**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF MARYLAND**

| | | |
|---|---|---|
| HOSPIRA, INC., | ) | |
| | ) | |
| Plaintiff, | ) | |
| | ) | |
| v. | ) | CIVIL ACTION NO. |
| | ) | 8:14-cv-02662-GJH |
| SYLVIA MATTHEWS BURWELL, *et al*., | ) | |
| | ) | |
| Defendants. | ) | |
| _____ | ) | |

**INTERVENOR-PLAINTIFF SANDOZ INC.'S MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF HOSPIRA'S MOTION FOR TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION**

Intervenor-Plaintiff Sandoz Inc. ("Sandoz") submits this memorandum of points and authorities in support of Plaintiff Hospira's Motion for a Temporary Restraining Order and Preliminary Injunction. Because Plaintiff Hospira and Plaintiff Intervenor Sandoz have a likelihood of success on the merits and will be irreparably harmed by the actions complained of, and the equities tip strongly in their favor, Sandoz respectfully seeks the entry of temporary and preliminary relief pending a full trial on the merits. Sandoz respectfully submits this Memorandum to provide further detail as to the likelihood of success on the merits, its irreparable harm and to the availability of the remedy sought by Plaintiffs.

## I. INTRODUCTION

The FDA has exceeded its authority under the Food Drug & Cosmetic Act ("FDCA") and the Administrative Procedure Act ("APA") by issuing an arbitrary and capricious decision that paves the way for approval of ANDAs for generic versions of PRECEDEX™ brand dexmedetomidine injection 100 mcg / mL (hereinafter "Precedex" or "dexmedetomidine injection") that fail to comply with plain statutory requirements. This action directly and irreparably injures Sandoz, which fought long and hard to achieve the 180-day exclusivity promised to generic applicants that challenge branded patents.

Hospira's '867 patent is a "method of use" patent listed in the FDA's "Orange Book" with respect to Precedex. That listing puts generic companies on notice that they must provide certain certifications or statements to the FDA with respect to that patent before the FDA may approve their applications. The statutory framework encourages generic companies like Sandoz to be the first to file Paragraph IV certifications to listed patents, and rewards them with a period of market exclusivity as to other generics. Thus, because Sandoz was the first applicant to file a Paragraph IV certification with respect to dexmedetomidine injection, other applicants filing a Paragraph IV certification may only launch ***after*** Sandoz does.

The alternative course, filing a section viii statement, is not available with respect to the '867 patent. Here, it is undisputed that no approved indication for Precedex is outside of the use

code for the ’867 patent; both approved indications for Precedex are covered by the ’867 patent at least in part. By its very terms, section viii does not apply.

Yet despite this statutory authority and regulatory framework, the FDA has suddenly decided that it ***may*** approve applications that unquestionably are seeking approval of uses admittedly covered by the ’867 patent. This conclusion is flatly contrary to the governing law, judicial precedent, and the FDA’s own regulations and prior decisions. And it operates immediately to Sandoz’s detriment, depriving Sandoz of its hard-won statutory exclusivity – the express incentive provided by Congress to encourage generics like Sandoz to challenge patents in Court. This injury cannot be recovered by Sandoz.

Sandoz was engaged in Paragraph IV litigation on its dexmedetomidine ANDA for more than three years, ultimately settling with Hospira to allow generic competition beginning in late 2014, five years before the natural expiration of the ’867 patent, and earning its statutory reward of 180 days of generic exclusivity for being the first ANDA filer with a Paragraph IV certification. That result, which is exactly what the Hatch-Waxman Act was designed to encourage, should not be disrupted by the FDA, and certainly cannot be disrupted based on the procedural end-run the FDA has employed. The FDA must be enjoined from allowing an unlawful circumvention of the carefully balanced Paragraph IV process. This Court has the authority to do so.

## II. ARGUMENT

In April 2009, Sandoz submitted ANDA No. 91-465, seeking approval from the FDA to market a generic dexmedetomidine product in the U.S. (Declaration of Scott Smith (“Smith Decl.”) ¶ 5.) Sandoz’s ANDA was the first ANDA referring to the Precedex NDA that included a Paragraph IV certification, thereby entitling Sandoz to 180 days of generic market exclusivity against any subsequent ANDA filer with a Paragraph IV certification before the ’867 patent’s expiration. *See* 21 U.S.C. § 355(j)(5)(B)(iv). In December 2013, after more than three 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 U.S. no later than December 26, 2014, approximately five years prior to the expiration of the '867 patent. (Smith Decl. ¶ 8-10.)

Sandoz joins Hospira in seeking temporary and preliminary relief in view of the recognized irreparable harm it would suffer if the FDA's action is allowed to stand. Permitting an ANDA filer to enter the market prematurely deprives Sandoz of the market exclusivity it won through the arduous and costly Paragraph IV process. Sandoz invested significant time and financial resources in that process, at a cost of pursuing other opportunities, and ultimately won the right to launch its generic dexmedetomidine in December 2014, with 180 days of market exclusivity. (Smith Decl. ¶ 10.) Sandoz will be irreparably harmed if a section viii filer is allowed to come on the market and deprive Sandoz of its statutory exclusivity; this harm cannot be quantified, and has been recognized as irreparable by the Courts. *Mova Pharm. Corp. v. Shalala*, 955 F. Supp. 128, 131 (D.D.C. 1997).

The four-part test for assessing injunctive relief[1] compels the conclusion that Hospira and Sandoz are entitled to the requested injunction against the FDA.[2] First, Hospira and Sandoz are likely to succeed on the merits, because there is no lawful carve-out for the Precedex label, and the FDA's endorsement of section viii ANDAs for this drug was arbitrary and capricious and

[1] In evaluating whether to issue a preliminary injunction or temporary restraining order, this Court must consider whether (1) the party seeking the injunction is "likely to succeed on the merits"; (2) the party seeking the injunction is "likely to suffer irreparable harm" if relief is withheld; (3) the "balance of hardships" tips in favor of the party seeking the injunction; and (4) "the injunction is in the public interest." *Metropolitan Reg'l Info. Sys. v. American Home Realty Network, Inc.*, 722 F.3d 591, 595 (4th Cir. 2013) (citing *Winter v. Natural Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008).

[2] Pursuant to the APA, agency decisions must be set aside if "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A); *N.C. Growers' Ass'n, Inc. v. United Farm Workers*, 702 F.3d 755, 763–64 (4th Cir. 2012). A court best provides oversight of an agency decision "by scrutinizing process and by determining whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment," and these tasks are "the heart of the judicial inquiry." *Id.* at 764 (quoting *Kennecott v. EPA*, 780 F.2d 445, 449 (4th Cir. 1985)). Although an agency decision is entitled to a presumption of regularity, "[w]here the agency has failed to provide a reasoned explanation, or where the record belies the agency's conclusion, [the court] must undo its action." *Petroleum Commc'ns, Inc. v. FCC*, 22 F.3d 1164, 1172 (D.C. Cir. 1994).

contrary to law. Second, Sandoz will suffer irreparable harm absent injunctive relief. Third, there will be no substantial or inequitable harm to the FDA or any other party if the injunction is granted. Finally, the public interest favors an injunction, because the requested relief will ensure that the Hatch-Waxman incentives for bringing generic drugs to market remain intact.

### A. Hospira and Sandoz Are Likely to Succeed On the Merits, Because There Is No Lawful Carve-Out for the Precedex Label

#### 1. Approval of a Section viii ANDA Is Foreclosed By the Overlap in the Approved Precedex Indications and the Scope of the Use Code for the '867 Patent

Although ANDAs with section viii statements are permitted in certain circumstances, in the case of Precedex, a section viii statement filed against the '867 patent is foreclosed by the interplay between the Precedex label and the use code for the patent.

It is undisputed by the FDA that "use [of dexmedetomidine] for procedural sedation may at times occur in an intensive care setting." Decision at 12. This is clear from a simple comparison of the use code for the '867 patent and the procedural sedation indication for PRECEDEX:

| Precedex Indication 1.2 | Use Code U-1472 for the '867 Patent |
|---|---|
| "Sedation of non-intubated patients prior to and/or during surgical and other procedures." | "intensive care unit sedation, including sedation of non-intubated patients prior to and/or during surgical and other procedures." |

The FDA's fundamental error is misinterpreting "section viii" itself. Section viii permits label carve-outs "for a method of use patent which <u>does not</u> claim a use for which the applicant is seeking approval." (emphasis added) Here, the second PRECEDEX indication claims "Sedation of non-intubated patients prior to and/or during surgical and other procedures." FDA's position is, essentially, that this indication can cover sedation that is not in the ICU, and thus not covered by Use Code U-1472. While that is true, it misses the point. That same indication also covers

uses the FDA admits do occur in the ICU. Thus, FDA has approved section viii carve-outs that FDA itself admits do claim a use for which the applicant is seeking approval. That is directly prohibited by the plain language of section viii. Accordingly, FDA has exceeded its statutory authority in approving section viii carve-outs here. By definition, then, such approvals are arbitrary and capricious.

Likewise, the Supreme Court's decision in *Caraco* contradicts the FDA's determination here. In *Caraco*, the Supreme Court held that "the FDA will not approve an ANDA if the generic's proposed carve out label overlaps at all with the brand's use code." 132 S. Ct. at 1677. The Supreme Court observed that the FDA may only approve a label with a section viii statement "if the use code provides sufficient space for the generic's proposed label." *Id*. But as shown above, there is no space between the procedural indication and the use code for the '867 patent. The FDA acknowledged as much (Decision at 12), yet defied the Supreme Court's teachings nonetheless. This again was legal error.

**2. Any ANDA Filer Seeking FDA Approval Prior to Expiration of the '867 Patent Must Follow the Paragraph IV Process**

Because the unexpired '867 patent is listed in the Orange Book and the use code for this patent covers both Precedex indications, proper application of the statutory and regulatory framework should have required all applicants for generic versions of PRECEDEX to submit a Paragraph IV certification to the '867 patent with their ANDAs in order to get FDA approval prior to patent expiration. Those filers, like Sandoz and any other Paragraph IV filer, could then have challenged the validity and/or infringement of the '867 patent in court, under the well-defined procedures set forth in the Hatch-Waxman Act.[3] What FDA cannot do is disregard the statutory framework to approve such applications under section viii here.

[3] In addition, to the extent that a section viii filer believed the U-1472 use code description improperly reflected the scope of the '867 patent, it could have asserted a counterclaim to that effect in the Paragraph IV litigation. That is precisely the mechanism envisioned by the Hatch-Waxman Act, 21 U.S.C. §355(j)(5)(C)(ii)(I), and expressly endorsed by the Supreme Court. *Caraco*, 132 S. Ct. at 1688.

The FDA's role insofar as Orange Book patent listings are concerned is purely ministerial. *See, e.g.*, *aai Pharma v. Thompson*, 296 F.3d 227, 241 (4th Cir. 2002), *cert. denied*, 123 S. Ct. 1582 (2003); *American Biosci., Inc. v. Thompson*, 269 F.3d 1077, 1084 (D.C. Cir. 2001). Under this approach, the FDA must rely exclusively on Hospira's representations about the scope of the '867 patent, *i.e.*, through the use code description supplied by Hospira. The FDA is not permitted to look beyond the use code to make substantive determinations about the patent's scope.

The FDA's statements in adopting its use code system establish this point. The FDA specifically considered whether it would be appropriate for ANDA applicants to unilaterally decide whether a listed method-of-use patent claims the use for which the ANDA applicant seeks approval. The FDA rejected that approach, concluding instead that:

> In the absence of explicit statutory language, we believe an approach that requires the NDA applicant or holder or patent owner to identify the approved methods of use protected by the patent is most consistent with the general balance adopted in Hatch-Waxman. 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.

The FDA observed then that if it did not adopt rules that encouraged these disputes to be resolved by litigation with the patent holder, "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." 68 Fed Reg 36676 at 36682 (June 18, 2003) (emphasis added). Indeed, the Supreme Court relied on this history in reaching its ruling in *Caraco. Caraco*, 132 S. Ct. at 1677 (citing FDA, Final Rule, Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,682-83 (June 18, 2003)).

In view of this history, and on these facts, the FDA cannot approve a version of generic dexmedetomidine injection with a "section viii" carve out.

### B. If the FDA Is Not Enjoined from Approving Section viii ANDAs for Dexmedetomidine, Sandoz Will Effectively Lose its Stautory Exclusivity

Sandoz will be irreparably harmed if a section viii filer is permitted to launch a generic dexmedetomidine product before Sandoz's 180 days of exclusivity expires. That is precisely why the Hatch-Waxman Act rewards the first filer of a Paragraph IV ANDA—the first step in a difficult and expensive process designed to clear the way for generic competition—with 180 days of market exclusivity.

Here, Sandoz litigated the '867 patent for more than three years, at substantial expense, in order to bring generic dexmedetomidine to market before the patent's expiration in 2019. Sandoz succeeded in that goal, earning the right to begin selling its generic dexmedetomidine product on December 26, 2014 with 180 days of market exclusivity. The FDA's decision to approve section viii ANDAs for this drug allows the section viii filers not only to begin selling generic dexmedetomidine immediately but also to flood the market with generic product so that subsequent generic entrants are at a substantial disadvantage. If the section viii ANDA approvals are not enjoined, Sandoz will enter a dexmedetomidine market on December 26, 2014 but will not have the exclusivity to which it is entitled and the market share that conveys. *See 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.").

Even if the section viii ANDA approvals are later found to have been granted improperly, Sandoz will have irrevocably lost the exclusive market position to which it was entitled. (Smith Decl. ¶ 15.) The harm to Sandoz from the FDA's actions will therefore be irreparable. Furthermore, the harm includes damage to Sandoz's industry reputation for failing to bring generic dexmedetomidine to market before other generic entrants, loss of goodwill, and damage to Sandoz's investment in future products for which it holds statutory 180-day exclusivity, which

would be placed in jeopardy by the FDA's actions here. (Smith Decl. ¶ 16.) The Fourth Circuit has recognized that such non-quantifiable harm is irreparable and warrants injunctive relief. *See Multi-Channel TV Cable Co. v. Charlottesville Quality Cable Operating Co.*, 22 F.3d 546, 551-52 (4th Cir. 1994) ("[I]rreparable injury is suffered when monetary damages are difficult to ascertain or are inadequate.") (quoting *Danielson v. Local 275*, 479 F.2d 1033, 1037 (2d Cir. 1973)).

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

Permitting the unprecedented label changes seen in this case would significantly frustrate the goals of the Hatch-Waxman system and harm the public interest. 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.

But more importantly, the FDA's injection of uncertainty into the use code process puts filers such as Sandoz at great risk that they might find their efforts without reward, usurped by a later filer seeking a novel interpretation of the law. *Caraco*, 132 S. Ct. at 1677. If a generic entrant cannot be reasonably certain that its successful Paragraph IV challenge will lead to 180 days of market exclusivity, and instead must worry that its exclusivity will be threatened by a later generic company pursuing a novel "carve-out" approach, it will be less willing to invest the resources to bring that Paragraph IV challenge in the first place, thereby reducing the number of important generic drugs that the company brings to market.

Although there is a public interest in bringing generic drugs to market as soon as possible, courts have repeatedly held 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. *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"); *Teva Pharms. USA, Inc. v. Sebelius*, 595 F.3d 1303 (D.C. Cir. 2010) (180-day exclusivity period is a "reward for generics that stick out their necks" by challenging a patent, and the statute "deliberately sacrifices the benefits of full generic competition at the first chance allowed by the brand manufacture's patents, in favor of the benefits of earlier generic competition" made possible by a Paragraph IV challenge).

## III. THE COURT HAS BROAD EQUITABLE POWERS TO DIRECT AN APPROPRIATE REMEDY

Because the August 18 Decision and the resulting launch of generic dexmedetomidine by section viii ANDA filers will irreparably harm Sandoz, Sandoz respectfully requests that the Court order the FDA to rescind ab initio any final ANDA approval of a generic version of Precedex based upon the August 18 Decision, order the FDA to recall any product sold or distributed under such an approval, direct that no further product be sold under such approvals, and enjoin the FDA from granting any further ANDA approvals based upon the August 18 Decision. The Court is invested with broad equitable powers to order the requested remedy, and such remedy is necessary to prevent the irreparable harm described above. *See Thompson v. United States HUD*, 404 F.3d 821, 830 (4th Cir. 2005) ("The district court must be free to exercise its equitable powers as necessary to remedy the problem."); *East Tenn. Natural Gas Co. v. Sage*, 361 F.3d 808 (4th Cir. 2004) (District court may exercise equitable power to grant an appropriate remedy through the issuance of a preliminary injunction.); *United States v. Barr Laboratories, Inc.*, 812 F. Supp. 458 (D.N.J. 1993) (requiring a drug product recall in the context of a preliminary injunction and recognizing that such recall is "consistent with the broad equitable relief powers district courts enjoy.").

In the alternative, Sandoz submits that the Court should at the very least (a) stay further approvals of dexmedetomidine ANDAs based on its Decision, and (b) enjoin further sales of product by entities that have received erroneous approvals.

## IV. CONCLUSION

Each of the four factors favors granting an injunction, and Hospira and Sandoz are entitled to the requested relief. For the foregoing reasons, Hospira's motion should be granted.

Dated: August 19, 2014

Respectfully submitted,

By: /s/

G. Brian Busey (Bar No. 03918)
Kirk A. Sigmon (*pro hac vice pending*)
Morrison & Foerster LLP
2000 Pennsylvania Avenue, NW, Suite 6000
Washington, D.C. 20006-1888
Phone: (202) 887-1500
Fax: (202) 887-0763
GBusey@mofo.com
KSigmon@mofo.com

Matthew M. D'Amore (*pro hac vice pending)*
Morrison & Foerster LLP
250 W. 55th Street
New York, NY 10019
Phone: (212) 468-8000
Fax: (212) 468-7900
MDAmore@mofo.com

Stephen D. Keane (*pro hac vice pending*)
Morrison & Foerster LLP
12531 High Bluff Drive
San Diego, CA 92130-2040
Phone: (858) 720-5100
Fax: (858) 720-5125
SKeane@mofo.com

Attorneys for Intervenor-Plaintiff Sandoz Inc.