

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARGENTUM PHARMACEUTICALS LLC

Petitioner

v.

CIPLA LIMITED

Patent Owner

Case No. IPR2017-00807

U.S. Patent No. 8,168,620

**CIPLA LIMITED'S REQUEST FOR REHEARING
PURSUANT TO 37 C.F.R. § 42.71(d)**

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Patent Trial and Appeal Board

U.S. Patent and Trademark Office

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I. Introduction

Patent Owner Cipla Limited requests rehearing under 37 C.F.R. § 42.71(d) of the Board's Decision on Institution ("Decision," Paper 11). The Board correctly denied institution of Ground 1, finding the challenged claims novel over Segal. But the Board wrongly instituted trial on the obviousness grounds (Grounds 2 and 3). At least two statements in the Decision evince that, in doing so, the Board misapprehended or overlooked key evidence and arguments in Cipla's Preliminary Response that warranted denial of trial on Grounds 2 and 3. These statements are: (1) the Board's conclusion that "no claim terms require express interpretation for purposes of this Decision;" and (2) the Board's conclusion that "Patent Owner does not identify any particular claim limitation as not disclosed in the prior art." (Paper 11, 7, 16.)

The first statement shows that the Board misapprehended or overlooked the importance of construing the terms "nasal spray" and "suitable for nasal administration." As Cipla explained in its preliminary response, even under the "broadest reasonable interpretation" standard, the terms "nasal spray" and "suitable for nasal administration" must be construed to mean "pharmaceutical formulations that are tolerable to patients, homogeneous, and can be suitably deposited onto the nasal mucosa." (*See* Paper 7, 9.)

This construction is important because the preliminary response then

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demonstrates that none of the combinations of cited art teach a person of ordinary skill in the art how to make the claimed fixed-dose combination “nasal spray” or formulation “suitable for nasal administration” with a reasonable expectation of success. This is because the Petition fails to show how Segal (even in combination with Hettche, Phillipps, and/or the Flonase[®] Label) teaches the composition that would provide for the claimed fixed-dose combination “nasal spray” formulation that is “suitable for nasal administration.” (Paper 7, 12-16, 24-25, 41-42.) None of Hettche, Phillipps, nor the Flonase[®] Label describe formulations with *two* active ingredients, and Segal does not teach how to successfully make a combination formulation suitable for nasal administration.

Because the Board misapprehended or overlooked the relevance of Cipla's proposed claim construction to demonstrating this threshold failure in Argentum's Petition, the Board should grant Cipla's motion for rehearing and reverse its decision to institute trial on Grounds 2 and 3.

II. Legal Standard

“A party dissatisfied with a decision may file a request for rehearing, without prior authorization from the Board.” 37 C.F.R. § 42.71(d). The “burden of showing a decision should be modified lies with the party challenging the decision,” and the request “must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was

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previously addressed in a motion, an opposition, or a reply.” *Id.* When rehearing a decision on petition, the Board will review the decision for abuse of discretion. 37 C.F.R. § 42.71(c).

Cipla's request satisfies 37 C.F.R. § 42.71(d) and demonstrates that the Board abused its discretion by overlooking Cipla's proposed claim construction and evidence in Cipla's preliminary response that demonstrates how the Petition failed to show that the cited art taught critical claim elements—“nasal spray” and “suitable for nasal administration.”

III. Argument

A. The Board misapprehended or overlooked the importance of the proper claim constructions of “nasal spray” and “suitable for nasal administration.”

In its Decision, the Board determined that “no claim term requires express interpretation for purposes of this Decision.” (Paper 11, 7.) In doing so, the Board misapprehended or overlooked that a key dispute between the parties is whether the combination of cited references in Grounds 2 and 3 disclose a “nasal spray” that is “suitable for nasal administration.” This is important because these elements appear in *every* challenged claim, yet they are not found in the art.

As Cipla explained in its preliminary response, the broadest reasonable interpretation of “nasal spray” or a formulation “suitable for nasal administration” is “pharmaceutical formulations that are tolerable to patients, that are

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homogeneous, and that can be suitably deposited onto the nasal mucosa.” (Paper 7, 9.) This interpretation arises from the ’620 patent specification (EX1001, 1:37-53 3:36-39) and amendments and arguments made during prosecution of the ’620 patent. (Paper 7, 10-11.) For example, during prosecution, the ’620 patent’s application was rejected over Example III in Cramer. In response to that rejection, Cipla scientists prepared and tested a formulation by following the teaching of Cramer Example III. The testing revealed that Cramer’s disclosed formulation had: “(1) unacceptable osmolality, which would irritate patients; (2) unacceptable spray quality, which would not have suitably deposited onto the nasal mucosa; and (3) unacceptable settling, which would have adversely effected homogeneity of the formulation.” (*Id.* (citing EX1002, 286-87, 220-21).) Cipla consequently distinguished its claimed inventions from Cramer by (1) amending several claims to recite “said pharmaceutical formulation is in a dosage form suitable for nasal administration,” and (2) emphasizing the limitation “nasal spray,” as it appeared in all other claims. (*Id.*) That is, the prosecution history shows that the inventors did not claim just *any* formulation—they claimed only “pharmaceutical formulations that are tolerable to patients, that are homogeneous, and that can be suitably deposited onto the nasal mucosa.” (Paper 7, 9-11.)

These amendments and arguments made during prosecution and their effect on claim construction of the ’620 patent claims should not be overlooked here.

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Indeed, the Federal Circuit has mandated that the Board “should [] consult the patent’s prosecution history in proceedings in which the patent has been brought back to the agency for a second review” to see if a given construction would be “legally incorrect.” *Microsoft Corp. v. Proxyconn, Inc.*, 789 F.3d 1292, 1298 (Fed. Cir. 2015); *D’Agostino*, 844 F.3d at 948. (Paper 11, 10.)

Had the Board adopted the proper claim construction, which Cipla proffered, the Board would not have instituted trial. Rather, the Board would have found that none of Argentum’s prior art references or arguments disclose a “nasal spray” formulation that is “suitable for nasal administration,” as discussed in detail in III.B., below.

B. The Board misapprehended or overlooked that Argentum’s prior art references do not teach a “nasal spray” that is “suitable for nasal administration.”

The Board’s conclusion that “no claim terms require express interpretation,” (Paper 11, 7), suggests that the Board misapprehended or overlooked Cipla’s arguments that the art fails to give any reason to a person of ordinary skill in the art to modify the cited art to arrive at the claimed “nasal spray” and formulation “suitable for nasal administration” with a reasonable expectation of success. (Paper 7, 41-42.) This is underscored by the Board’s assertion that “Patent Owner does not identify any particular claim limitation as not disclosed in the prior art.” (Paper 11, 16.) To the contrary, Cipla showed in its preliminary response that the claim

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elements “nasal spray” and formulation “suitable for nasal administration,” as properly construed, are not taught in the art.

1. The Board overlooked that Segal is even more deficient than the closer prior art (Cramer) which Cipla overcame.

In finding that Cipla did not identify any particular claim limitation that was not disclosed in the prior art, the Board overlooked Cipla's evidence that Cramer and Segal share the same teachings relevant to these proceedings, (Paper 7, 12-16), and that Segal is even more deficient, as confirmed by the testimony of Argentum's experts, Dr. Schleimer and Dr. Donovan.

Attempting to avoid the irreparable deficiencies in Cramer's disclosure established during prosecution and confirmed in district court litigation, Argentum instead relies on the more general teachings from the Segal reference to anchor its obviousness Grounds 2 and 3. But not only does Segal fail to cure Cramer's shortcomings, it exacerbates them. There can be no dispute that Segal's disclosure is a “less specific” version of Cramer's teachings. That is how Argentum's expert, Dr. Schleimer, described the two references during his testimony in district court. (Paper 7, 12 (quoting CIP2019, 65:17-20).) That description is accurate: Segal discloses more than 800 million hypothetical drug combinations, as the Board found, (Paper 11, 13.), and contains no formulation examples or other description of ingredients or concentrations. (See CIP2007, ¶29; see generally EX1012.)

In contrast to Segal, Cramer—which Cipla overcame during prosecution by

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clarifying or inserting the “nasal spray” and “suitable for nasal administration” claim elements—*does* provide specific example formulations and other descriptions of ingredients and concentrations. Dr. Govindarajan, upon whose testing Argentum's expert Dr. Donovan relied in the district court, attempted to recreate Cramer Example III. But his attempted formulations exhibited the same shortcomings that Cipla had shown during prosecution. (Paper 7, 42 (citing CIP2007, ¶¶42-47; CIP2030, 31, 39.)

If Cramer's specific disclosure does not teach a POSA how to make a “nasal spray” that is “suitable for nasal administration,” then Segal surely cannot. (Paper 7, 12-16, 40, 41-42.) Indeed, Argentum's Petition shows no basis to assume it could.

2. The Board misapprehended or overlooked that Ground 2 is deficient because Argentum's alleged art is missing key claim limitations: “nasal spray” and “suitable for nasal administration.”

As the Board correctly recognized, Segal does not anticipate the '620 patent claims. (Paper 11, 10-14.) Consequently, a person of ordinary skill in the art must modify Segal in order to stand any chance of arriving at the claimed formulations. But Cipla's preliminary response highlights how a person of ordinary skill in the art would have had no reasonable expectation that the POSA could successfully modify Segal to arrive at a “nasal spray” formulation “suitable for nasal administration.” In fact, as Cipla explained in its Preliminary Response, testing by

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Dr. Govindarajan that Dr. Donovan relied on in the district court showed that even modifications of Cramer (and thus, Segal) that might be considered routine in the art, still did not yield the claim elements. Both Dr. Govindarajan's efforts and additional testing conducted by Cipla (including varying the viscosities of the HPMC thickening agent, varying the micronization of triamcinolone, applying heat, and applying high-speed mixing steps) all showed that various so-called "routine" modifications failed to cure the deficiencies that Cipla exposed during prosecution. (Paper 7, 42 (citing CIP2007, ¶¶48-50, CIP2030, 27; CIP2105, 4-6; CIP2110, 4-7, CIP2040, 4; CIP2029, 3; EX1002, 285-86; CIP2030, 30-31, 33, 36, 37).) These failed results underscore that parameters necessary for a "nasal spray" that is "suitable for nasal administration" within the meaning of the claims are interrelated, such that modifying the formulation to address one problem will have adverse consequences for other parameters. And the scant formulation guidance in Segal would not have taught a person of ordinary skill in the art how to modify a combination of azelastine and fluticasone to make it suitable for nasal administration with any reasonable expectation of success. (Paper 7, 38-42).

The Board concluded that Cipla's preliminary response creates "disputed issues of fact" as to whether a person of ordinary skill in the art would have had a reasonable expectation of success. (Paper 11, 20.) There is no such dispute: in district court, both Argentum's and Cipla's experts provided testing of numerous

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changes to Cramer's formulation and the process for making the same (each of which would fall within the scope of Segal's unspecific teachings). (Paper 7, 42.) The results of these formulation tests cannot be disputed, and each test was unsuccessful. The repeated failures do not give rise to any expectation of success, reasonable or otherwise. (*Id.*, 41-42.) For Argentum's expert to testify otherwise does not create a dispute of fact where the testing she previously relied upon proves that there is no dispute. *See Brand Management, Inc. v. Menard, Inc.*, 135 F.3d 776, *9 (Fed. Cir. 1998) (rejecting a later declaration that contradicted a witness's earlier deposition testimony).

3. *Ground 3 also fails because it relies upon deficient Ground 2.*

The Board's decision to institute Ground 3 also overlooks the importance of the correct construction of the limitations, "nasal spray" and "suitable for nasal administration." As with Ground 2, there can be no dispute that the same limitations above are missing from Ground 3. But Cipla highlighted additional shortcomings in Ground 3 that the Board would have found persuasive had it not overlooked the correct claim construction.

Specifically, the Board found that "Patent Owner's contention that the Petition fails to articulate a motivation to combine Hettche, Phillipps and Segal with the Flonase[®] Label is an issue for trial," and that "Patent Owner's arguments and evidence" regarding teaching away and the additional excipients "raise a

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disputed issue of fact that is best resolved on a complete record.” (Paper 11, 21-22.)

First, Cipla explained that the use of either CMC or MCC was inconsistent with the homogeneity requirement of the correctly construed claims. CMC and MCC—both thickening agents intended to keep the fluticasone suspended—were expected to precipitate out of solution in the presence of cationic drugs. (Paper 7, 44-45.) Azelastine hydrochloride is cationic. (*Id.*, 45.) Thus, by using CMC or MCC in a formulation with azelastine, a POSA would not expect fluticasone to stay properly suspended, which in turn yields a non-homogeneous formulation. (*Id.*) The Board's finding that this is a disputed issue is an abuse of discretion: the pre-invention art unambiguously established this expectation, and post-invention testing by Meda Pharmaceuticals confirmed the expectation. (*Id.*, 45-46.)

Second, Cipla explained that Segal itself teaches that Argentum's proposed combination is inconsistent with the tolerability requirement of the correctly construed claims. Segal teaches that “[p]reservative-free compositions are preferred due to reduced sensitivity and increased patient acceptance.” (Paper 7, 47 (quoting EX1012, 6:15-19).) There can be no dispute that this is what Segal teaches. And the parties also do not dispute that a POSA would have known that Astelin[®] is the commercial embodiment of Hettche. (*Compare* Paper 7, 47, *with* Paper 2, 12 (“[Hettche], issued in 1982, is the patent that covers Astelin[®].”).) Both

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drugs—Astelin[®] and Flonase[®]—contain two preservatives: BKC and EDTA in Astelin[®] and BKC and phenyl ethyl alcohol in Flonase[®]. (Paper 7, 47 (citing EX1008, 2; EX1010, 1).) Putting them together, as Argentum proposes in Ground 3, yields *three* preservatives and increased concentration in the formulation. (Paper 7, 47.) But Segal teaches away from that very result, particularly in a situation where, as here, the formulation must be tolerable to patients. In finding that Cipla's arguments "raise a disputed issue of fact," the Board overlooked that *there is no dispute of fact*: Segal teaches not to increase preservative content, but that is precisely what Argentum's purported combination achieves. (*See* Paper 2, 44-45 (listing EDTA, BKC, and phenylethyl alcohol as preservatives).)

In short, the Board's misapprehension of the correct construction of terms "nasal spray" and "suitable for nasal administration" compounded its misapprehension of the arguments presented in Ground 3. The undisputed facts are sufficient to show that Ground 3 should not have been instituted.

IV. Once the Board's claim construction oversight/misapprehension is cured, it is appropriate to grant rehearing and deny institution on Grounds 2 and 3.

The Board's precedent establishes that rehearing is particularly appropriate in situations where it either arrived at an incorrect claim construction and the correct construction would change the outcome of its original decision. *See, e.g., WesternGeco LLC v. PGS Geophysical AS*, IPR2015-00313, Paper 45 (Feb. 3,

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2017) (granting rehearing and reversing original opinion when corrected claim construction changed the import of prior art); *AVX Corp. v. Greatbatch, Ltd.*, IPR2015-00710, Paper 13 (Jan. 13, 2016) (same).

Cipla showed that the broadest reasonable interpretation of the claim terms “nasal spray” and “suitable for nasal administration” is “pharmaceutical formulations that are tolerable to patients, that are homogeneous, and that can be suitably deposited onto the nasal mucosa.” (Paper 7, 9-11.) Cipla also established that these claim elements are absent from Argentum’s cited prior art. (*See supra.*) Accordingly, the Board should grant Cipla’s request for rehearing, construe these claim terms, and reverse its decision to institute because Argentum’s Petition failed to show that either element was known in the prior art.

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V. Conclusion

The Board misapprehended or overlooked various critical (and indisputable) facts raised in Cipla's Preliminary Response that warrant denial of institution of Argentum's Grounds 2 and 3. Argentum's arguments alleging that Segal taught a "nasal spray" formulation that is "suitable for nasal administration," within the proper meaning of these terms, is at odds with its own experts' prior testimony. Cipla, therefore, respectfully requests that the Board grant rehearing and deny institution on Grounds 2 and 3.

Respectfully Submitted,

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Date: September 5, 2017

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CERTIFICATE OF SERVICE (37 C.F.R. §§ 42.6(e))

The undersigned hereby certifies that the above-captioned “Cipla Limited’s Motion for Rehearing Pursuant to 37 C.F.R. § 42.71(d)” was served in its entirety on September 5, 2017, upon the following parties via email:

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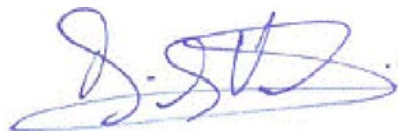
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