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Paper 7
Date: July 31, 2020

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GLAXOSMITHKLINE
CONSUMER HEALTHCARE HOLDINGS (US) LLC,
Petitioner,

v.

CIPLA LTD.,
Patent Owner.

IPR2020-00368
Patent 8,163,723 B2

Before JO-ANNE M. KOKOSKI, ZHENYU YANG, and CHRISTOPHER M. KAISER, *Administrative Patent Judges.*

YANG, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 325(d)

INTRODUCTION

GlaxoSmithKline Consumer Healthcare Holdings (US) LLC ("Petitioner") filed a Petition (Paper 1 ("Pet.")), seeking an *inter partes* review of claims 1–28 of U.S. Patent No. 8,163,723 B2 (Ex. 1002, "the '723 patent"). Cipla Ltd. ("Patent Owner") filed a Preliminary Response. Paper 6 ("Prelim. Resp.").

For the reasons provided below, we exercise our discretion under 35 U.S.C. § 325(d) and deny institution of an *inter partes* review.

Related Matters

According to the parties, the '723 patent is the subject of *Meda Pharmaceuticals Inc. v. Teva Pharmaceuticals USA, Inc*., No. 1:15-cv-00785-LPS (D. Del.); *Meda Pharmaceuticals Inc. v. Perrigo UK FINCO Ltd*., No. 1:16-cv-00794-LPS (D. Del.); and *Meda Pharmaceuticals, Inc. v. Apotex Inc*., No. 1:14-cv-01453-LPS (D. Del.). Pet. 56; Paper 5, 1. All three cases have been dismissed by stipulation. Pet. 56; Paper 5, 1.

The parties also identify *Argentum Pharmaceuticals LLC v. Cipla Ltd.*, IPR2017-00807 (PTAB) ("the Argentum IPR") as a related matter. Pet. 56; Paper 5, 1. The Argentum IPR challenged the parent of the '723 patent, U.S. Patent No. 8,168,620 B2 (Ex. 1001, "the '620 patent"). There, the Board instituted trial but terminated it prior to issuing a final written decision. Pet. 56, 58; Paper 5, 1.

Petitioner concurrently filed three other petitions, challenging patents related to the '723 patent: IPR2020-00369 (challenging the '620 patent), IPR2020-00370 (challenging U.S. Patent No. 9,259,428 B2 (Ex. 1003)), and IPR2020-00371 (challenging U.S. Patent No. 9,901,585 B2 (Ex. 1004, "the '585 patent").

The '723 Patent

The '723 patent discloses and claims pharmaceutical compositions comprising azelastine (or its pharmaceutically acceptable salt) and fluticasone (or its pharmaceutically acceptable ester) in a dosage form suitable for nasal administration. *See generally* Ex. 1002. It teaches that azelastine is an antihistamine useful for treating allergy-related conditions. *Id.* at 1:30–33 (stating "it is known to use the antihistamine azelastine (usually as the hydrochloride salt) as a nasal spray against seasonal or perennial allergic rhinitis"). It also teaches that it was known in the art to treat allergic rhinitis with corticosteroids, "which will suppress nasal and ocular inflammatory conditions." *Id.* at 1:35–37. The '723 patent lists fluticasone as a corticosteroid "known for nasal use." *Id.* at 1:37–38.

According to the '723 patent, "[i]t would be highly desirable, however, to provide a treatment that combines the effects of anti-histamine treatments and steroid treatments, in a pharmaceutically acceptable formulation, which is tolerated in situ, without significantly disrupting the potency of the constituent pharmaceuticals." *Id.* at 1:43–47.

The '723 patent states that the inventors found that, "very surprisingly, azelastine . . . can advantageously be combined with a steroid . . . to provide a stable, very effective combination product or formulation" for nasal treatment. *Id.* at 1:48–57. Such a combination, according to the '723 patent, "can provide, in a single administration or dosing regime, the antihistaminic properties of azelastine and the anti-inflammatory (and/or other) properties of the steroid, without any significant interference between the two, or adverse reaction in situ." *Id.* at 1:58–62.

The '723 patent discloses that the pharmaceutical compositions are preferably in the form of nasal drops, eye drops, nasal sprays, nasal inhalation solutions, aerosols, or insufflation powders. *Id.* at 2:16–18. Of these, the '723 patent states that a nasal spray is a particularly preferred form. *Id.* at 2:24–26. The '723 patent also teaches that the formulations may contain pharmaceutically acceptable excipients, such as preservatives, stabilizers, auxiliary substances, isotonization agents, thickening agents, and buffers. *Id.* at 2:32–3:65.

Illustrative Claim

Claim 1 is the only independent claim and is reproduced below:

> 1. A method for the prophylaxis or treatment in a mammal of a condition for which administration of one or more anti-histamines and/or one or more steroids is indicated, comprising intranasal administration to said mammal of a therapeutically effective amount of a pharmaceutical composition comprising (a) azelastine, or a pharmaceutically acceptable salt thereof; and (b) pharmaceutically acceptable ester of fluticasone.

The Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability:

Claims Challenged	35 U.S.C. §	References
1–28	103(a)	PDR 1999,[1] Segal[2]
1–28	103(a)	Cramer,[3] PDR 1999

In support of its patentability challenge, Petitioner relies on the Declarations of Maureen D. Donovan, Ph.D. (Ex. 1058) and Robert P. Schleimer, Ph.D. (Ex. 1062).

[1] Physicians' Desk Reference (53rd ed. 1999) (Ex. 1010).
[2] WO 98/48839 A1, published Nov. 5, 1998 (Ex. 1012).
[3] EP 0 780 127 A1, published June 25, 1997 (Ex. 1011).

DISCUSSION

Patent Owner asks us to exercise our discretion under 35 U.S.C. § 325(d) and deny this Petition. Prelim. Resp. 20–28. Patent Owner argues that "[t]he Office has already evaluated—and rejected—Petitioner's arguments." *Id.* at 20. According to Patent Owner, Cramer and Segal were addressed by the Examiner during prosecution, and while PDR 1999 was not previously considered, "its teachings are cumulative of information already considered (and rejected) by the Office." *Id.* at 21. We find Patent Owner's arguments persuasive.

Under § 325(d),

> In determining whether to institute or order a proceeding under . . . chapter 31, the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.

In evaluating whether to exercise our discretion under § 325(d), we weigh the following non-exclusive factors ("*BD* factors"):

> (a) the similarities and material differences between the asserted art and the prior art involved during examination;
>
> (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
>
> (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
>
> (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;
>
> (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
>
> (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of prior art or arguments.

Becton, Dickinson & Co. v. B. Braun Melsungen AG, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential as to § III.C.5, first paragraph).

Factors (a), (b), and (d) relate to whether the art and arguments presented in the petition are the same or substantially the same as those previously presented to the Office. *Advanced Bionics, LLC v. Med-El Electromedizinishe Geräte GmbH*, IPR2019-01469, Paper 6 at 10 (PTAB Feb. 13, 2020) (precedential). Factors (c), (e), and (f) "relate to whether the petitioner has demonstrated a material error by the Office" in its prior consideration of that art or arguments. *Id.* Only if the same or substantially the same art or arguments were previously presented to the Office do we then consider whether petitioner has demonstrated error. *Id.*

BD Factors (a), (b), and (d)

We first consider whether Petitioner asserts the same or substantially the same prior art or arguments that previously were presented to the Office. We conclude that Petitioner does so.

Cramer

Petitioner acknowledges that "*Cramer* was cited by the examiner during prosecution." Pet. 58. Indeed, during the prosecution of the parent '620 patent, the Examiner repeatedly relied on Cramer to reject the claims as anticipated or obvious. *See* Ex. 2001, 497–512, 603–22, 721–42. Cramer was also specifically discussed during an Examiner interview. *Id.* at 494.

The Examiner found that "Cramer teaches a nasal spray composition comprising about 0.001 to about 0.2% concentration of a glucocorticosteroid (i.e. beclomethasone, flunisolide, triamcinolone, fluticasone, mometasone,

bedusonide and pharmaceutically acceptable salts), 0.01 to about 4% concentration of an antihistamine (i.e. azelastine or pharmaceutically acceptable sale thereof, and an intranasal carrier)." *See, e.g.*, *id.* at 732. Referring to Example III of Cramer as "disclos[ing] an intranasal pharmaceutical composition prepared by combining" azelastine and triamcinolone acetonide, a glucocorticoid agent, the Examiner recognized that "Cramer does not exemplify a composition comprising azelastine and fluticasone." *Id.* at 732–33. Nevertheless, the Examiner concluded that "one of ordinary skill in the art would have been motivated to make a composition comprising azelastine and fluticasone because Cramer suggests that the combination of a glucocorticoid (i.e. fluticasone) and antihistamine (i.e. azelastine) provide improved relief of symptoms associated with seasonal or perennial allergic rhinoconjunctivitis."[4] *Id.* at 733.

Petitioner relies on the same teachings of Cramer. For example, Petitioner asserts that "*Cramer* discloses 'pharmaceutical formulations for nasal administration comprising . . . a safe and effective amount of a glucocorticoid,' such as 'fluticasone,' and 'a safe and effective amount of a leukotriene inhibiting antihistamine,' such as 'azelastine' or 'pharmaceutically acceptable salts thereof.'" Pet. 27 (quoting Ex. 1011, 2:36–44). Like the Examiner, Petitioner also points to Cramer's Example III for disclosing "an 'intranasally administered pharmaceutical composition' comprising 'azelastine HCl' (or azelastine hydrochloride), which is a

[4] During prosecution of the '723 patent, the Examiner suggested certain amendments to "accord with prior art identified during prosecution of the ['620 patent]." Ex. 1006, 3. After the applicant did so, the Examiner allowed the claims, stating that "[t]he claims as amended are free of the prior art of record." *Id.* at 22.

pharmaceutically acceptable salt of azelastine, and 'triamcinolone acetonide,' which is a pharmaceutically acceptable ester of triamcinolone." *Id.* at 27–28 (quoting Ex. 1011, 6:26–51). Petitioner further refers to Example III for disclosing that "substantially similar results are also obtained using, in whole or in part, equivalent amounts of other glucocorticoid agents such as fluticasone." *Id.* at 28 (quoting Ex. 1011, 6:44–46).

In sum, Cramer was previously presented to the Office, and Petitioner makes the same arguments the Office previously considered regarding Cramer.

Segal

During the prosecution of the '620 patent, the applicant listed Segal on an IDS and the Examiner initialed it. Ex. 2001, 786. Although the Examiner did not rely on Segal in any rejections, the Examiner explicitly stated that the reference was considered. *See* Ex. 1008, 36–39.

Segal was asserted against the '620 patent claims in the Argentum IPR petition. The Examiner, in allowing the claims of the '585 patent, a later-issued patent related to the challenged '723 patent, stated that "all the references cited by the Argentum Petition are of record and have been previously evaluated, or disclose information redundant to information of record." *Id.* at 37. And Petitioner admits that "the Argentum IPR was instituted based on the cited prior art and similar arguments" as in this Petition. Pet. 58. Accordingly, Segal was previously presented to the Office and Petitioner makes the same arguments the Office previously considered regarding Segal.

PDR 1999

PDR 1999 was not before the Examiner during prosecution. We agree with Patent Owner, however, that the teachings of PDR 1999 do not differ "in any material way from the art and arguments already considered and overcome during prosecution." Prelim. Resp. 24.

PDR 1999 discloses monotherapy nasal spray formulations comprising either azelastine hydrochloride or fluticasone propionate. Ex. 1010, 1122 (PDR 1999 entry for Flonase, fluticasone propionate nasal spray), 3191 (PDR 1999 entry for Astelin, azelastine hydrochloride nasal spray). Petitioner relies on PDR 1999 for those teachings, as well as for disclosing certain excipients the challenged claims require. *See* Pet. 4–5, 28–29.

As Patent Owner points out, these teachings were already considered by the Examiner because "the specification itself recognizes that azelastine and fluticasone as monotherapies to treat allergy-related conditions were known in the art." Prelim. Resp. 14 (citing Ex. 1001,[5] 1:20–30).

In addition, Patent Owner argues that Cramer, which was considered by the Examiner, as well as declarations submitted during prosecution to traverse the rejections, described the prior-art practices of using antihistamines and corticosteroids as monotherapies. *Id.* at 14–15. For example, Patent Owner points to statements from medical practitioners that azelastine alone and fluticasone alone were used to treat seasonal allergic rhinitis. *Id.* at 15 (citing Ex. 2001, 577, 581).

[5] Although Patent Owner cites the specification of the '620 patent, the '723 patent contains the same passages. *See* Ex. 1002, 1:28–39.

Furthermore, the Argentum IPR asserted similar references with essentially the same teachings. *See* Argentum IPR, Paper 11, 6. For example, Hettche[6] discloses a nasal medicine that contains azelastine or a physiologically acceptable salt of azelastine, and each of Phillipps[7] and Flonase Label[8] discloses nasal spray formulations comprising fluticasone propionate and other pharmaceutical carriers or excipients. *Id.* at 14–22. As discussed above, in allowing the claims of the '585 patent, a later-issued patent related to the challenged '723 patent, the Examiner stated that "all the references cited by the Argentum Petition are of record and have been previously evaluated, or disclose information redundant to information of record." Ex. 1008, 37. And Petitioner admits that "the Argentum IPR was instituted based on the cited prior art and similar arguments" as in this Petition. Pet. 58.

Thus, PDR 1999 is cumulative of the art the Examiner considered during prosecution and Petitioner makes the same arguments that the Office previously considered.

BD Factors (c), (e), and (f)

Because we find that the "same or substantially the same prior art or arguments previously were presented to the Office," we turn to whether Petitioner demonstrates that the Office erred in a manner material to the patentability of the challenged claims. We conclude that Petitioner has failed to do so.

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[6] U.S. Patent No. 5,164,194, issued Nov. 17, 1992 (Ex. 1013).
[7] U.S. Patent No. 4,335,121, issued June 15, 1982 (Ex. 1009).
[8] FLONASE® (fluticasone propionate) Nasal Spray, 50 mcg Product Information (Dec. 1998) (Ex. 2020).

Petitioner does not discuss the factors listed in the Board's precedential decision *Becton, Dickinson*. Nevertheless, Petitioner asserts that, during prosecution, the applicant overcame the rejections over Cramer "based solely on alleged objective indicia of nonobviousness, none of which demonstrates nonobviousness." Pet. 58. Petitioner is correct that the Examiner allowed the claims of both the challenged '723 patent and the parent '620 patent after considering objective indicia of nonobviousness. Ex. 2001, 195–98; Ex. 1006, 22. Petitioner, however, has not shown sufficiently that the Examiner erred in doing so.

During the prosecution of the '620 patent, the applicant submitted several declarations from inventor Geena Malhotra as evidence supporting unexpected stability of the claimed formulation and the inoperability of Cramer's Example III. Ex. 2001, 336–39, 568–70, 698–700. The applicant also submitted declarations from Mr. Nikhil Chopra, Joachim Maus, M.D., and Sujeet Rajan, M.D. to support the assertions of commercial success, unexpected results, and long-felt need, respectively. *Id.* at 328–34, 358–64, 458–62.

After considering those declarations, the Examiner allowed the claims. *See id.* at 192–99. In the Reasons for Allowability, the Examiner discussed in detail the Chopra, Maus, and Rajan declarations. *Id.* at 195–98. The Examiner found "the Chopra Declaration supports that the product of the invention has been a commercial success for both the inventors and the copiers . . . [and] that the product of the invention has filled a long-felt, but unmet need for an improved treatment for allergic rhinitis." *Id.* at 196. The Examiner found Dr. Rajan's declaration "also supports that the invention fills a long unmet need." *Id.* In addition, the Examiner found that "Dr. Maus

concludes that the superior results obtained with the combination of nasal fluticasone propionate and azelastine HCl would have been unexpected at the time of filing of the application. On the basis of this information and declaration, the examiner concurs in this conclusion." *Id.* at 197 (internal citation omitted). Accordingly, the Examiner concluded "the invention [of the '620 patent] is unexpectedly and surprisingly unobvious over, different from, and superior to the prior art of record." *Id.* at 198.

Similarly, the Examiner allowed the challenged claims of the '723 patent, relying on the applicant's evidence on objective indicia of nonobviousness. Ex. 1006, 22. The Examiner repeats:

> The unobviousness of the method is supported by a proper Declaration by Mr. Chopra attesting to commercial success of the product, as used in the claimed method. Also, a proper Declaration by Dr. Rajan supported that the invention fills a long unmet need. A third proper Declaration by Dr. Maus supported the notion that contemporary publications found no clinical benefit or minimal clinical benefit to a combination of oral antihistamine and nasal steroid.

Id.

Petitioner argues that there are no "unexpected results supportive of nonobviousness" because, during prosecution, the applicant did not compare "the claimed invention to the closest prior art." Pet. 53. According to Petitioner, "the closest prior art is a pharmaceutical nasal formulation comprising both azelastine and fluticasone, such as those taught by *Cramer* and *Segal*." *Id.* Thus, Petitioner asserts that the applicant did not show unexpected results because it did not present "results comparing the claimed invention to a pharmaceutical nasal formulation comprising both azelastine and fluticasone . . . or to co-administration of commercially available

azelastine hydrochloride nasal spray and fluticasone propionate nasal spray." *Id.* at 54.

Assuming, without deciding, that Petitioner is correct that the applicant did not compare the claimed invention to the closest prior art, Petitioner has not shown sufficiently that the Examiner erred in allowing the challenged claims. After all, the Examiner did not allow the claims solely based on the applicant's showing of unexpected results. Rather, the Examiner also found persuasive the applicant's evidence on commercial success and long-felt need, including the Chopra and Rajan declarations. Ex. 1006, 22.

Petitioner does not discuss either of these declarations. In fact, Petitioner does not even mention commercial success. As to long-felt but unmet need, Petitioner's analysis, in its entirety, reads: Patent Owner "Cipla has not shown that the claimed invention satisfied a long-felt but unmet need, for at least the reason that Cipla has not shown that any such need that was not already satisfied by co-administration of commercially available azelastine hydrochloride and fluticasone propionate nasal sprays." Pet. 55–56. This attorney argument, without supporting evidence, is not enough to show that the Examiner committed any material error.

Moreover, Petitioner's argument is substantially similar to one made in the Argentum IPR. *Compare* Pet. 54, *with* IPR2017-00807, Paper 2, 55. During prosecution of the later-issued, related '585 patent, the Examiner considered that argument made in the Argentum IPR. Ex. 1008, 37 ("With regard to the Declaration by Maus, the Argentum Petition asserts that the relevant comparator for the inventive formulation is concurrent use of fluticasone propionate nasal spray and azelastine nasal spray."). The

Examiner determined that assertion "is not persuasive because at the time of the invention, the field as a whole was divided as to whether oral or nasal administration of antihistamine was better." *Id.* Yet Petitioner does not attempt to explain how the Examiner erred in that determination. Nor does Petitioner discuss the Maus declaration,[9] which the Examiner found persuasive. *See, e.g.*, Ex. 1008, 41 (describing the Maus declaration as reviewing several studies, including "a non-prior art study which concludes that there is no evidence that a combination of intranasal corticosteroids with intranasal antihistamines provides any additional therapeutic benefit, in comparison with intranasal steroids alone").

In sum, the record demonstrates that the Examiner determined the claims were unobviousness based on the totality of the evidence. Petitioner has not demonstrated a material error by the Office in the prior consideration of the same or substantially the same art or arguments presented in the Petition.

CONCLUSION

Weighing the *BD* factors, we conclude that, on the record presented, the circumstances of this case warrant exercise of our discretion to deny institution based on § 325(d). The Petition relies on the same and substantially the same references, and presents arguments that are substantially the same as those the Examiner considered during prosecution.

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[9] Petitioner also argues that a declaration by inventor Geena Malhotra does not support nonobviousness. Pet. 54. But, as Petitioner acknowledges, "the Examiner did not cite [the Malhotra] declaration in issuing the patents." *Id.* Thus, we do not find Petitioner's arguments directed to the Malhotra declaration as relevant in determining whether Petitioner shows that the Examiner erred in a manner material to patentability.

Petitioner has not demonstrated that the Examiner materially erred in that consideration. Thus, we exercise our discretion and deny institution of a trial under 35 U.S.C. § 325(d).[10]

ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *denied*, and no trial is instituted.

[10] Patent Owner argues that we should deny institution for several other reasons. Prelim. Resp. 5–11, 29–61. Because we deny the Petition under § 325(d), we do not reach those additional arguments.

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