UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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,

Petitioners

v.

ELI LILLY AND COMPANY,

Patent Owner.

Case IPR2016-00318[1]
U.S. Patent 7,772,209

PETITIONER SANDOZ INC.'S RESPONSE TO PATENT OWNER'S MOTION FOR OBSERVATIONS ON THE DEPOSITION OF EXPERT RON D. SCHIFF, M.D., PH.D.

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[1] Cases IPR2016-01429, IPR2016-01393, and IPR2016-01340 have been joined with the instant proceeding.

I. PATENT OWNER'S MOTION FOR OBSERVATIONS INCLUDES IMPROPER ARGUMENTS AND SHOULD BE EXPUNGED

Petitioner respectfully requests that the Board dismiss Patent Owner's Motion for Observations on the Deposition of Petitioner Sandoz's Expert Dr. Ron Schiff ("Motion" or "Mot.") and expunge its supporting exhibits because the purported observations in the Motion are a masked attempt to submit additional argumentative sur-reply pages in contravention of the Board's guidance and prior decisions. Instead of a short statement of relevance, Patent Owner's observations include argument, some of which spans several sentences or is strung together with a series of semicolons. *E.g.*, Paper 67, Mot. at 3, 7, 9, 10. Moreover, many of Patent Owner's arguments are new; they do not match the positions taken on the portions of the prior briefing Patent Owner cites. Sandoz discusses particularly egregious examples in further detail in its responses below.

As the Office Patent Trial Practice Guide makes clear, "[a]n observation should be a concise statement of the relevance of identified testimony to an identified argument or portion of an exhibit . . . . [I]t is not an opportunity to raise new issues, re-argue issues, or pursue objections." 77 Fed. Reg. 48,755, 48,767-68 (Aug. 14, 2012). The Board has further noted that "each item included as an observation on cross-examination should be precise, preferably no more than one short sentence in the explanation of relevance. Observations on cross-examination

are not meant to serve the purpose of an argumentative surreply." *Atrium Med. Corp. v. Davol Inc.*, IPR2013-00189, Paper 48 at 2 (February 28, 2014).

"The Board may refuse entry of excessively long or argumentative observations (or responses)," such as the observations contained in Patent Owner's Motion. *See* 77 Fed. Reg. 48,755, 48,767-68 (Aug. 14, 2012). In fact, the Board has previously considered proposed observations similar to the Patent Owner's submissions and dismissed them as containing improper argument. In *Medtronic, Inc. v. Nuvasive, Inc.*, the Board reviewed proposed observations that "cite[d] several pages of [the witness's] testimony, as opposed to one portion" and "proceed[ed] to present an argument that the testimony is relevant . . . ." IPR2013-00506, Paper 37 at 3-4 (October 15, 2014). The Board found the statements improper, dismissed the Motion, and expunged the relevant exhibits. *Id.*; *see also LG Elecs., Inc. v. ATI Techs. ULC*, IPR2015-00325, Paper 52 at 2-5 (January 25, 2016). While Petitioner maintains that the Board should dismiss the Motion without considering Patent Owner's proposed observations due to their inclusion of argument, Petitioner has responded to the proposed observations below.

II. SANDOZ'S RESPONSES TO PATENT OWNER'S OBSERVATIONS

Response to Observation 1

Patent Owner's observation concerns Dr. Schiff's testimony relating to the use of vitamin B_{12} (in the form of crude liver extract) and folic acid, as described in

Farber's 1948 study. According to Lilly, Farber's early work with aminopterin somehow shows "that vitamin B_{12} pretreatment would not have been obvious because over many decades of the use of antifolates and recognition of antifolate toxicity problems, vitamin B_{12} pretreatment was not used" since Farber 1948 was published. Paper 67 at 2. Not only is this an improper new argument under the Board's rules, but it also ignores Dr. Schiff's full testimony. Dr. Schiff explained that Farber's early experiments involving other antifolates provided proof of principle that folic acid and vitamin B_{12} can alleviate antifolate toxicity (Exhibit 2136 at 45:10-46:25, 52:7-53:21) and that vitamin B_{12} was in fact used with other antifolates such as 5-FU between Farber's work in the 1940s and the discovery in the 1990s of pemetrexed (*e.g.*, Ex. 2136, at 102:8-105:5 (citing Ex. 1028, Tisman)).

Response to Observation 2

Patent Owner makes an improper argument that a POSA would look only to the folic acid dose used in Hammond "rather than to trials of other drugs or doses used in other contexts," which, as noted above, violates the Board's rules and should be expunged. Paper 67 at 3.

Moreover, in making this improper argument, Patent Owner's observation ignores Dr. Schiff's testimony. Dr. Schiff explained that for various antifolates "certain findings will be transferable from one situation to another" but that a

POSA would understand it "would certainly be a mistake to assume that what one found with one antifolate compound would apply exactly to another . . . ." Ex. 2136 at 30:23-31:14. Likewise, Patent Owner omits Dr. Schiff's explanation of how a POSA would understand that Hammond used a very "high dose" of folic acid in order to offset toxicities that might occur while escalating the dose of pemetrexed beyond the known safe Phase II dose. Ex. 2136 at 196:16-197:20. Dr. Schiff's explained that a POSA would look to published literature concerning the use of folic acid with other antifolates such as lometrexol and the "community standard for folic acid dose" in order to determine an appropriate dosage of folic acid outside the context of pemetrexed dose escalation of Hammond. Ex. 2136 at 212:25-214:13. The referenced testimony is provided below:

> Q. . . . . Would the person of ordinary skill have understood why Hammond was structured as a dose escalation study as opposed to simply giving the folic acid with the maximum tolerated dose that had previously been seen and seeing if the toxicity could be reduced?
>
> A. Yes.
>
> Q. What's the reason for that?
>
> A. I think a person of ordinary skill would have understood that and attributed it to the fact that if you wanted to see whether folic acid has a protective effect on toxicity, you would want to use high doses of pemetrexed, which includes dose escalation and not just the Phase II dose, and you'd want to use a high dose of folic acid itself. So maybe I misspoke. You'd want to use a high dose of pemetrexed in a

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