

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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SANDOZ INC., APOTEX INC., APOTEX CORP.,  
EMCURE PHARMACEUTICALS LTD., HERITAGE PHARMA LABS  
INC., HERITAGE PHARMACEUTICALS INC.,  
GLENMARK PHARMACEUTICALS, INC., USA,  
GLENMARK HOLDING SA, GLENMARK PHARMACEUTICALS,  
LTD., MYLAN LABORATORIES LIMITED, TEVA  
PHARMACEUTICALS, USA, INC., FRESENIUS KABI USA, LLC, and  
WOCKHARDT BIO AG,  
Petitioner,

v.

ELI LILLY & COMPANY,  
Patent Owner.

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Case IPR2016-00318<sup>1</sup>  
Patent 7,772,209 B2

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Before JACQUELINE WRIGHT BONILLA, MICHAEL P. TIERNEY,  
*Vice Chief Administrative Patent Judges*, and LORA M. GREEN,  
*Administrative Patent Judge*.

GREEN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION

Determining That Claims 1–22 Have Not Been Shown to Be Unpatentable  
*35 U.S.C. § 318(a) and 37 C.F.R. § 42.73*

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<sup>1</sup> Cases IPR2016-01340, IPR2016-01393, and IPR2016-01429 have been  
joined with the instant proceeding.

## I. INTRODUCTION

Sandoz Inc. filed a Petition requesting an *inter partes* review of claims 1–22 of U.S. Patent No. 7,772,209 B2 (Ex. 1001, “the ’209 patent”). Paper 2 (“Pet.”). Eli Lilly & Company (“Patent Owner” or “Lilly”) filed a Preliminary Response to the Petition. Paper 11 (“Prelim. Resp.”). We determined that the information presented in the Petition and the Preliminary Response demonstrated that there was a reasonable likelihood that Petitioner would prevail in challenging claims 1–22 as unpatentable under 35 U.S.C. § 103(a). Pursuant to 35 U.S.C. § 314, we instituted trial on June 16, 2016, as to all of the challenged claims of the ’209 patent. Paper 14 (“Institution Decision” or “Dec. Inst.”).

Thereafter, other parties filed three additional Petitions challenging the same claims based on the same ground of unpatentability over the same prior art as those instituted by the Board in the instant case, as well as motions for joinder. Specifically, Apotex Inc., Apotex Corp., Emcure Pharmaceuticals Ltd., Heritage Pharma Labs Inc., Heritage Pharmaceuticals Inc., Glenmark Pharmaceuticals Inc., USA, Glenmark Holding SA, Glenmark Pharmaceuticals Ltd., and Mylan Laboratories Limited requested *inter partes* review of claims 1–22 of the ’209 patent in IPR2016-01429, and joinder to the instant proceeding. IPR2016-01429, Papers 2 and 3. On October 6, 2016, the Board instituted *inter partes* review in that case, and granted joinder. IPR2016-01429, Paper 11. Teva Pharmaceuticals USA, Inc. and Fresenius Kabi USA, LLC requested *inter partes* review of claims 1–22 of the ’209 patent in IPR2016-01340, as well as joinder to the instant proceeding. IPR2016-01340, Papers 2 and 3. *Inter partes* review was instituted in that case and joinder granted on October 6, 2016. IPR2016-

IPR2016-00318  
Patent 7,772,209 B2

01340, Paper 9. Finally, Wockhardt Bio AG also requested *inter partes* review of claims 1–22 of the '209 patent in IPR2016-01393, and joinder to the instant proceeding. IPR2016-01393, Papers 1 and 3. *Inter partes* review was instituted and joinder granted on November 21, 2016. IPR2016-01393, Paper 9. We collectively refer to all enjoined Petitioners in this Final Written Decision as “Petitioner.”

Patent Owner filed a Response (Paper 36, “PO Resp.”), Petitioner filed a Reply (Paper 49), and Patent Owner filed a Sur-reply (Paper 68). In addition, Petitioner filed a Motion to Exclude (Paper 64, “Mot. Exclude”), to which Patent Owner filed an Opposition (Paper 72, “Opp. Mot. Exclude”), and Petitioner filed a Reply (Paper 77). Oral hearing was held on March 16, 2017, and a transcript of that hearing has been entered into the record. Paper 81 (“Tr.”).

We have jurisdiction under 35 U.S.C. § 6. Petitioner bears the burden of proving unpatentability of the challenged claims, and the burden of persuasion never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). To prevail, Petitioner must establish facts supporting its challenge by a preponderance of the evidence. *See* 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

Based on the record before us, we conclude that Petitioner has failed to demonstrate by a preponderance of the evidence that claims 1–22 of the '209 patent are unpatentable. We also *deny* Petitioner’s Motion to Exclude.

A. *Related Proceedings*

The '209 patent is the subject of litigation in the U.S. District Court for the Southern District of Indiana, including *Eli Lilly & Co. v. Sandoz Inc.*, No. 1:14-cv-2008 (S.D. Ind.) (filed Dec. 5, 2014). Pet. 2–3; Paper 5, 2–3.

The '209 patent also has been challenged in IPR2016-00237 and in IPR2016-00240 by Neptune Generics, LLC. IPR2016-01190, IPR2016-01335, and IPR2016-01341 have been joined with IPR2016-00237, and proceedings IPR2016-01191, IPR2016-01337, and IPR2016-01343 have been joined with IPR2016-00240.

B. *The '209 Patent*

The '209 patent issued on August 10, 2010, listing Clet Niyikiza as the sole inventor. Ex. 1001. The '209 patent claims priority to a series of applications, the earliest of which was filed on June 30, 2000. *Id.* at 1:2–10.

“As cancer cells are actively proliferating, they require large quantities of DNA and RNA.” Ex. 1047, 35.<sup>2</sup> Antifolates are a well-studied class of antineoplastic agents that inhibit one or several key folate-requiring enzymes of the thymidine and purine biosynthetic pathways. Ex. 1001, 1:19–20, 1:36–41. Because antifolates interfere with DNA and RNA synthesis, antifolates are used as chemotherapeutic drugs to treat certain types of cancer. Ex. 1004 ¶¶ 28–29, 31.

A limitation on the use of antifolate drugs is “that the cytotoxic activity and subsequent effectiveness of antifolates may be associated with substantial toxicity for some patients.” Ex. 1001, 1:62–64. Homocysteine levels have been shown to be a predictor of cytotoxic events related to the

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<sup>2</sup> We note that, unless otherwise indicated, the page numbers refer to the page numbers of the original references, and not to those added by a party.

use of certain antifolate enzyme inhibitors. *Id.* at 2:16–26. The ’209 patent states that folic acid has been shown to lower homocysteine levels. *Id.* Additionally, the patent states that it was known in the art to treat and prevent cardiovascular disease with a combination of folic acid and vitamin B12, but that “the use of the combination for the treatment of toxicity associated with the administration of antifolate drugs was unknown heretofore.” *Id.* at 2:50–54.

The ’209 patent describes “[a] method of administering an antifolate to a mammal in need thereof.” *Id.*, Abstract. The method is said to improve the therapeutic utility of antifolate drugs by administering a methylmalonic acid (“MMA”) lowering agent, such as vitamin B12, to the host undergoing treatment. *Id.* at 2:37–46. The ’209 patent also states that a combination of a MMA lowering agent, such as vitamin B12, and folic acid “synergistically reduces the toxic events associated with the administration of antifolate drugs.” *Id.* at 2:47–50.

The term antifolate is said to encompass chemical compounds that inhibit at least one key folate-requiring enzyme of the thymidine or purine biosynthetic pathways. *Id.* at 4:28–34. Pemetrexed disodium is the most preferred antifolate for the ’209 patent. *Id.* at 4:28–43. Pemetrexed is also referred to in the art as the “multitargeted antifolate” (“MTA”).<sup>3</sup> Ex. 1015, 129, Abstract 620P.

### *C. Illustrative Claims*

Petitioner challenges claims 1–22 of the ’209 patent. Claims 1 and 12 are independent, and are reproduced below:

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<sup>3</sup> We use “pemetrexed” and “MTA” interchangeably throughout this Decision.

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