IN THE UNITED STATES COURT OF APPEALS
FOR THE FOURTH CIRCUIT

HOSPIRA, INC., *Appellant,* v. SYLVIA MATHEWS BURWELL, *et al.* *Appellees*.	Case No. 14-1920

INTERVENOR SANDOZ INC.'S RESPONSE IN SUPPORT OF HOSPIRA'S EMERGENCY MOTION FOR INJUNCTION PENDING APPEAL

INTRODUCTION

FDA has taken an unprecedented and unlawful approach in approving abbreviated new drug applications ("ANDAs") for generic dexmedetomidine. Where a branded company like Hospira identifies patents covering its product, the Hatch-Waxman Act requires ANDA filers to follow a very specific certification process to gain approval, except in the case of "a method of use patent which does not claim a use for which the applicant is seeking approval." 21 U.S.C. § 355(j)(2)(A)(viii). Sandoz followed that certification process (known as a "Paragraph IV" certification), battled a years-long patent litigation with Hospira, and, as the first ANDA filer to do so, earned the reward promised under the statute

to generic companies who bring patent challenges—180 days of market exclusivity against other challengers to the listed patents.

Yet in this case, the FDA wrongly permitted Mylan and Par to come to market ***without*** challenging Hospira's patents under the statutory certification procedure and ***without*** waiting for Sandoz's statutory exclusivity to expire. This occurred even though Hospira's patent ***does*** "claim a use for which [Mylan and Par are] seeking approval." 21 U.S.C. § 355 (j)(2)(A)(viii). This wrongful approval directly and irreparably injures Sandoz by depriving it of its hard-earned statutory exclusivity.

The injunction requested by Hospira will protect Sandoz's exclusivity until the merits of this dispute are resolved, thereby ensuring that the Hatch-Waxman incentives for bringing generic drugs to market remain intact. Sandoz respectfully submits this Response in support of Hospira's motion to provide additional background with respect to the irreparable harm and public interests at stake.

BACKGROUND

In April 2009, Sandoz submitted ANDA No. 91-465, seeking approval from FDA to market a generic dexmedetomidine product in the United States. Declaration of Scott A. Smith ("Smith Decl."), ECF No. 14-1 at ¶ 5 (Exhibit A). Sandoz contributed substantial resources to that effort. *Id.* ¶ 14. Pursuant to the FDCA, Sandoz's ANDA included a Paragraph IV certification to U.S. Patent No.

6,716,867 ("'867 patent"). *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV). Sandoz certified that the '867 patent was invalid, unenforceable, and/or would not be infringed by the Sandoz generic dexmedetomidine product. *Id.*

Sandoz's ANDA was the first ANDA for Precedex that included a Paragraph IV certification to the '867 patent, thereby entitling Sandoz to 180 days of generic market exclusivity against any subsequent ANDA filer with a Paragraph IV certification to that patent. Smith Decl. ¶ 8. *See* 21 U.S.C. § 355(j)(5)(B)(iv). Following FDA acceptance of Sandoz's ANDA for filing, and pursuant to the FDCA, Sandoz notified '867 patent owner Hospira of the Paragraph IV certification and was subsequently sued by Hospira for patent infringement in the District of New Jersey, as the Hatch-Waxman scheme envisioned. Smith Decl. ¶ 9. *See* 35 U.S.C. § 271(e)(2)(A).

In December 2013, after more than four years of litigation, including a bench trial on the merits and full appellate briefing, Sandoz and Hospira entered into a settlement agreement under which Sandoz is permitted to market its generic dexmedetomidine product in the United States on December 26, 2014, or earlier in certain circumstances. That is approximately five years prior to the expiration of the '867 patent. Smith Decl. ¶ 10.

According to public court dockets, at least six other drug manufacturers (in addition to Sandoz) filed ANDAs with Paragraph IV certifications seeking to make

generic versions of Precedex: Caraco Pharmaceutical Laboratories, Ltd., Akorn Inc., Accord Healthcare Inc., Actavis plc, Bedford Laboratories, and Aurobindo Pharma Ltd.[1] These entities followed a path similar to Sandoz, filing Paragraph IV certifications and exposing themselves to suit by Hospira. Each has been sued and is litigating with Hospira. But even if these other companies win a judgment defeating the '867 patent or obtain a favorable settlement, each must wait at least 180 days after Sandoz launches its generic dexmedetomidine before they can enter the market with that certification, because they filed their certifications after Sandoz did. 21 U.S.C. § 355(j)(5)(B)(iv).

That is how the Paragraph IV system works. The Hatch-Waxman Act, under which Paragraph IV disputes occur, provides the 180-day exclusivity as an incentive to generic companies for challenging patents covering brand drugs and investing the resources to litigate over such patents. *See* 21 U.S.C. § 355(j); *Teva Pharms. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1318 (D.C. Cir. 2010).

As set forth by Hospira, this case arose after the FDA issued a decision in a public docket, in which it wrongly concluded that it could approve generic applications for dexmedetomidine without requiring those applications to go

[1] Docket No. 2:10-CV-14514 (E.D. Mich.); Docket No. 1:14-CV-2811 (N.D. Ill.); Docket No. 1:14-CV-336 (M.D.N.C.); Docket No. 1:14-CV-488 (D. Del.); Docket No. 1:14-CV-487 (D. Del.); Docket No. 1:14-CV-1008 (D. Del.); Docket No. 1:14-CV-486 (D. Del.).

through the Paragraph IV process with respect to the '867 patent. Because Sandoz's statutory rights were jeopardized by the FDA's approval, the district court permitted Sandoz to intervene as a plaintiff in this suit by Hospira.

ARGUMENT

A. Sandoz Will Suffer Irreparable Harm in the Absence of Injunctive Relief

The FDA, and now the district court, have wrongly permitted Mylan and Par to sell their generic versions of dexmedetomidine regardless of Sandoz's exclusivity. Absent an injunction, Sandoz will suffer serious, irreparable harm—it will be denied the benefit of the statutory exclusivity to which it is entitled. This cannot be undone; Sandoz will forever lose its first-to-market status. An injunction is therefore necessary to protect Sandoz's market exclusivity before its statutorily-entitled benefits are lost.

It cannot be disputed that Sandoz faces irreparable and non-compensable harm from the loss of its 180-day statutory exclusivity as the first generic to challenge the dexmedetomidine patents in Hatch-Waxman litigation. Mylan itself acknowledged the irreparable nature of such harm just a few months ago in similar litigation, in a case where Mylan claimed its own first-to-market exclusivity:

> [A]s the D.C. Circuit Court of Appeals stated in *Teva Pharms., Inc.*, 595 F.3d at 1311, ***a first-filer who is unlawfully denied marketing exclusivity is irremediably harmed*** because the "'first-mover advantage' is a valuable asset." *See also Mylan Pharms., Inc. v. U.S. Food & Drug Admin.*, 454 F.3d 270, 272-73 (4th Cir. 2006) (noting

> that the first applicant to file "enjoys a unique advantage" and that the 180-day exclusivity period "is a significant boon to the recipient"). . . . Likewise, in *Apotex, Inc. v. FDA.*, No. 06-0627, 2006 WL 1030151, at *17 (D.D.C. Apr. 19, 2006), the court recognized that "[o]nce the statutory entitlement [to marketing exclusivity] has been lost, it cannot be recaptured." Unsurprisingly, ***the loss of 180-day exclusivity has been expressly held to be a form of irreparable injury sufficient to justify preliminary injunctive relief against FDA.*** *Mova Pharm. Corp.*, 140 F.3d at 1067 n.6.

Memorandum of Law in Support of Plaintiffs' Motion for Preliminary Injunction at 34-35, *Mylan Pharmaceuticals Inc. v. U.S. FDA*, Case No. 1:14-CV-75 (N.D. W. Va. April 28, 2014) (emphasis added), ECF No. 62-3 (Exhibit B).

Unless Mylan and Par are enjoined from further sales, Sandoz will irrevocably lose the exclusive market position to which it was entitled. Smith Decl. ¶¶ 14-15. *See also Mova Pharm. Corp. v. Shalala,* 955 F. Supp. 128, 131 (D.D.C. 1997) ("[D]epriving [first-filer] Mova of a 180-day statutory grant of exclusivity and giving [later-filer] Mylan an officially sanctioned head start in the market . . . will cause injury to Mova. All parties recognize that the earliest generic drug manufacturer in a specific market has a distinct advantage over later entrants."), *aff'd*, 140 F.3d 1060 (D.C. Cir. 1998).

Indeed, Mylan argued forcefully below that it should be permitted to obtain these first-to-market advantages for itself. *See* ECF 39-3 at ¶ 12 ("Mylan Institutional's approval presents unique and irreplaceable advantages to Mylan Institutional, including the opportunity to market as a first generic market entrant,

access to important customers that would otherwise be unavailable, the opportunity to form unique commercial relationships with customers, and the opportunity to expand Mylan Institutional's entire portfolio of low-cost products, among others.").

Appellee Par went further, noting that because Mylan and Par had usurped Sandoz's exclusivity, Sandoz "would gradually garner a 20 percent market share," compared to the 40 percent share that Mylan and Par would achieve by taking away Sandoz's exclusive rights to market first. ECF 111-1 (declaration in support of Par's motion for bond) at ¶ 6. Par noted that "***Sandoz' lower share reflects the late mover disadvantages*** associated with long-term supply contracts and other customer switching costs that would constrain its market penetration." *Id.* (emphasis added). In other words, instead of its first-mover advantage due to its 180 days of statutory exclusivity, Sandoz would be irreparably injured in the market due to the premature entry of Mylan and Par.

These first-mover advantages now claimed by Mylan and Par are the advantages that Sandoz secured by obtaining a statutory 180 days of exclusivity, at great expense and effort. Mylan and Par are not entitled to claim those benefits for themselves, particularly when the legal challenge to FDA's approval of the Mylan and Par ANDAs has not yet been resolved.

Nor can Mylan's and Par's arguments about injury to themselves be viewed as outweighing Sandoz's. Unlike Mylan and Par, Sandoz's harm is non-monetary, based on an express statutory right with which Mylan and Par seek to interfere. *See Apotex, Inc. v. FDA*, No. 06–0627-JDB, 2006 WL 1030151, at *17 (D.D.C. Apr. 19, 2006) ("[U]nlike the harm that Apotex allegedly faces, the potential injury that the [exclusivity-holders] face is not 'merely economic.' Rather, they stand to lose a statutory entitlement, which is a harm that has been recognized as sufficiently irreparable . . . Once the statutory entitlement has been lost, it cannot be recaptured.") (citations omitted), *aff'd*, 449 F.3d 1249 (D.C. Cir. 2006).

To secure its statutory entitlement, Sandoz made a substantial investment of millions of dollars, many years of litigation, and significant personnel resources. Smith Decl. ¶¶ 8-15. Absent an injunction, that investment and statutory entitlement will be lost; as Par expressly recognized, Sandoz will be relegated to a fraction of its expected market share during the 180 days it is supposed to have exclusive rights. Furthermore, the harm to Sandoz in the absence of injunctive relief includes damage to its industry reputation for failing to bring generic dexmedetomidine to market before other generic entrants, loss of goodwill, and a jeopardized investment in future products for which it holds statutory 180-day exclusivity, which is threatened if the FDA's actions are not enjoined here. Smith Decl. ¶ 16. Such non-quantifiable harm is irreparable and warrants permanent

injunctive relief. *See Douglas Dynamics, LLC v. Buyers Products Co.*, 717 F.3d 1336, 1344 (Fed. Cir. 2013) ("Irreparable injury encompasses different types of losses that are often difficult to quantify, including lost sales and erosion in reputation and brand distinction."). Again, while Mylan and Par claim such harm for themselves, it cannot compare to the intrusion onto the express, well-recognized injury to statutory rights that their conduct causes Sandoz.

Sandoz has already been injured by the improper market entry of Mylan and Par, which poses a direct threat to the investment of time and personnel to make Sandoz's statutory "first filing" of a dexmedetomidine ANDA a reality. As explained in Hospira's motion, in the 36-hour period between FDA approval and the district court's TRO, Par released a 6-week supply of generic dexmedetomidine into the market, and Mylan transferred "tens of millions" of dollars' worth of generic dexmedetomidine to wholesalers and customers. Hospira Mot. at 7. Failure to enjoin further sales by Mylan and Par during the pendency of this appeal will result in permanent harm to Sandoz, and this factor therefore strongly favors the requested injunctive relief.

Moreover, in light of the district court's judgment, other dexmedetomidine ANDA filers who submitted a Paragraph IV certification to the '867 patent are likely to attempt to convert to a section viii statement, and receive immediate FDA approval, rather than await FDA approval at the expiry of Sandoz's exclusivity

period as they originally intended. Such conversion will allow immediate entry of these filers into the generic dexmedetomidine market, further reducing any prospects for Sandoz to realize the early entrant advantages to which it is entitled. The harm to Sandoz from the judgment below is therefore far from limited to the commercial activities of Mylan and Par. If the FDA's August 18, 2014 Decision is not stayed and FDA approves these additional dexmedetomidine ANDAs, Sandoz's statutory exclusivity will be utterly worthless.

Finally, Sandoz has no remedy at law to compensate for the harm it will suffer in the absence of injunctive relief. As explained above, the loss of Sandoz's statutory exclusivity is itself a real and recognized irreparable injury. *See Mova Pharm.*, 955 F. Supp. at 131; *Apotex, Inc.*, 2006 WL 1030151, at *17. And that loss will additionally cause both economic and non-economic harm, including non-quantifiable harm to Sandoz's industry reputation, loss of goodwill, and a jeopardized investment in future products for which Sandoz holds statutory 180-day exclusivity. Such non-quantifiable harm warrants injunctive relief. *Douglas Dynamics*, 717 F.3d at 1344. Moreover, in the circumstances of this case, the FDA's sovereign immunity further supports a finding of irreparable harm and weighs in favor of injunctive relief. *See Smoking Everywhere, Inc. v. FDA*, 680 F. Supp. 2d 62, 77 n.19 (D.D.C. 2010), *aff'd sub nom. Sottera, Inc. v. FDA*, 627 F.3d 891 (D.C. Cir. 2010); *Senior Execs. Ass'n v. United States*, 891 F. Supp. 2d 745,

755 (D. Md. 2012). The unavailability of monetary damages to compensate Sandoz's significant harm therefore further supports injunctive relief.

B. The Balance of Hardships and the Public Interest Favor an Injunction

For similar reasons, the balance of the hardships and the public interest also favor an injunction. Sandoz pursued its challenge to the validity of the '867 patent at its substantial expense, ultimately receiving a license to launch generic dexmedetomidine well before the expiration of the patent, along with 180 days of statutory market exclusivity. As the FDA's conduct would deprive Sandoz of these hard-fought statutory rights, the balance of hardships thus tips in its favor.

The FDA has already recognized the strong interest in encouraging patent disputes to be heard through the "Paragraph IV" system. FDA recognized that this approach "permits the NDA applicant or holder to determine which patents claim its approved drug product and then, when appropriate, to resolve disputes over infringement of those patents through patent litigation." 68 Fed. Reg. 36676 at 36682; *see also id.* at 36683 ("A fundamental assumption of the Hatch-Waxman Amendments is that the courts are the appropriate mechanism for the resolution of disputes about the scope and validity of patents.") (cited and quoted in *Caraco Pharm Labs., Ltd v. Novo Nordisk A/S*, __ U.S. __, 132 S. Ct. 1670, 1676 (2012)).

Indeed, FDA concluded that such a framework was "most consistent with the general balance adopted in Hatch-Waxman," specifically cautioning that:

> If ANDA and 505(b)(2) applicants could always avoid the possibility of a 30-month stay by asserting in a section viii statement that certain labeling for which the applicant is seeking approval is not protected by a listed method-of-use patent—despite the NDA holder's assertion to the contrary—there would be little reason for any applicant to submit a paragraph IV certification for a method-of-use patent. This approach would essentially eliminate the certification, notice, and litigation process as to any listed method-of-use patent, producing an outcome that is inconsistent with the act.

Id. at 36682. FDA reached this conclusion even though it recognized that other approaches to section viii might otherwise speed the entry of generic drugs to market. Yet the FDA's decision here encourages the conduct it sought to avoid in 2003.

In short, although there is a public interest in bringing generic drugs to market as soon as possible, the FDA and the courts have repeatedly observed that such an interest is outweighed by the public interest in ensuring that the first Paragraph IV ANDA filer receives its 180 days of exclusivity—because that ensures that generics are encouraged in the future to bring the kind of challenges brought by Sandoz in this case. *See Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998) (affirming district court's finding that "the public's interest in the 'faithful application of the laws'" concerning first-filer market exclusivity "outweighed its interest in immediate access to [later-filer] Mylan's generic product").

As the D.C. Circuit has explained:

> ***The statute's grant of a 180–day delay in multiple generic competition for the first successful paragraph IV filer is a pro-consumer device.*** And it happens to be precisely the device Congress has chosen to induce challenges to patents claimed to support brand drugs. The statute thus deliberately sacrifices the benefits of full generic competition at the first chance allowed by the brand manufacturer's patents, in favor of the benefits of earlier generic competition, brought about by ***the promise of a reward for generics that stick out their necks (at the potential cost of a patent infringement suit) by claiming that patent law does not extend the brand maker's monopoly as long as the brand maker has asserted.*** As Congress deliberately created the 180–day exclusivity bonus, the FDA cannot justify its interpretation by proudly proclaiming that it has eviscerated that bonus.

Teva Pharms., 595 F.3d at 1318 (emphasis added).

This analysis equally applies here: the public interest strongly favors affirming Sandoz's exclusivity, to support and affirm the framework Congress designed to foster generic competition in the market.

CONCLUSION

For the foregoing reasons, and as more fully set forth in Hospira's Emergency Motion, injunctive relief that protects Sandoz's market exclusivity should be granted pending this appeal, and Sandoz respectfully requests that Hospira's proposed order be entered.

Dated: September 7, 2014

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on this 7th day of September 2014, a copy of the foregoing document was delivered, via electronic filing, to Paul F. Strain, pfstrain@venable.com; Maggie Teresa Grace, mtgrace@venable.com; Steven M. Klepper, sklepper@kg-law.com; Michael Randolph Shebelskie, mshebelskie@hunton.com; and James Patrick Ulwick, julwick@kg-law.com. I further certify that the following were served by electronic mail:

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