine that his declaration testimony may be useful to the Board in resolving the dispute at hand.

b) The Certificate of Translation Accompanying Muratore (Ex. 1010)

Petitioner provides an English translation of Muratore (Ex. 1010) translated from the Italian language. Patent Owner objects to the Translator’s Declaration, dated April 10, 2018, and signed by Ms. Laura Archiapatti of Park IP Translations. Ex. 1010 (last page). Ms. Archiapatti attests that she possesses “advanced knowledge of the Italian and English languages” and that the translation provided “has been translated by me and

to the best of my knowledge and belief, is a true and accurate translation of” the Italian version of Muratore. *Id.*

Patent Owner rests on bare attorney argument challenging Ms. Archiapatti’s “qualification or expertise regarding language translation” and questioning the sufficiency of the wording of her oath. Paper 13, 5. Patent Owner does not demonstrate that Ms. Archiapatti’s oath fails to comply with the form of evidence required for foreign language translations in our forum. 37 C.F.R. § 42.63(b). Nor does Patent Owner come forward with any objective evidence tending to cast doubt on the content of Ms. Archiapatti’s translation (for example, a conflicting translation provided under oath by a translator of Patent Owner’s choice). Paper 13, 5. We find unpersuasive Patent Owner’s conclusory challenge to the information provided under oath by Ms. Archiapatti. We overrule the objection.

3. Petitioner’s Objections to Exhibits 2002, 2003, and 2004

Petitioner objects to Exhibits 2002, 2003, and 2004, which Patent Owner submits in support of the Response to the Petition. Paper 17; Resp. 30. Exhibits 2002 and 2003 are advanced as Orange Book information about neridronic acid. Resp. 30. Exhibit 2004 is the Declaration of Mr. Brent A. Johnson and may relate to whether the FDA had approved oral neridronate products by the time of the invention. Paper 17, 1. Petitioner argues that those exhibits are irrelevant and unfairly prejudicial to Petitioner. *Id.* We overrule those objections because they go to weight to

which the evidence is entitled, not admissibility. Further, Petitioner does not explain adequately why those exhibits are unfairly prejudicial. *Id.*

Petitioner further asserts that Exhibits 2002 and 2003 (the Orange Book information) constitute “inadmissible hearsay.” *Id.* at 2. The gravamen of Petitioner’s objection, however, goes to whether Orange Book information reported years after the critical date is persuasive – which may affect the weight, but not the admissibility, of the evidence. *Id.*

B. The Asserted Patentability Challenges

We next turn to the merits of the patentability challenges. We organize this section into three subparts: First, we address the level of ordinary skill in the art. Second, we resolve several disputed issues of claim construction. Third, we turn to the merits of the patentability challenges asserted in the Petition. We divide that third section into four subparts that address the challenges based, respectively, on anticipation, obviousness, lack of written description support, and lack of enablement.

1. Level of Ordinary Skill in the Art

We consider the grounds of unpatentability in view of the understanding of a person of ordinary skill in the art at the time of the invention. Petitioner argues that an ordinarily skilled artisan would have had “an M.D. or a Ph.D. in a pain-medicine-relevant discipline, such as clinical health psychology or neuroscience, and at least 3–5 years of experience in the treatment of CRPS or related chronic pain conditions, or in the study of CRPS or related types of chronic pain.” Pet. 13 (citing Ex. 1003 ¶¶ 17–21).

Patent Owner responds that the ordinarily skilled artisan “would have [had] an M.D. or a Ph.D. in a discipline related to the interaction of drugs

with a human body, such as biology, pharmacology, etc., and experience in supervising, carrying out, or collaborating in animal or human testings, including off-label treatment of patients, related to drug development in the pain area.” Resp. 1–2. Patent Owner avers, “[t]raining in an area such as clinical health psychology is not relevant to treatment of pain conditions using a medication.” *Id.* at 2.

On this record, we find that the prior art is sufficient to demonstrate the level of ordinary skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (the prior art itself can reflect the appropriate level of ordinary skill in the art). To the extent that a more specific definition is required, we adopt Petitioner’s view, which is consistent with the prior art and supported by Dr. Poree’s unrefuted declaration testimony. *Compare* Pet. 13 (citing Ex. 1003 ¶¶ 17–21), *with* Resp. 1–2 (identifying no record support for Patent Owner’s counterarguments). Alternatively, we find that any “differences between Petitioner’s and Patent Owner’s definitions have no impact on the asserted grounds.” Reply 3; *see* Sur-Reply 1–25 (nowhere contesting that view).

2. Claim Construction

The Board interprets claims in an unexpired patent using the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.200(b) (2017).⁵ Under that standard, we assign

⁵ A recent amendment does not apply because the Petition was filed prior to November 13, 2018. *See* “Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board,” 83 Fed. Reg. 51,340 (Oct. 11, 2018) (amending 37 C.F.R. § 42.200(b) effective November 13, 2018); *see* Pet. (filed April 18, 2018).

claim terms their ordinary and customary meaning as understood by one of ordinary skill in the art at the time of the invention, within the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Only claim terms in controversy need be construed, and then only to the extent necessary to resolve the dispute. *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999).

Petitioner proposes the following definitions for terms included in the challenged claims. Pet. 14–15 (and evidence cited therein).

Term	Claims	Petitioner’s Proposed Construction
“A method of treating pain associated with complex regional pain syndrome (CRPS)” and “to a human being with CRPS”	1–30	Requires that neridronic acid be administered to a human being having CRPS for the purpose of diagnosing, curing, mitigating, or preventing pain associated with CRPS, or for activity that otherwise affects the structure or any function of the body in a human being with CRPS
“predisposing event for CRPS”	1–30	Synonymous with a “precipitating event” or “triggering event,” i.e., an event that causes or contributes to the occurrence or onset of CRPS.

We first address the preamble, “[a] method of treating pain associated with” CRPS. Ex. 1001, 84:59. Petitioner argues, and Patent Owner does not disagree, that the preamble is limiting because “it recites essential structure or steps, or . . . is necessary to give life, meaning, and vitality to the claim.” Pet. 14–15; *see* Resp. 1–2 (Patent Owner, presenting arguments consistent with that position). We agree with Petitioner’s assertions in that regard, because the body of the claim refers twice to CRPS, and the entire thrust of

the Specification is directed to the use of bisphosphonates to treat pain associated with CRPS. *See, e.g.*, Ex. 1001, code (54) (Title), code (57) (Abstract), 5:49–7:34 (detailed description invention); 84:59–63 (claim 1).

As Petitioner points out, the Specification expressly defines “[t]he term ‘treating’ or ‘treatment’ broadly” to include “any kind of treatment activity” – such as “diagnosis, cure, mitigation, or prevention of disease in man or other animals, or any activity that otherwise affects the structure or any function of the body of man or other animals.” Ex. 1001, 6:57–61; *see* Pet. 15; Ex. 1003 ¶ 31 (both quoting the cited disclosure of the Specification). Patent Owner counters that such activity falls outside the scope of the claim term “unless it affects the pain associated with CRPS . . . in a way that is beneficial.” Resp. 3. Petitioner has the better position, because the Specification includes a clear definition for “treating” that supports Petitioner’s construction. Ex. 1001, 6:57–61. Patent Owner does not address adequately that definitional statement. Resp. 2–3. Nor does Patent Owner effectively rebut Dr. Poree’s testimony that an ordinarily skilled artisan at the time of the invention would have applied the construction advanced by Petitioner. Ex. 1003 ¶¶ 31–34.

We adopt also Petitioner’s proposed construction for the second claim phrase identified above. Petitioner’s construction aligns with the plain words of the claim, is consistent with the prosecution history of the ’245 patent, finds support in the uncontroverted testimony of Dr. Poree, and is not contested by Patent Owner. Pet. 16; Ex. 1022, 518; Ex. 1003 ¶¶ 36–38; *see* Resp. 2–3 (Patent Owner, nowhere opposing that construction).

3. Grounds of Unpatentability

We next turn to the grounds of unpatentability advanced in the Petition: (1) anticipation by Varena; (2) obviousness over Varena alone or in combination with one or more other references; (3) lack of written description support; and (4) lack of enablement. Pet. 8; Dec. 21.

a) Anticipation

Petitioner asserts that Varena anticipates claims 1–4, 9, 10, 12, 14, 16–18, 23, 24, and 27–29. Pet. 8. Varena is listed on the face of the '245 patent but was not substantively evaluated during patent prosecution. Ex. 1005 (Varena); Ex. 1001, code (56) (listing Varena among cited publications); Exs. 1021, 1022 (prosecution history). We first address independent claim 1, then turn to the dependent challenged claims.

(1) Claim 1

Claim 1 specifies a method of treating CRPS in humans, where bone fracture is a predisposing event of the CRPS, by administration of the acid or salt form of neridronic acid. Ex. 1001, 84:59–63. During prosecution of the '245 patent, the Examiner found that an ordinarily skilled artisan would have recognized that bisphosphonates generally are useful and effective for mitigating pain associated with CRPS in humans. Ex. 1022, 453, 510. Neither party raises evidence from which we reasonably can conclude that the Examiner erred in finding that “bisphosphonates [were] known to be useful in treating CRPS” and, further, that the particular bisphosphonate at issue here (namely, “neridronic acid”) would have been “reasonably expected to be effective” for that purpose. Ex. 1022, 454. We adopt those findings here.

Varennna discloses the administration of neridronic acid “to a human being with CRPS.” Pet. 36–37 (citing Ex. 1005, 534, 536; Ex. 1003 ¶¶ 81–82).⁶ The reference reports “the efficacy of the amino-bisphosphonate neridronate in patients with” CRPS, including “clinically relevant and persistent benefits” associated with the administration of neridronate. *Id.* at 35 (citing Ex. 1005, 534; Ex. 1003 ¶ 76). Significantly, Varennna expressly teaches that neridronate effectively mitigates pain associated with CRPS in patients presenting with “bone fracture” as “a predisposing event for” that condition. Ex. 1001, 84:61–62; see Pet. 37–39 (citing, for example, Ex. 1005, 535–36, 538–39, Table 1; Ex. 1003 ¶¶ 83–88).

Of particular significance, on that last point, is Varennna’s identification of a subset of patients in a human clinical study that experienced bone “fracture” as a “[p]recipitating event” for CRPS. Ex. 1005, 536 (Table 1). Varennna reports that, in that subset of patients, the administration of neridronate effectively mitigated pain. Pet. 32–33, 37–39 (and evidence cited therein); Ex. 1005, 534, 536; Ex. 1003 ¶¶ 73, 83–88.

Claim 1 does “not require any particular measure or level of efficacy against pain associated with CRPS.” Ex. 1003 ¶ 34; Pet. 15; see Ex. 1001, claim 1. Accordingly, Patent Owner’s position that Varennna must expressly disclose “at least some level of diagnosing, curing, mitigating, or preventing pain associated with CRPS” in order to anticipate claim 1 is not persuasive. Sur-Reply 1. “Efficacy is not a limitation of any challenged claim,” and

⁶ A preponderance of the evidence demonstrates that the term “neridronate” in Varennna refers to the salt or acid form of the compound. Pet. 36 (citing Ex. 1005, 535; Ex. 1003 ¶¶ 78–80, 85); see *generally* Resp. (nowhere refuting that factual contention).

Patent Owner's view "that anticipation requires 'conclusive' evidence of efficacy from a large clinical trial is . . . incorrect." Reply 7; Resp. 2, 19–20.

Several other facts confirm our above analysis. Varena informs, "[i]n patients with acute CRPS-I," the intravenous administration of neridronate is "associated with clinically relevant and persistent benefits." Ex. 1005, 534; *see* Pet. 35–39 (and evidence cited therein). Varena reports results that provide "conclusive evidence that the use of bisphosphonates . . . is the treatment of choice for CRPS-I." Ex. 1005, 534. "CRPS was known in the prior art as a severely debilitating pain syndrome that sometimes develops after trauma such as a bone fracture." Pet. 1; *see* Ex. 1003 ¶ 22 (citing Ex. 1005, 534). Varena discloses with anticipatory specificity the mitigation of pain in patients suffering from CRPS (including those in which that pain syndrome was triggered by bone fracture) by treatment with neridronate. Pet. 32–33, 37–39; Ex. 1005, 534, 536; Ex. 1003 ¶¶ 73, 83–88.

Here, the disclosure of Varena, standing alone, supports our determination of anticipation. Petitioner, however, directs us to additional persuasive evidence regarding how and why an ordinarily skilled artisan would have understood Varena to reveal "the particular type of precipitating event did not influence outcomes in the study, indicating that patients with all types of precipitating events, including fractures, benefited from the neridronate treatment." Pet. 39 (citing Ex. 1003 ¶ 88); *see* Ex. 1005, 538 (Varena, explaining, "[i]n multivariate regression analysis," no "baseline variables except treatment assignment" "appeared to influence outcome measures"). In our decision instituting review, we expressly invited Patent Owner to challenge that factual contention. Dec. 12. Patent Owner, however, identifies no persuasive objective proof (such as counter

testimony from a witness qualified to opine about the perspective of an ordinarily skilled artisan) on point. We accept Dr. Poree's opinions, which explain how and why Varennia anticipates each limitation of claim 1. Ex. 1003 ¶¶ 74–88 (and citations to Varennia therein).

Patent Owner attempts to parse Dr. Poree's words in a manner that would suggest he has failed to explain how or why Varennia necessarily anticipates every element of claim 1. Resp. 16–18; Sur-Reply 15. We reject that endeavor. Patent Owner's bare attorney argument, in that regard, is insufficient to cast doubt on the plain disclosures in Varennia identified by Dr. Poree in his testimony, or the clarity of the explanations provided in his declaration. Ex. 1005, 535, 538 (Varennia); Ex. 1003 ¶¶ 83–88 (Dr. Poree's declaration testimony on point, explaining with sufficient clarity how disclosures identified with specificity in Varennia anticipate claim 1).

As Petitioner correctly observes, "Patent Owner's unsupported attorney argument does not and cannot refute Dr. Poree's expert opinions concerning how a" person of ordinary skill in the art "would interpret Varennia." Reply 10. Patent Owner does not take account adequately of Varennia's express disclosures pertaining to the effective use of neridronate to treat pain (that is, CRPS) in fracture patients. Reply 10–13 (and evidence cited therein). Accordingly, we determine that Petitioner demonstrates by a preponderance of the evidence that Varennia anticipates claim 1 of the '245 patent. Pet. 32–39 (and evidence cited therein).

(2) Dependent Claims

Varennia also anticipates the subject matter of dependent claims 2–4, 9, 10, 12, 14, 16–18, 23, 24, and 27–29. See Pet. 39–46 (including

substantial evidence cited therein). Patent Owner raises no new argument directed to any of those independent claims. Resp. 15–20. Instead, Patent Owner relies on argument presented in the context of claim 1. *Id.* Our analysis pertaining to claim 1 applies with equal force to dependent claims 2–4, 9, 10, 12, 14, 16–18, 23, 24, and 27–29.

b) Grounds Based on Obviousness

We next turn to Petitioner’s contention that claims 1–30 (all of the challenged claims) are unpatentable as obvious. We first consider whether the subject matter of claim 1 would have been obvious from the disclosure of Varena alone or in combination with one or more additional reference. Pet. 8, 46–67. We then turn to the dependent claims.

(1) Claim 1

If Varena does not “specifically disclose treatment of pain associated with CRPS wherein fracture was a predisposing event,” we find that this reference, at minimum, suggests that limitation. Pet. 46. Further, if Varena does not suggest that limitation, we find that the subject matter of claim 1 would have been obvious over the combined disclosures of Varena, Bruehl, Gatti, La Montagna, and Muratore. *Id.* at 8, 46–67.

As Petitioner observes, Varena “shows that 11 of the 41 patients enrolled in the neridronate arm of the study”—that is, “26.8%” of the patients evaluated—“had fracture as a precipitating event for CRPS.” *Id.* at 46 (citing Ex. 1005, 536 (Table 1)). “Of the 41 patients enrolled in the placebo arm, 17 had fracture as a precipitating event for CRPS (41.4%).” *Id.* (citing Ex. 1003 ¶ 124); see Ex. 1005, 536 (Table 1). Eventually, “the patients who had been on placebo were given neridronate following the

same regimen (four 100-mg infusions over 10 days) as in the double-blind phase.” *Id.* (citing Ex. 1005, 535).

Given those facts, we agree that Varennna, at minimum, suggests that neridronic acid effectively mitigates pain in patients presenting with bone fracture as a predisposing event for CRPS. Pet. 46–47 (citing Ex. 1003 ¶¶ 124–128 (Dr. Poree’s unrebutted and well-supported declaration testimony on point)). Patent Owner’s counterarguments rest on bare attorney argument about the skill and understanding of an ordinarily skilled artisan. The Response is replete with unsupported statements about what the ordinarily skilled artisan would have “recognized,” “understood,” “reasonably expected,” or been “motivated” to do at the time of the invention. Resp. 4, 5, 21, 29–33. Counsel’s views are unsupported by persuasive objective evidence and, therefore, do not effectively undercut Dr. Poree’s declaration testimony, explaining how and why an ordinarily skilled artisan would have found the subject matter of claim 1 obvious over the disclosure of Varennna. Ex. 1003 ¶¶ 124–128.

Dr. Poree explains in detail why, from the perspective of an ordinarily skilled artisan, the disclosure of Varennna in combination with the other asserted prior art references would have suggested the administration of neridronic acid to a human being having CRPS with a reasonable expectation of success in treating pain. *See* Ex. 1003 ¶¶ 123–128 (Dr. Poree, explaining why the subject matter of claim 1 would have been obvious over the disclosure of Varennna alone); *see also id.* ¶¶ 129–144 (Dr. Poree, further explaining why the combined disclosures of Varennna, Gatti, Muratore, and La Montagna would have reasonably expected such a treatment to be effective and useful to treat pain associated with CRPS); *see especially id.*

¶¶ 140–141 (clear explanation for why an ordinarily skilled artisan would have combined the asserted prior art references). Patent Owner’s observation that “[m]ost patients in Varena receiving neridronic acid in the randomized study did not have bone fracture” does not effectively rebut Dr. Poree’s declaration testimony. Resp. 21. Nor does Patent Owner’s further observation that Varena does not “include bone fracture as a precipitating event in its baseline variables.” *Id.* Ultimately, neither of those assertions adequately supports Patent Owner’s contention that “Varena would not have motivated a [person of ordinary skill in the art] to select patients with bone fracture for using neridronic acid to treat CRPS.” *Id.* We find that conclusory statement ineffective to counter persuasively Dr. Poree’s well-supported opinions provided under oath.

Dr. Poree’s testimony identifies objective support for his opinions, namely, specific disclosures in Varena, reporting a course of intravenous administration of neridronate that improves clinical signs and functional status in patients experiencing CRPS (by definition, a pain syndrome) triggered by bone fracture—thereby, suggesting that the treatment mitigates pain. Pet. 47; Ex. 1005, 536, 538; Ex. 1003 ¶¶ 124–128. Dr. Poree’s opinions stand unrefuted: An ordinarily skilled artisan would have recognized bone fracture as a common triggering event for CRPS, understood that neridronic acid was effective for treating pain associated with CRPS, and been led to administer neridronate to successfully relieve pain in patients presenting with CRPS triggered by bone fracture. Pet. 47–53; Ex. 1003 ¶¶ 118–144 (Dr. Poree’s testimony on point).

As it did during patent prosecution, Patent Owner submits results reported by Varena in 2017 to demonstrate unexpected results that inure to

the subject matter of the claimed invention. Resp. 23–24; *see* Ex. 1022, 516–518, 548. Even Patent Owner acknowledges that, by 2017, an ordinarily skilled artisan would have been well aware that “fracture patients respond better than patients with other predisposing events” to treatment with neridronate. Resp. 25–26 (quoting Ex. 1003 ¶ 177). The relevant question is whether substantial evidence supports a finding that the results obtained by Varenna in 2017 would have been truly unexpected at the time of the invention (namely, on or about May 14, 2013 (*see supra* note 2)). On that key point, for reasons that follow, we determine that the evidence does not support a finding that the results obtained by Varenna in 2017 would have been truly surprising or unexpected at the time of the invention.

Patent Owner makes essentially no showing that the results reported by Varenna in 2017 would have been truly unexpected or surprising to a person of ordinary skill in the art at the time of the invention. *See In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) (a showing of unexpected results requires evidence “that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected”). Here again, we take note that Patent Owner’s assertions are backed up by no witness testimony from a person qualified to opine about the understanding of a person of ordinary skill in the art at any time. Resp. 23–28 (Patent Owner’s position that the increase reported in Varenna 2017 would have been “unexpected” to an ordinarily skilled artisan); *see especially id.* at 25 (Patent Owner’s position that an ordinarily skilled artisan would view those results as “unexpectedly better than treating patients with other predisposing events”).

In fact, Patent Owner directs us to no record evidence tending to show that the results reported in Varena 2017 would have been truly surprising to an ordinarily skilled artisan when compared to the results disclosed by Varena (Ex. 1005) in 2012. Significantly, in that regard, we assess an assertion of unexpected results from the perspective of an ordinarily skilled artisan comparing the claimed invention with the closest prior art. *In re Fracallossi*, 681 F.2d 792, 794 (CCPA 1982); *In re Reuter*, 670 F.2d 1015, 1023 (CCPA 1981); *In re Fenn*, 639 F.2d 762, 765 (CCPA 1981). In this case, Varena (Ex. 1005) represents the closest prior art. Patent Owner does not attempt to articulate, with any clarity or persuasive effect, how or why the disclosure of Varena 2017 establishes that results obtained by the inventors at the time of the invention would have been truly surprising to an ordinarily skilled artisan in view of the disclosure of Varena (Ex. 1005). Resp. 23–28. Instead, Patent Owner compares internal results obtained and reported by Varena in 2017 – offering nothing, not even attorney argument, to explain how or why an ordinarily skilled artisan would have viewed those results as surprising over the results obtained by Varena (Ex. 1005) in 2012. Resp. 23–28.

We acknowledge Dr. Poree’s observation that Varena (Ex. 1005) reported no differences in outcome based on the triggering event. We find unpersuasive, however, Patent Owner’s argument that Dr. Poree’s observation suggests an ordinarily skilled artisan would not have expected the results reported by Varena in 2017. Resp. 23. Dr. Poree addresses, and effectively refutes, that suggestion by reference to express disclosures within the four corners of Varena 2017. Pet. 64; Ex. 1003 ¶¶ 174–178. We find persuasive Dr. Poree’s testimony, regarding how an ordinarily skilled artisan

would have interpreted Varennia 2017, including the disclosure that “[t]he differences in effectiveness observed between the different regimens are small.” Ex. 1015, 1137; Ex. 1003 ¶ 178. We recognize that Patent Owner interprets that disclosure differently, but find significant that Patent Owner comes forward with no evidence that an ordinarily skilled artisan would have adopted that different interpretation. Resp. 26–28; Sur-Reply 21–23.

We find Dr. Poree’s testimony on point credible and reliable, because it is consistent with the disclosure of Varennia 2017. Immediately after reporting that “this study suggests that patients” with “fracture as a triggering event” for CRPS “are more likely to respond to treatment with bisphosphonates,” Varennia states, “[t]he differences in effectiveness observed between the different regimens are small and likely to be related to the need for these drugs to be used at the appropriate dosage.” Ex. 1015, 1137. Dr. Poree is the only witness in this review qualified to opine about how an ordinarily skilled artisan would have understood that disclosure, and his interpretation is reasonable, given that Varennia discusses “fracture as a triggering event” in the sentence immediately preceding the disputed disclosure. *Id.*; see Ex. 1003 ¶¶ 175, 177 (Dr. Poree’s opinion testimony).

In the alternative, we find no disclosure in Varennia 2017 indicating that the response to treatment seen in patients with fracture-induced CRPS would have been truly “surprising” or “unexpected” to a person of ordinary skill in the art. See *generally* Ex. 1015 (Varennia 2017, nowhere describing the results obtained as “surprising” or “unexpected”). At best, Varennia 2017 describes the improved results in such patients as “more likely.” *Id.* at 1137. On this record, we agree with Petitioner that Varennia 2017 discloses “at most a ‘difference in degree,’ not a ‘difference in kind’” sufficient to rebut

the substantial evidence of obviousness in this case. Pet. 64 (quoting *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014)).

Although not clearly raised by Patent Owner, we recognize, and assign some weight to, the Examiner's finding that Varena 2017 demonstrates unexpected results assignable to the claimed invention. Ex. 1022, 516–518 (data from Varena 2017, which was submitted during patent prosecution to show that humans suffering from CRPS were nearly three times as likely to respond favorably to bisphosphonate treatment when bone fracture was a predisposing event), 547 (notice of allowance). Nonetheless, we are directed to no evidence that the Examiner compared the results reported by Varena in 2017 to results reported in the closest prior art of record here, namely, Varena (Ex. 1005). We are mindful, in that regard, that although Patent Owner identified Varena (Ex. 1005) to the Examiner during patent prosecution (Ex. 1022, 430), neither party contends that the file history includes any evidence that the Examiner considered or evaluated the disclosure of Varena 2017 against the work completed by Varena in 2012 (and reported in Exhibit 1005). See Exs. 1021, 1022 (file history of record).

In the alternative, even if we assign some weight to the statements in Varena 2017 as evidence of unexpected results, that evidence does not change our ultimate conclusion. Petitioner makes out a relatively strong showing of obviousness in this case, a showing not outweighed by the evidence of unexpected results on this record. See *Sud-Chemie, Inc. v. Multisorb Techs., Inc.*, 554 F.3d 1001, 1009

(Fed. Cir. 2009) (“[E]vidence of unexpected results and other secondary considerations will not necessarily overcome a strong prima facie showing of obviousness”); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 719 (Fed. Cir. 1991) (secondary considerations may be insufficient to override primary considerations that support a conclusion of obviousness).

(2) Dependent Claims

We next turn to whether Petitioner shows by a preponderance of the evidence that the subject matter of dependent claims 2–30 would have been obvious to an ordinarily skilled artisan at the time of the invention. Pet. 8 (statement of grounds). We determine that Petitioner makes out that showing. *Id.* at 46–57 (and evidence cited therein).

Patent Owner first raises arguments about claims 2–29 that are the same as those presented in the context of claim 1. *See* Resp. 20–28 (arguing claims 1–29 as a group). Our discussion above in connection with claim 1 applies with equal force to those arguments.

Dependent claims 5–8, 21, and 26 further require oral administration of neridronate. Patent Owner submits, in connection with those claims, that “Petitioner has not provided a valid motivation to combine Varenna with Manicourt.” *Id.* at 29. We disagree. Petitioner directs us to persuasive evidence that a person of ordinary skill in the art “would have been motivated to combine” those two references because both “concern clinical trials investigating the use of bisphosphonates to treat CRPS, and both included patients with fracture as a predisposing event.” Ex. 1003 ¶ 160; Pet. 58. Further, “[a]s of 2012,” a person of ordinary skill in the art “reading

Varennna” was aware of multiple bisphosphonates suitable for oral administration, and “would have been motivated to look to other prior art examples of orally administered bisphosphonates, like Manicourt.”

Ex. 1003 ¶ 161; Pet. 58–59. Patent Owner’s argument that Petitioner fails to provide a valid reason to combine the references lacks merit. Resp. 29.

Also in connection with claims 5–8, 21, and 26, Patent Owner asserts, “neither Varennna nor Manicourt, or any other reference cited by Petitioner, actually discloses oral neridronic acid.” Resp. 29–31. That assertion is unpersuasive in view of Dr. Poree’s undisputed testimony that an ordinarily skilled artisan “would have understood that the treatment options available” would have included oral administration of neridronate. Reply 19 (quoting Ex. 1003 ¶ 172); see Pet. 61; Resp. 19–20; Ex. 1003 ¶¶ 25, 27, 169, 171, 173; Ex. 1020, 249; Ex. 1006 (supporting Petitioner’s view on this point).

Based on the information presented, we determine that Petitioner demonstrates by a preponderance of the evidence that claims 2–29 are unpatentable as obvious based on the grounds stated in the Petition.

c) Ground Based on Lack of Written Description Support

Petitioner asserts that claims 1–30 lack written description support in the ’245 patent specification. Pet. 8, 23–29. “[T]he hallmark of written description is disclosure.” *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). A patent disclosure is sufficient if it “reasonably conveys to those skilled in the art that the inventor had

possession of the claimed subject matter as of the filing date,” based on an “objective inquiry into the four corners of the specification.”⁷ *Id.*

This ground depends on Petitioner’s assertion that “nothing in the specification even indicates or suggests that the use of neridronic acid to treat pain associated with CRPS resulting from a particular predisposing event is part of the invention.” Pet. 24 (citing Ex. 1003 ¶ 53). That argument appears to us as an attempt to revisit an issue expressly raised during patent prosecution. *See, e.g.*, Ex. 1022, 514 (applicant, directing the Examiner to specification support for the claims, including Examples 3 and 9 in the Specification), 548 (reasons for allowance).

In any event, Petitioner does not show sufficiently that the Specification fails to support the use of neridronic acid to mitigate pain associated with fracture-induced CRPS. On the contrary, the Specification indicates that “bisphosphonate” compounds generally are useful “to relieve” pain associated with “complex regional pain syndrome” and “pain associated with vertebral crush fractures.” Ex. 1001, 7:54–57, 65. The Specification repeatedly calls out neridronic acid, in particular, as a bisphosphonate that is useful for practicing the claimed invention. *See, e.g., id.* at 3:29, 15:55, 29:61; *see especially id.* at 64:40–42 (Embodiment 79, disclosing “[a] method of treating complex regional pain syndrome comprising administering neridronic acid to a human being in need thereof”).

⁷ We follow the parties’ convention and cite to the Specification of the ’245 patent in our analysis of the ground based on lack of written description support. Pet. 24–26; Resp. 4–6.

We read those statements, pertaining to neridronic acid, within the context of the full disclosure of the Specification, including Example 3. *Id.* at 43:1–44:43 (Example 3). Example 3 describes a method of oral administration of zoledronic acid to treat “CRPS” in a “rat tibia fracture model” in which “CRPS was induced in the rats by fracturing the right distal tibia of the animals and casting the fractured hindpaws for 4 weeks.” *Id.* at 43:6–10. The Specification explains that the rat model had “been shown to replicate the inciting trauma” “such as a fracture” “observed in human CRPS patients.” *Id.* at 43:11–15. Where the Specification contains further information describing suitable dosing regimens, when neridronic acid is selected as the bisphosphonate for use in the treatment method (*see, e.g., id.* at 28:5–11, 28:42–45, 29:59–30:50), we find Petitioner directs us to evidence insufficient to show that the inventors lacked possession of the subject matter of claim 1. Pet. 23–29.

We observe that Petitioner’s analysis of the ground based on lack of written description support appears to focus exclusively on the limitations of claim 1. Pet. 23–29; *see especially id.* at 28–29 (bridging paragraph) (sum total of analysis of dependent claims, averring that all claims require a method of using neridronic to treat a “human being with CRPS, wherein bone fracture was a predisposing event for CRPS” according to claim 1, therefore, all claims “are unpatentable for lack of written description”). We discern in the Petition no argument or evidence advanced to demonstrate that any additional limitation (such as a dosing regimen) set forth in claims 2–30

lacks written description support in the '245 patent Specification.⁸ *Id.* Accordingly, Petitioner does not demonstrate on this record that any challenged claim is unpatentable for lack of written description support.

d) Ground Based on Lack of Enablement

We next address the ground based on lack of enablement. Pet. 29–32. We evaluate enablement by considering whether the patent disclosure, at the time of filing,⁹ would have enabled a person of ordinary skill in art to make and use the subject matter of the claims. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The touchstone of enablement is whether undue experimentation would have been required to practice the claimed invention. *Id.* At the outset, we observe that Varena appears to anticipate most of the challenged claims. *See supra*. That circumstance appears inconsistent with Petitioner's further view that the degree of detail provided in the Specification is inadequate in view of the state of the prior art as revealed by the disclosure of Varena. Pet. 31–32.

⁸ In PGR008, the Board found unpatentable, for lack of written description support, claims in “the same patent family” as the '245 patent. Pet. 5; *see* PGR008, Paper 43 (final written decision). The claims challenged there specified a dosing regimen of “about 80 to about 500 mg of zoledronic acid” in a method for treating CRPS. PGR008, Paper 43, 15; *see id.* at 3–6, 10–21 (explaining why, based on the record developed in PGR008, the claimed dosing regimen lacked written description support). The parties declined our invitation to explain whether the Petition articulates reasoning sufficient to demonstrate that any limitation of claims 2–30, including any limitation pertaining to a dosing regimen, lacks written description support. Dec. 17 n.2 (citing Pet. 23–29); Resp. 3–10; Reply 21–23.

⁹ Except where otherwise noted, we follow Petitioner's convention of referring to the Specification when discussing the ground based on lack of enablement. Pet. 30–31.

We find that the disclosure of Varena would have informed an ordinary artisan, well before the critical date, exactly how to administer neridronic acid to humans having fracture-induced CRPS with an expectation of mitigating pain associated with that condition. Ex. 1005, 534 (Abstract), 535 (study design), 536 (Table 1 and results and efficacy data), 538 (Table 2 and discussion of improvement in pain symptoms upon treatment with neridronate). That finding is fully consistent with views formed by the Examiner during patent prosecution. Ex. 1022, 454 (“[T]he dosage forms and the herein claimed routes of administration and the dosing regimens are all well-known according to the teachings of the cited prior art. The dosage of neridronic acid taught in the prior art encompasses the herein claimed dosage.”). On that point, we observe that Varena (Ex. 1005), which is cited on the face of the ’245 patent (Ex. 1001, code (56)), was among the prior art references before the Examiner.

The information advanced in the Petition does not account adequately for the fact that Varena establishes a level of ordinary skill in the art that makes reasonable the degree of detail set forth in the Specification. Pet. 29–32. “The specification need not disclose what is well known in the art.” *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). On this record, the Petition does not advance information from which we reasonably can find that any experimentation, much less undue experimentation, would have been necessary to enable the claimed invention. Here we take account of both the disclosures set forth within the Specification and the general knowledge of an ordinarily skilled artisan as demonstrated by Varena. *See, e.g.*, Ex. 1001, 28:5–45, 43:1–44:43, 55:1–64:42 (patent disclosures); Ex. 1005 (Varena). The state of the prior art informs our decision that the

Specification includes details and explanations that, under the particular facts and circumstances of this case, sufficiently enable the claims.

An enabling disclosure need not disclose any working examples or demonstrate that the claimed invention was actually reduced to practice at the time of filing. *Alcon Research Ltd. v. Barr Labs, Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014). Where there is no need for an actual reduction to practice, we are not persuaded that the failure to include a working example, specific to neridronic acid, supports a conclusion that undue experimentation would have been necessary to make and use the claimed invention. *See* Pet. 30–31 (arguing that the failure to include a working example directed to neridronic acid, in particular, supports a finding of lack of enablement).

In reaching our conclusions on the ground based on enablement, we take notice that “a considerable amount of routine experimentation” is permitted without rising to the level of undue experimentation under a correct enablement analysis. *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996). Petitioner does not address, much less explain adequately, how or why any required experimentation would have risen above the routine, given the state of the art as exemplified by the disclosure of Varena. Pet. 29–32. Accordingly, we are not persuaded that Petitioner demonstrates that any challenged claim is unpatentable for lack of an enabling disclosure.

III. CONCLUSION

Petitioner establishes by a preponderance of the evidence that claims 1–30 of the '245 patent are unpatentable as follows.

Claims	Reference(s)	Basis	Claim(s) Shown Unpatentable	Claims Not Shown Unpatentable
1–4, 9, 10, 12, 14, 16– 18, 23, 24, 27– 29	Varenna	§ 102	1–4, 9, 10, 12, 14, 16–18, 23, 24, 27–29	
1–29	Varenna, Bruehl, Gatti, La Montagna, Muratore	§ 103	1–29	
5–8, 21, 25	Varenna, Manicour	§ 103	5–8, 21, 25	
30	Varenna, Schwarzer, Bruehl, Gatti, La Montagna, Muratore	§ 103	30	
1–30		§ 112 (written description)		1–30
1–30		§ 112 (enablement)		1–30
Overall Outcome			1–30	

IV. ORDER

It is
ORDERED that claims 1–30 of the '245 patent are unpatentable; and
FURTHER ORDERED that, because this is a Final Written Decision,
any party to the proceeding seeking judicial review of the decision must
comply with the notice and service requirements of 37 C.F.R. § 90.2.

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