

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GRÜNENTHAL GMBH,
Petitioner,

v.

ANTECIP BIOVENTURES II LLC,
Patent Owner.

Case PGR2018-00001
Patent 9,539,268 B2

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

OBERMANN, *Administrative Patent Judge*.

REHEARING DECISION
Denying Patent Owner's Request for Rehearing
37 C.F.R. § 42.71(d)

I. INTRODUCTION

Patent Owner filed a Request for Rehearing (Paper 49, “Req. Reh’g”) seeking review of the Board’s Final Written Decision (Paper 48, “Dec.”), in which we held unpatentable claims 3–30 of U.S. Patent No. 9,539,268 B2 (Ex. 1001, “the ’268 Patent”). With Board pre-authorization (Paper 50), Petitioner filed a Response to the Request for Rehearing. Paper 51 (“Reh’g Resp.”). This Decision also refers to the Petition (Paper 2, “Pet.”), the Patent Owner’s Response (Paper 22, “Resp.”), Petitioner’s Reply (Paper 36, “Reply”), and Patent Owner’s Sur-Reply (Paper 39, “Sur-Reply”).

Upon request for rehearing, we review our decision for an abuse of discretion. 37 C.F.R. § 42.71(c). “The burden of showing a decision should be modified lies with the party challenging the decision.” 37 C.F.R. § 42.71(d). “The request must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, or a reply.” *Id.* Based on an application of those principles, we deny the Request for Rehearing.

II. DISCUSSION

The claimed invention relates to unenhanced dosage forms of zolendronic acid that achieve a bioavailability in humans “from about 1.1% to about 4%.” Dec. 6 (quoting claim 1). In a nutshell, we found that the written description of the ’268 Patent lacks guideposts sufficient to enable an ordinarily skilled artisan to practice the claimed invention, because the description does not explain how to differentiate dosage forms that achieve the required bioavailability from those that do not. *Id.* at 12–21.

Patent Owner requests modification of the Final Written Decision on four grounds. First, Patent Owner submits, the Board misattributed a statement made by Petitioner’s witness to Patent Owner’s witness. Req. Reh’g 2–3. Second, Patent Owner contends that the Board overlooked or misapprehended information bearing on the issue of enablement. *Id.* at 3–11. Third, Patent Owner argues that the Board overlooked or misapprehended an alleged admission by Petitioner that an ordinarily skilled artisan “could achieve a bioavailability above 1% for zoledronic acid without using a bioavailability enhancing agent.” *Id.* at 12. Fourth, Patent Owner argues that the Board misapplied or misunderstood principles governing the evidentiary showing applicable to enablement. *Id.* at 13. We address in turn each of those asserted grounds for modification.

A. Alleged Misattribution of Testimonial Evidence

We agree with Patent Owner that, in one instance, the Board misattributed testimony of Petitioner’s witness, Dr. Clive G. Wilson, to Patent Owner’s witness, Dr. William Wargin. Req. Reh’g 2 (citing Dec. 14). That circumstance does not persuade us of reversible error, however, or otherwise compel modification of the Final Written Decision.

Dr. Wilson, not Dr. Wargin, likened the belief that unenhanced zoledronic acid dosage forms could achieve bioavailabilities as high as 1.1% to “a belie[f] in ‘fairies.’” Req. Reh’g 2 (quoting Dec. 14; Ex. 2014, 137:21–138:8). That testimony represents a small fraction of the totality of evidence that undergirds our finding that an ordinarily skilled artisan generally would have expected that attaining a human bioavailability for zoledronic acid above 1% required an enhancer. *See* Dec. 12–21 (citing

substantial evidence for that proposition). Even if we set aside the testimony misattributed to Dr. Wargin, substantial evidence supports that finding.

Patent Owner unequivocally admitted as much, stating that an ordinarily skilled artisan at the time of the invention would have “believed that the oral bioavailability in humans of *all* forms for zoledronic acid could not be above 1% without an enhancer.” Resp. 1 (emphasis in original). That admission is consistent with other persuasive evidence on point, including the Specification of the ’268 Patent, which indicates that the bioavailability of unenhanced zoledronic acid forms is low, with some forms having a bioavailability as low as 0.01%. Dec. 13 (citing Ex. 1001, 13:57–59), 14 (citing Ex. 1001, 14:8–11).

The Final Written Decision turns on the lack of guideposts in the Specification (for example, the absence of any pharmacokinetic data or disclosure of even one example of a dosage form that meets the challenged claims). *Id.* at 13–14 (citing Ex. 1005 ¶¶ 64–65, 69). The lack of a working example, however, is just one fact contributing to the totality of circumstances that support our holding of non-enablement. At its core, this case turns on the lack of disclosure in the Specification combined with the unpredictable nature of the field of invention of pharmaceutical formulation. *Id.* at 12. Substantial evidence of record points in one direction; that an ordinarily skilled artisan generally would have expected unenhanced zoledronic acid dosage forms to exhibit a bioavailability in humans of 1% or lower. *Id.* at 12–13. Neither the Specification, nor any general understanding in the art, would have equipped an ordinarily skilled artisan to distinguish unenhanced dosage forms that achieve the bioavailability required by the

challenged claims from those that do not, absent undue experimentation. *Id.* at 13–21.

Alternatively, the testimony at issue carries some weight even when properly attributed to Dr. Wilson. Significantly, on that point, Dr. Wargin’s testimony aligns with Dr. Wilson’s testimony. Dr. Wargin similarly testifies that an ordinarily skilled artisan “would not have expected that the oral bioavailability of zoledronic acid could be above 1% in human beings without using an enhancer.” Reh’g Resp. 1–2 (quoting Ex. 2017 ¶ 98). The witnesses, in essence, agree on the underlying technical fact at hand. Patent Owner does not show reversible error based on the isolated instance in which the Board misattributed Dr. Wilson’s testimony to Dr. Wargin.

In sum, substantial evidence supports our determination that the disclosure of the ’268 Patent lacks guideposts sufficient to illuminate a path toward unenhanced dosage forms that fall within the scope of the challenged claims. *See* Dec. 15–20 (citing evidence on point). Accordingly, as Petitioner points out, the misattribution of testimony was inconsequential. Sur-Reply 1 (heading).

B. Alleged Failure to Comprehend Evidence of Enablement

Patent Owner asserts that the Board, in four instances, reversibly erred by overlooking or misapprehending arguments and evidence pertaining to enablement. Req. Reh’g 3–4. All four instances generally relate to our finding that an ordinarily skilled artisan would have expected unenhanced zoledronic acid “to have an oral bioavailability of less than 1%” and that the ’268 Patent lacks guidance sufficient to explain how to identify unenhanced dosage forms that meet the claim limitation requiring a bioavailability in humans from about 1.1% to about 4%. Req. Reh’g 3

(citing Dec. 17–18); *see* Ex. 1001, claims 1 and 3 (independent claim specifying that bioavailability range); *see also id.* at claim 23 (independent claim specifying an unenhanced dosage form of zolendronic acid that exhibits a human bioavailability from “about 1.2% to about 4%”).

First, Patent Owner directs us to testimony of Dr. Wargin pertaining to “a human clinical trial using a dosage form” of zolendronic acid that included “no bioavailability enhancing agents,” but nonetheless achieved “a bioavailability occupying a significant portion of the” ranges required by the challenged claims. Req. Reh’g 4 (citing Ex. 2017 ¶¶ 54–78 (discussing Ex. 2026)). That evidence is an undated, four-page summary document bearing the legend “CONFIDENTIAL.” Ex. 2026. Patent Owner first introduced that evidence in the Response in connection with a dosage form denoted as “AZS-02.” Resp. 23 (citing Ex. 2026); *see id.* at 1, 8, 10 (for additional argument pertaining to that undated summary document).

Patent Owner made no showing in the Response (or any other brief of record) that Exhibit 2026 would have been publicly accessible or otherwise available to inform the understanding of an ordinarily skilled artisan at the time of the invention. *See generally* Resp.; *see also* Reply 8–10 (Petitioner, explaining that the data in Exhibit 2026, which Patent Owner advances in the Response to establish the bioavailability achieved in Aronhime (Ex. 1035), was not available at the time of filing of the Petition).

After Patent Owner filed Exhibit 2026 in support of the Response, the parties argued at some length about its evidentiary impact. *See, e.g.,* Reply 8–10; Sur-Reply 4–6. Petitioner asserted that, if Dr. Wargin is correct that the summary document (Ex. 2026) demonstrates that an unenhanced dosage form of zolendronic acid disclosed in another document (identified

by the parties as Aronhime (Ex. 1035)) inherently meets the bioavailability range required by the challenged claims, then Aronhime (Ex. 1035) represents an anticipatory reference. Reply 8–11. Relevant to enablement, however, Patent Owner nowhere asserted, much less established, that an ordinarily skilled artisan would have been privy to the summary results (Ex. 2026) or otherwise would have been aware of the bioavailability achieved by Aronhime (Ex. 1035). Sur-Reply 5 (referring to an unenhanced dosage form of zoledronic disodium tetrahydrate that could achieve with “95% confidence” a bioavailability of up to “3.06%” (as disclosed in Exhibit 2026) but arguing that “Aronhime does not expressly disclose an oral dosage form containing” the same “excipients” as the form discussed in Exhibit 2026 “and there is no way of knowing that an oral dosage form containing other excipients would have the same bioavailability”).

In any event, the critical question is not whether one particular unenhanced dosage form of zoledronic acid disclosed in Aronhime or Exhibit 2026 would have attained a bioavailability that falls within the scope of the challenged claims. The key is whether an ordinarily skilled artisan, reading the disclosure of the '268 Patent, would have been equipped to practice the full scope of the claimed invention. We did not overlook or misapprehend Exhibit 2026. We correctly determined that, in this unpredictable field of pharmaceutical formulation, an ordinarily skilled artisan would have required direction (lacking in the Specification or the prior art) explaining how to prepare dosage forms that meet the full range of bioavailabilities embraced by the challenged claims, including the specified high endpoint human bioavailability of about 4%. *See, e.g.*, Dec. 11–12

(citing undisputed evidence of unpredictable nature of the field of invention (Ex. 1005 ¶ 60)).

Significantly, on that point, Dr. Wargin states he was privy to information regarding Exhibit 2026 as part of this proceeding but does not suggest that this information would have been publicly available at the time of the invention. *See, e.g.*, Ex. 2017 ¶ 54 (Dr. Wargin’s testimony that his opinions were formed based on information, which was made available to him in connection with this proceeding, including “access to individuals” having personal knowledge of the clinical trial). Exhibit 2026 includes, on every page, a notation that the document was, at least at some point, treated as confidential. Ex. 2026 (summary of results from the clinical trial, marked on every page as “CONFIDENTIAL”). Patent Owner directs us to no persuasive evidence that an ordinarily skilled artisan, seeking to practice the claimed invention, could or would have turned to the summary document of the clinical trial (Ex. 2026) for direction at the time of the invention.

Alternatively, even if we accept that the summary document (Exhibit 2026) would have been publicly accessible at the time of the invention, Patent Owner directs us to no persuasive evidence that the document enables the full scope of the challenged claims. Exhibit 2026 discloses a dosage form that may have exhibited a bioavailability of “3.06%” – which falls well short of the 4% endpoint specified in the challenged claims. Ex. 2026, 2. Patent Owner does not explain how or why an ordinarily skilled artisan, privy to that result, would have been equipped to prepare an unenhanced dosage form with a reasonable expectation of attaining a bioavailability in humans of “about 4%” — that is, the high

endpoint of the specified bioavailability ranges. Ex. 1001, claims 1, 3, and 23; Req. Reh’g 4.

Multiple variables, including the form of the active ingredient, its degree of solubility, and the process by which it is manufactured, would have been understood to “have unpredictable effects on bioavailability.” Dec. 12. Given that unpredictability, we correctly found the Specification lacking in disclosure sufficient to guide one to dosage forms that attain the full range of human bioavailabilities specified in the challenged claims (including the high endpoint of 4%). A preponderance of evidence supports our finding that the identification of workable dosage forms would have required more than an exercise of ordinary skill in this particular field of endeavor. *Id.* at 11–20 (including citations to evidence that the ’268 Patent lacks sufficient guidance in view of the unpredictable nature of the technical field of the invention).

Second, Patent Owner avers that the Board erroneously held “that unenhanced zoledronic acid in oral dosage forms cannot have a bioavailability over 1%.” Req. Reh’g 5. On the contrary, we held that the Specification lacks information that “would have guided the artisan to a selection of zoledronic acid dosage forms” that meet “the full range of claimed bioavailabilities.” Dec. 13. On that point, even Patent Owner acknowledges, “an ordinarily skilled artisan would have ‘believed that the oral bioavailability in humans of *all* forms for zoledronic acid could not be above 1% without an enhancer.’” *Id.* at 13 (quoting Resp. 1). Even if, as Patent Owner now asserts, that artisan would have expected some unenhanced dosage forms to exhibit a bioavailability above 1%, no showing is made that one would have understood how to formulate a dosage form

that achieves the high endpoint of human bioavailability (of about 4%) encompassed by the challenged claims.

Petitioner did not argue, and the Board did not find, “that all unenhanced zoledronic acid dosage forms had a bioavailability of less than 1%, nor did Petitioner claim that the prior art asserted that bioavailabilities greater than 1% were impossible to achieve with zoledronic acid in the absence of an enhancer.” Reh’g Resp. 3. The crucial distinction is that, at the time of the invention, “[t]he prior art would have *suggested*” the difficulty of identifying, without guidance, dosage forms of unenhanced zoledronic acid that attain a bioavailability of 1% or more in humans. *Id.* at 3–4 (citing Pet. 20) (emphasis in original). Although the claims broadly embrace unenhanced dosage forms that attain a bioavailability in humans of up to about 4%, neither the written description nor the prior art of record explains how to identify those dosage forms.

Patent Owner contends that the Board erroneously credited “four sources” of evidence advanced by Petitioner to demonstrate that unenhanced forms of zoledronic acid would have been understood at the time of the invention to have an oral bioavailability of less than 1%. *Id.* at 4–5. That assertion relates to Patent Owner’s erroneous assumption that the Decision rests on a finding that no unenhanced oral dosage forms of zoledronic acid could, in fact, exhibit a bioavailability over 1%. *Id.* The rationale that undergirds our Decision, however, is that distinguishing dosage forms that fall within the scope of the claims, from those that do not, would have required more than an exercise of ordinary skill in the art; such an endeavor would have required undue experimentation. Dec. 12–20.

Third, according to Patent Owner, the Board failed to comprehend evidence that the '268 Patent does, in fact, provide guidance adequate “to prepare a dosage form having a bioavailability” that falls within the challenged claims. Req. Reh’g 7. Here again, however, the relevant question is not whether the disclosure provides guidance sufficient to practice a single embodiment of the invention. The question is whether the disclosure enables the full scope of the challenged claims. As we stated in the Decision, the Specification includes no “instructions or guidance as to how to achieve the recited range” of human bioavailability “without the use of enhancers.” Reh’g Resp. 7 (citing Dec. 16). “Even if,” as Patent Owner submits, the '268 Patent discloses “one embodiment of the claims, this is insufficient to” establish enablement with respect “to the full scope of the claims,” including the high endpoint human bioavailability of about 4%. *Id.* (footnote omitted).

Fourth, Patent Owner submits, “clinical trials are routine experimentation and therefore *not* undue experimentation”—a position allegedly overlooked or misapprehended by the Board. Req. Reh’g 9. Patent Owner argues that both parties’ witnesses described as routine experimentation “the one year of work and one million dollars” that would have been required to demonstrate that even one dosage form exhibits the human bioavailability required by the challenged claims. *Id.* at 11. Patent Owner reargues that issue without identifying with any particularity reversible error in our reasoning. *Id.* Simple disagreement with the result does not show reversible error in our rationale. *See* Dec. 15–20 (including citations to substantial evidence undercutting Patent Owner’s view that the identification of workable dosage forms would have required no more than an exercise of ordinary skill in the art). Further, as Petitioner points out, this

is not a case in which the patent disclosure “gives instructions as to how to vary the parameters of interest.” Reh’g Resp. 7. “The fact that clinical trials might be considered ‘routine’ experimentation in certain circumstances misses the point.” *Id.* at 6. Here, given the broad range of human bioavailabilities encompassed by the challenged claims (ranging from about 1.1% up to about 4%), “it would require multiple, extensive clinical trials to enable the practice of the full scope of the claims.” *Id.* Under the circumstances, Patent Owner does not show reversible error.

C. Alleged Failure to Comprehend Admission

Patent Owner asserts that the Board overlooked or misapprehended “the fact that Petitioner admitted that a” person of ordinary skill in the art “could achieve a bioavailability above 1% for zoledronic acid without using a bioavailability enhancing agent.” Req. Reh’g 12 (emphasis omitted). For support, Patent Owner directs us to a statement from Petitioner’s Reply: “Patent Owner does not explain why a bioavailability of 1.59-2.08% for a disodium salt form of zoledronate is unexpected in light of higher reported bioavailabilities for other similar bisphosphonates.” *Id.* (quoting Reply 16). In Patent Owner’s view, that statement amounts to an admission “that a bioavailability over 1% for a disodium salt form of zoledronic acid is not unexpected—that it is indeed expected.” *Id.* (emphasis omitted).

Patent Owner contends that the Board’s failure to address that alleged “admission” regarding unexpected results amounts to reversible error. *Id.* Petitioner counters that the Board did not need to address the alleged admission regarding unexpected results, “because the Board declined to reach Petitioner’s obviousness grounds” implicating such results. Reh’g Resp. 9. Petitioner’s argument, however, misses the mark because that

alleged admission does represent an element of extrinsic evidence suggesting that attaining a dosage form that falls within the claimed bioavailability ranges would have been within the grasp of the ordinarily skilled artisan.

That modicum of extrinsic evidence, however, does not compel a modification of the Final Written Decision. The alleged admission is offset by other extrinsic evidence; namely, testimony of Patent Owner's own witness, unequivocally asserting that an ordinarily skilled artisan "would not have expected that the oral bioavailability of zoledronic acid could be above 1% in human beings, without using an enhancer." *Id.* at 8 (quoting Ex. 2017 ¶ 98). Here again, for reasons explained above, the critical question is whether it would have been within the level of ordinary skill in the art to practice, without undue experimentation, the full scope of the claims, a feat that requires identifying unenhanced dosage forms that exhibit the high endpoint of human bioavailability (about 4%) embraced by the challenged claims. On balance, the extrinsic evidence cited by Patent Owner does not improve the guidance in the Specification or otherwise establish that an ordinarily skilled artisan would have understood how to achieve an unenhanced dosage form of zoledronic acid characterized by a human bioavailability of "about 4%." Ex. 1001, claims 1, 3, and 23; *see* Req. Reh'g 12 (citing Reply 16, which generally refers to bioavailabilities higher than 2.08% without directing us to persuasive intrinsic support).

In sum, Patent Owner does not show that the asserted admission tips the totality of evidence towards a finding that an ordinarily skilled artisan would have been equipped to practice the full scope of the challenged claims without undue experimentation.

D. Alleged Failure to Apply Applicable Evidentiary Standards

Patent Owner argues, “The fact that a [person of ordinary skill in the art] might not believe the disclosure” of the Specification (namely, that some dosage forms of unenhanced zolendronic acid are capable of achieving a human bioavailability as high as about 4%) “does not defeat enablement.” Req. Reh’g 13. In Patent Owner’s view, that circumstance indicates “expert skepticism” as a secondary indicium of nonobviousness. Req. Reh’g 13. The Board did not address any ground based on obviousness; therefore, Patent Owner’s assertion regarding alleged objective indicia of nonobviousness is misplaced. *See* Dec. 20 (conclusions on patentability of claims 3–30).

Further, even if we accept Patent Owner’s view that the inventors recognized (and disclosed) that unenhanced forms of zolendronic acid (contrary to general belief) are capable of attaining the high endpoint bioavailability (of about 4% in humans), that circumstance does not end the inquiry. Req. Reh’g 13. The Board conducted an appropriate analysis grounded in the *Wands* factors¹ to conclude that the Specification provides insufficient guidance to enable an ordinarily skilled artisan to identify “even one” unenhanced dosage form that meets the bioavailability requirements of the challenged patent claims – much less equip that artisan to attain the full range of human bioavailabilities specified in the challenged claims. Dec. 17. Accordingly, Patent Owner does not establish reversible error based on an alleged failure of the Board to apply the governing evidentiary standards applicable to enablement.

¹ *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (listing non-exclusive factors to assist in resolving the issue of enablement).

III. CONCLUSION

For the above reasons, we deny Patent Owner's Request for Rehearing of the Board's Final Written Decision in this proceeding.

V. ORDER

It is

ORDERED that Patent Owner's Request for Rehearing of the Final Written Decision is *denied*.

PETITIONER:

Bruce C. Haas
Stephen Yam
VENABLE LLP
GrunenthalPGR@Venable.com
BCHaas@Venable.com
SYam@Venable.com

PATENT OWNER:

Brent A. Johnson
R. Parrish Freeman
Michael I. Katz
MASCHOFF BRENNAN
bjohnson@mabr.com
pfreeman@mabr.com
mkatz@mabr.com