UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ENDO PHARMACEUTICALS INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civil Action 12-1936 (RBW)
	)	
UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,	)	
	)	
	)	
Defendants.	)	

DEFENDANTS' RESPONSE TO THE COURT'S NOVEMBER 30, 2012 ORDER

On November 30, 2012, Endo Pharmaceuticals Inc., ("Endo") filed a complaint and motion for preliminary injunction against the U.S. Food and Drug Administration, Commissioner Hamburg, and the U.S. Department of Health and Human Services Secretary Sebelius (hereinafter, "FDA").[1] The case concerns the drug product oxymorphone HCl, extended-release tablets, marketed by Endo since 2006 under the brand-name Opana ER. On the same day the case was filed, and before setting a briefing schedule or hearing date, this Court ordered FDA to respond to two questions. This filing is FDA's response to that Court order.

I. Does the Court have jurisdiction to entertain the plaintiff's motion prior to the date on which FDA is required to act under 21 U.S.C. § 355(j)(6) and 21 C.F.R. § 314.161(a)?

The Court has jurisdiction to entertain Endo's motion for preliminary injunction to the extent it claims that FDA has unreasonably delayed rendering a decision whether, under 21

[1] FDA notes that Endo failed to satisfy its duty to confer under LCvR 7(m). Counsel first notified FDA of this matter Friday afternoon at 3:56 pm and did not attempt to confer with agency counsel prior to filing its complaint or motion for preliminary injunction.

U.S.C. § 355(j)(6) and 21 C.F.R. § 314.161, the original Opana ER product was removed from the market for safety or effectiveness reasons. However, that claim fails under Federal Rule of Civil Procedure 12(b)(6) because FDA has no duty to act before December 31, 2012, despite Endo's arguments to the contrary.

Endo filed a citizen petition with FDA dated August 10, 2012,[2] that asks FDA to take several actions including, as relevant to the Court's jurisdictional question, making a determination, under 21 C.F.R. § 314.161, that the original Opana ER was removed from the market for safety reasons.[3] A recent amendment to the Federal Food, Drug, and Cosmetic Act gives FDA 270 days from the date of submission to respond substantively to a citizen petition requesting such a determination. *See* 21 U.S.C. § 355(w). Mention of this statutory deadline is conspicuously absent from Endo's filings. Yet, despite a statutory deadline for FDA's response that is many months away, Endo nonetheless argues that FDA has unreasonably delayed responding to its citizen petition. This claim is subject to dismissal under Fed. R. Civ. P. 12(b)(6) because Endo has not shown that FDA has a duty to act prior to May 10, 2013 -- 270 days after Endo's citizen petition was submitted to FDA.

Endo's unreasonable delay claim fails not only because of the statutory 270-day deadline, but also because it is far from unreasonable for FDA to take sufficient time to make the requested determination. Endo does not suggest that the withdrawn product is less safe than the

[2] Endo filed a second citizen petition with FDA, dated August 31, 2012, but that petition does not involve application of 21 U.S.C. § 355(j)(6) or 21 C.F.R. § 314.161 and is therefore not relevant to the Court's questions.

[3] On August 30, 2011, FDA determined, in response to a citizen petition from a generic manufacturer, that two strengths of the original Opana ER (7.5 mg and 15 mg) were *not* withdrawn from the market for reasons of safety or effectiveness. *See* 76 Fed. Reg. 53908 (Aug. 30, 2011). This determination was made before Endo's new formulation of Opana ER was approved in December 2011. Endo's citizen petition requesting a 314.161 determination is not limited to any particular strengths of the original Opana ER.

new formulation for the intended user. Instead, Endo's request that FDA make a section 314.161 determination raises *inter alia* complex and novel legal issues concerning: (1) whether a product that was previously considered safe and effective must now be found unsafe or ineffective because a manufacturer claims that a safer or more effective product has been introduced to the market; and (2) whether the potential for misuse of a drug product by a population other than the intended user constitutes a safety concern under 21 U.S.C. § 355(j)(6) and 21 C.F.R. § 314.161 that requires FDA to conclude the drug was withdrawn for safety or effectiveness reasons. In addition, if FDA were to conclude that Endo's original Opana ER product was removed from the market for safety or effectiveness reasons, FDA would then have to decide what process is required to withdraw approval of previously approved products.

To determine these issues, FDA must also resolve the complex scientific question whether Endo's new formulation for Opana ER is safer or more effective than Opana's old formulation, particularly in light of the fact that FDA has approved no labeling for Opana's new formulation that suggests a reduced potential for abuse exists. *Compare* new Opana ER label (available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/201655lbl.pdf) *with* old Opana ER label (available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/021610s013lbl.pdf) (the only relevant difference between the labels is the description of the tablets' shape (round vs. octagonal); the "abuse potential" sections of the labels are identical). Because FDA needs adequate time to consider and analyze the relevant legal and factual issues, including analysis of data relating to the alleged safety advantage of the new formulation (which Endo submitted just weeks ago, on November 13), the agency has not yet determined whether all strengths of the original Opana ER were removed from the market for safety reasons, and is not likely to reach such a determination by December 31, as Endo desires. In these circumstances, any alleged

"delay" on FDA's part is eminently reasonable. Endo's urgent desire to block previously approved generics from competing in the marketplace, which competition Endo believes will begin on January 1, 2013, does not translate into a mandatory requirement that FDA reorder its priorities and respond to Endo's citizen petition by December 31, 2012.

Apart from the 270-day deadline that governs FDA's response to Endo's citizen petition in this case, neither 21 U.S.C. § 355(j)(6) nor 21 C.F.R. § 314.161(a) establish a deadline by which FDA must determine whether Endo's product was removed from the market for safety reasons. Endo reads into both the statutory provision and the regulation a requirement that FDA act by December 31, 2012. There is no statutory or regulatory support for Endo's claim. Indeed, the December 31 date is a function of Endo's own creation necessitated by its own commercial decision-making. In settlement of patent litigation, Endo granted a license to a generic manufacturer, Impax Laboratories Inc. ("Impax"), that permits Impax to begin marketing a generic version of the original Opana ER on January 1, 2013. But a different generic version of two strengths of the original Opana ER, marketed by Actavis South Atlantic ("Actavis"), was introduced in July 2011, *see* http://www.actavis.us/en/oxymorphone.htm, and it is FDA's understanding that those strengths continue to be marketed today. Endo's self-inflicted December 31 deadline is a thinly-veiled attempt to maintain its market-share and block generic competition from Impax.[4]

[4] Notably, Endo has patent protections on its new formulation of Opana ER that have the potential to prevent generic competition until approximately 2029. *See* http://www.accessdata.fda.gov/scripts/cder/ob/docs/patexclnew.cfm?Appl_No=201655&Product_No=007&table1=OB_Rx (Orange Book entry showing the drug substance patent that is listed only for the new formulation of Opana ER, patent number 7,851,482, expires on July 10, 2029).

II. Would the FDA authorize the marketing of a generic drug that has already been approved prior to reaching a determination under 21 U.S.C. § 355(j)(6) and 21 C.F.R. § 314.161(a) whether the plaintiff's product was withdrawn from the market for safety reasons?

FDA does not authorize the marketing of generic drugs separately from approving those products. Once FDA issues a final approval under 21 U.S.C. § 355(j), which is a finding by FDA that the generic product meets all the requirements for generic approval and therefore the product is safe and effective, the manufacturer can immediately begin marketing the approved product. As Endo noted in its Memorandum Of Points And Authorities In Support Of Plaintiff's Motion For Preliminary Injunction ("PI Mem."), two abbreviated new drug applications ("ANDAs") for generic versions of the original Opana ER were approved in December 2010, before Endo removed its product from the market. PI Mem. at 2. Those ANDAs belong to Impax and Actavis. As noted above, Actavis began marketing two strengths of its generic product on July 15, 2011. *See* http://www.actavis.us/en/oxymorphone.htm. In FDA's view, Impax was also permitted to begin marketing its product immediately upon approval. Impax, however, is apparently blocked by a patent license agreement with Endo from marketing until January 1, 2013. S*ee* PI Mem. at 13, n.20. FDA was not, and is not, a party to that licensing agreement.

FDA assures the Court that it will not approve any other ANDAs that reference the original Opana ER without first determining whether the product was removed from the market for reasons of safety or effectiveness, in accordance with 21 U.S.C. § 355(j)(6) and 21 C.F.R. § 314.161(a). However, products that have already been approved (including Impax's product, Actavis' product, and Endo's own original product) may continue to be lawfully marketed unless and until FDA determines that Endo's original Opana ER was in fact removed from the market for reasons of safety and effectiveness. Indeed, Endo itself could resume marketing its original

Opana ER tomorrow should it choose, because FDA's finding that Endo's product is safe and effective remains, as of this date, unchanged. The fact that Endo's own labeling for the new Opana ER product is largely identical to the original Opana ER label except for the description of the tablets' shape, as explained above, confirms that Endo's true interest in expedited FDA consideration stems from business concerns rather than protection of the public health.

* * *

Because Endo has no likelihood of success on its ill-conceived, eleventh-hour motion for exigent relief, the Court should deny it on that basis alone. Alternatively, FDA requests that the Court set a reasonable, non-expedited briefing schedule on Endo's motion for preliminary injunction together with the government's anticipated motion to dismiss Endo's unreasonable delay claim.

Respectfully submitted,

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