IN THE UNITED STATES COURT OF APPEALS
FOR THE FOURTH CIRCUIT

Hospira, Inc.	*	
Appellant,	*	
v.	*	Case No. 14-1920
Sylvia Mathews Burwell, et al.	*	
Appellees.	*	

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HOSPIRA'S REPLY MEMORANDUM IN SUPPORT OF MOTION FOR INJUNCTION ON APPEAL

Reply Argument

Appellees' oppositions to Hospira's motion for an injunction coupled with Hospira's request for an expedited schedule are revealing for what they fail to say.[1] With respect to the merits, the central premise of all the oppositions is that FDA simply followed its usual, longstanding rule in its decision (and then in approving Mylan's and Par's ANDAs). This premise is refuted by some jarringly inconsistent and undisputed facts. Appellees do not, for example, explain why FDA opened a docket, which it denominated a "rulemaking" docket, or why it said

[1] FDA agrees with Hospira's proposed schedule so long as it gets its usual 30 days to prepare and file its brief, which Hospira's schedule proposes. Remarkably, Mylan and Par oppose Hospira's proposed schedule even though they would receive the standard 30-day time for briefing, while proposing that if they lose on the present motion they would want to propose their own, more draconian schedule that, based on any reasonable review of the calendar, would not be possible without curtailing FDA's briefing time.

that one of its reasons for doing so was "to guide future decisions," if it already had a rule to follow. Nor do appellees explain why FDA asked those who submitted comments to the docket to consider whether it would be permissible to *add* language to the indication contained in the carved-out labeling to avoid the obvious overlap with Hospira's use code if, as they all now chant in unison, there is no overlap or the overlap does not matter.

With respect to the balance of harms, Par and Mylan admit that they flooded the market with generic Precedex before the district court could act. They are no doubt engaged in similar conduct while this motion is pending. Unless this Court orders a halt, they will do so throughout the pendency of Hospira's appeal.

Appellees fail to explain why they should be able to get into the market before Sandoz, which complied with the rules. They fail to explain why the advantages of first-to-market status, of such incalculable value to them, should be shrugged off in Sandoz's case; or why Hospira should lose its exclusivity rights. They do not explain why the Court should be concerned about their claimed "lost sales" even though their submissions fail to put real numbers on this loss, and when they admit that the market is now inundated with an estimated 6 weeks' supply, which was dumped into the market in the approximately 32-hour period between the docket decision and the court's TRO. And, again, there is no telling what volume of product they have pushed out since the lower court ruled.

With respect to the public interest, FDA fails to explain why, if the public interest is so strong, it took the agency seven months to issue its decision. And all appellees fail entirely to explain why the public cannot wait the relatively brief period needed to decide this appeal. The claims that the public is somehow at risk for missing out on "lower cost generics" is, at best, misleading. Par filed documents under seal showing that it sells its generic product at a price many multiples of Par's cost.

Hospira believes it will prevail on the merits of this appeal. An injunction now is necessary to assure that Hospira's victory will be meaningful.

I. The Court Should Grant An Injunction Pending Appeal.

A. Standard Of Review

Mylan's opposition misstates the standard for whether a motion for stay should be granted. *Pashby v. Delia*, 709 F.3d 307, 320-21 (4th Cir. 2013), does not require the Court to find that each *Hilton v. Braunskill*, 481 U.S. 770, 776 (1987) factor be met. Doc. No. 35-1, at 14. That is an open question in this Circuit. Doc. No. 5, at 9 & n.2. It is when "the motion for stay has received full consideration by a trial judge" that the movant's burden of persuasion is "substantially greater." *Long v. Robinson*, 432 F.2d 977, 979 (4th Cir. 1970).[2]

[2] While this may be "especially so" where the lower court has adversely determined the merits, *Blackwelder Furniture Co. of Statesville, Inc. v. Seilig Mfg. Co.*, 550 F.2d 189, 194 (4th Cir. 1977), *rev'd on other grounds*, 575 F.3d 342 (4th

Here, Hospira moved orally at a teleconference late in the day on September 5, 2014; the teleconference was held without the benefit of a recording. Ex. B to Doc. No. 5. The lower court's letter order denying post-judgment injunctive relief states that "the Court agrees that this case presents complicated issues." *Id.*

Hospira meets all of the *Hilton* factors, albeit it need not. This case demonstrates why, on appeal, a party should not be required to make the requisite showing under each *Hilton* factor. *See Brady v. NFL*, 640 F.3d 785, 789 (8th Cir. 2011) ("Ultimately, we must consider the relative strength of the four factors, 'balancing them all.'"); *Service Emps. Int'l Union Local 1 v. Husted*, 698 F.3d 341, 343 (6th Cir. 2012) ("'These factors are not prerequisites that must be met, but are interrelated considerations that must be balanced together.'"). "The four factors should be balanced; thus, for example, if the balance of the harms tips heavily enough in the stay applicant's favor then the showing of likelihood of success need not be as strong, and vice versa." Wright & Miller, *Federal Practice and Procedure* § 3954 (citing cases; footnotes omitted); *see also Brady*, 640 F.3d at 794 ("In sum, we think the League has met its burden to demonstrate that it likely will suffer some degree of irreparable harm without a stay, and the balance of the equities does not favor the Players so decidedly that it should outweigh our present view about likelihood of success on the merits.").

Cir. 2009), the district court found here in favor of Hospira on the first *Hilton* factor. Ex. B to Doc. No. 5.

The district court's legal conclusions are reviewed de novo. *See Stone v. Instrumentation Lab Co.*, 591 F.3d 239, 242-43 (4th Cir. 2009) ("a question of statutory interpretation is reviewed *de novo*); *N.C. Growers' Ass'n v. United Farm Workers*, 702 F.3d 755, 763 (4th Cir. Cir. 2012) (decision awarding summary judgment reviewed de novo).

B. There Is A Substantial Likelihood That Hospira Will Prevail On The Merits.

With respect to Hospira's claim that FDA's decision violated the relevant provision of the Hatch-Waxman Amendments to the Food, Drug and Cosmetic Act, *see* 21 U.S.C. § 355(j)(2)(A)(viii), the oppositions focus entirely on *Chevron* step one, Mylan going so far as to claim (incorrectly) that Hospira "did not address *Chevron* step two below." Doc. No. 35-1, at 13. *But see* ECF No. 106, at 4-5 ("[I]f the Court gets to *Chevron* step two (which it should not), FDA would be entitled to little, if any, deference because of the agency's severe lack of consistency in its interpretation of section viii." (citing numerous cases)).

Hospira's position is that FDA's decision fails at *Chevron* step one because Hospira's use code "claims a use [sedation in an intensive care unit (ICU) which includes procedural sedation in an ICU] for which the [section viii] applicant[s] . . . seek[] approval." 21 U.S.C. § 355(j)(2)(A)(viii). FDA's consistent reading of this statute – that is, how FDA has stated it determines if a use code "claims a use for which the applicant is seeking approval" – has been that section viii is unavailable

if, as here, "the generic's proposed carve-out label overlaps at all with the brand's use code." *Caraco Pharm Labs., Ltd. v. Novo Nordisk A/S*, 132 S. Ct. 1670, 1677 (2012) (citing FDA's statements in 68 Fed. Reg. 36682-36683 (2003)). As noted in Hospira's opening motion papers, the Supreme Court's categorical statement of no "overlap at all" was drawn virtually verbatim from the brief of the United States filed in *Caraco*. Thus, FDA's position has been, as Hospira's position is now, that the statute is unambiguous.

The federal appellees state in the first paragraph of their opposition that FDA's decision sets forth the rule that "permits generic manufacturers to obtain approval of ANDAs for drugs covered by method-of-use patents if – but only if – the indications and other information in the proposed ANDA labeling omit references to patented uses of the drug." Doc. No. 30, at 1. First, Hospira disputes the legal correctness of FDA's new rule because it is contrary to the statute. In any event, the rule in FDA's decision is undeniably at variance with the agency's prior position and it is because of this lack of consistency that FDA's decision here is entitled to no deference. *See Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 212-13 (1988) (deference not given where agency had taken inconsistent positions).

The district court decision relied heavily on, but misapplied, this Court's decision in *Sigma-Tau Pharmaceuticals, Inc. v. Schwetz*, 288 F.3d 141 (4th Cir.

2002). In that case, there was plainly no overlap between the approved generic indication for levocarnitine (for inborn metabolic disorders) and the innovator's protected indication (for end-stage renal disease). Recognizing this, the innovator argued – unsuccessfully – that FDA should nevertheless have denied the generic's ANDA on the grounds that the generic drug, notwithstanding its indication for inborn metabolic disorders only, would foreseeably be used off-label for end-stage renal disease, which would practically nullify any patent protection the innovator enjoyed. That is not the case here. Here, there is no question that the *indicated, on-label* use of generic Precedex for procedures that take place in an ICU—a use that is not hypothetical, as demonstrated by FDA's decision and the administrative record (A.R. 000813-16, 000979, 000982-984)—overlaps with Hospira's use code describing sedation in an ICU (including Precedex procedures that take place there) and the '867 patent claims. That difference is why the FDA originally considered establishing a different kind of rule than the one it ultimately adopted—a rule that would allow an ANDA applicant to add language to its carved out label so that its procedural indication explicitly precluded procedural use in the ICU. A.R. 000001-3.

Similarly, there is a substantial likelihood that Hospira will prevail on the merits of its Administrative Procedure Act rulemaking claim (as to which Par proffers no defense and the federal appellees and Mylan offer limited responses).

One of the several reasons why rulemaking was required here is because FDA opened a "rulemaking" docket, solicited comments, and adopted a new rule at variance with repeated past statements, including in the *Federal Register* and to the Supreme Court. *See N.C. Growers'*, 702 F.3d at 765-66 (putting into effect new and different formulations of a rule constitutes rulemaking). Even if, as FDA argues (contrary to what it told the Supreme Court) it never had a "no overlap" rule, what is plain is that, for the situation presented in Hospira's case FDA, at best, had no rule, and needed to come up with one to "guide future decisions."

C. Hospira Will Suffer Irreparable Harm.

If the Court denies a stay and Hospira ultimately wins on appeal, Hospira will have been irreparably harmed. Hospira will have been deprived of its statutory right to exclusivity. There is no remedy for that. The suggestion that this harm can somehow be avoided by Hospira's pursuing other claims is without merit; Hospira is entitled to insist that FDA follow the law. There are two generics on the market now via section viii statements and, if FDA's decision goes unchecked, there almost certainly will be more approvals granted while this matter is pending. If Hospira prevails on the merits, those approvals will have been unlawful, but, in the meantime, Hospira's harm will have been compounded.

With the inevitable flood tide of generic entry, Hospira will be forced to terminate its U.S. brand drug sales force of approximately 130 persons. Ex. C.

¶ 20; *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1063 (affirming grant of injunctive relief where damage from layoffs caused by generic entry would be significant and unquantifiable); *see also Par Pharms. v. TWi Pharms.* No. CCB-11-2466, 2014 U.S. Dist. LEXIS 110963, at *10-11 (D. Md. Aug. 12, 2014) (finding that Par demonstrated irreparable harm by presenting evidence that lost revenue would likely force entire branded division to shut down, which was an alleged "small portion of Par's overall business"). This sales force sells brand drugs and Precedex is Hospira's overwhelmingly predominant brand drug.

Further, Mylan and Par make much of Sandoz's entry to market in December 2014. Sandoz's generic entry does not lessen Hospira's irreparable harm. Rapid sales and price erosion are common upon entry of multiple generics due to the generic practices of pricing at a discount to the brand to ensure uptake and placing multiple months of the generic product in the wholesale distribution channel immediately on FDA approval. Ex. C to Doc. No. 5, ¶ 21. Significant price erosion is used to acquire market share; this is in contrast to a situation in which there is one generic during a 180-day exclusivity period (*i.e.*, Sandoz). *Id.* That price erosion, loss of market share, and loss of customers will not be recoverable. *Id.*; *see also Multi-Channel TV Cable Co. v. Charlottesville Quality Cable Operating Co.*, 22 F.3d 546, 551-52 (4th Cir. 1994) (irreparable harm is demonstrated where "the failure to grant preliminary relief creates the possibility

of permanent loss of customers to a competitor or the loss of goodwill).

D. Granting The Requested Injunction Will Not Substantially Injure The Other Parties And The Public Interest Favors Injunctive Relief Here.

The core public interest/balance of the equities considerations here are that agencies should follow the law, here including that Hatch-Waxman be implemented as Congress intended, and that decisions authorizing drug approvals should be lawful. These considerations strongly favor granting Hospira's request for injunctive relief.

To deflect the Court from those issues and related issues, the federal appellees boldly criticize Hospira for allegedly "delay[ing] the lawful marketing of [generic Precedex] for nearly three weeks," Doc No. 30, at 18-19, when FDA delayed for seven months before making its decision on the docket which was the predicate for ANDA approvals. Mylan and Par argue that the public interest is hurt by an injunction because the public "wants less expensive drugs." Doc. No. 33. They have, however, by their admissions, already flooded the market. ECF No. 40 Pera Dec. ¶ 13 (Par); ECF No. 39-3 ¶ 8(Mylan).

Conclusion

The Court should grant an injunction during the pendency of this appeal.

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 Reply Memorandum In Support Of Motion For Injunction On Appeal was delivered, via electronic filing, to George Brian Busey, gbusey@mofo.com; Steven M. Klepper, sklepper@kg-law.com; Michael Randolph Shebelskie, mshebelskie@hunton.com; and julwick@kg-law.com. I further certify that the following were served by electronic mail:

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