IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

Otsuka Pharmaceutical Co., Ltd., et al.,	*	
	*	
Plaintiffs,	*	
	*	
v.	*	
	*	Civil No. 15-CV-0852-GJH
Sylvia Mathews Burwell, Secretary	*	
U.S. Department of Health and Human	*	
Services, et al.,	*	
	*	
Defendants.	*	
	*****	

FEDERAL DEFENDANTS' MOTION TO DISMISS AND
OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

TABLE OF AUTHORITIES

Federal Cases

Federal Statutes

Federal Regulations

I. INTRODUCTION

This case reflects the efforts of plaintiffs Otsuka Pharmaceutical Co., Ltd., Otsuka Pharmaceutical Development & Commercialization, Inc., and Otsuka American Pharmaceutical, Inc. ("Otsuka") to maintain their monopoly for Abilify (aripiprazole), a blockbuster antipsychotic drug. Otsuka raises two counts, each of which lacks merit and should be dismissed outright.

First, Otsuka claims that FDA unlawfully broadened the scope of its approval for a Tourette's Disorder indication for Abilify, but FDA has not taken any such action: the approval for this indication, as reflected in the approved labeling, which embodies the scope of approval, has remained the same. For Count I, FDA has not taken any judicially reviewable final action, and Otsuka lacks standing to challenge an action that has caused it no injury. Moreover, there is no relief this Court may grant that could redress an "injury" that Otsuka has not suffered.[1]

Through Count II, Otsuka is attempting to block generic competition by asking this Court to stop the Food and Drug Administration's ("FDA's") approval of a generic competitor before FDA has even determined whether a generic product may be approved. But Otsuka must await an FDA decision before it can raise a judicially reviewable claim.

Moreover, Otsuka raises a claim that its orphan drug exclusivity for ***one*** indication should block generic approvals of Abilify for ***all*** indications, including those without any patent or exclusivity protection. FDA has yet to decide that issue in the context of aripiprazole or take any final, reviewable action, pursuant to its delegated authority to determine whether a generic drug may be approved. In any event, no generic competitor may be approved before April 20, 2015,

[1] In its recent Motion to Compel (Dkt. No. 38), Otsuka attempts to change the action challenged in Count I. Defendants address Otsuka's arguments in this regard in section V.A, *infra*.

because of a patent extended by pediatric exclusivity. FDA would only make a determination about whether or not a generic drug may be approved on or after that date.

Otsuka lacks standing to bring this challenge, and its request for an injunction to block any such approvals in advance is manifestly unripe at this time, before the agency has acted and, consequently, not yet compiled a complete administrative record to support a decision that has yet to be made. Otsuka's premature request for relief is contrary to established principles of judicial review of agency action under the Administrative Procedure Act ("APA").

If FDA were to decide the exclusivity issue adversely to Otsuka, the company may challenge the agency's decision at that time. Otsuka's desire to circumvent FDA to obtain a favorable judicial decision before the agency has had the opportunity to act in the first instance does not outweigh FDA's interest in the thoughtful and careful exercise of its authority to make generic approval decisions and the timing of those decisions. Only when FDA makes such decisions, supported by a full administrative record, would judicial review be appropriate.

Accordingly, for the reasons set forth more fully below, this Court should grant Defendants' motion to dismiss and deny Otsuka's motion for summary judgment.

II. STATUTORY AND REGULATORY BACKGROUND

A. New Drug Applications and Supplemental New Drug Applications

Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), pharmaceutical companies seeking to market the initial version of a drug (also known as the "innovator" or "pioneer" drug) must first obtain FDA approval by filing a new drug application ("NDA") containing extensive scientific data demonstrating the safety and effectiveness of the drug. 21 U.S.C. § 355(a), (d). A sponsor may thereafter submit a supplemental new drug application ("sNDA") seeking FDA's approval of a new indication of an already approved drug. 21 C.F.R. § 314.70(b). Drug

sponsors must justify the labeling change proposed in the supplement by submitting data supporting the safety and effectiveness of the drug for the new indication. 21 U.S.C. § 355(a) and (d); 21 C.F.R. § 314.70(b)(3)(iv)-(v). FDA will refuse to approve the supplement if, *inter alia*, the sponsor's investigations do not show that the drug is safe or effective for "the conditions of use prescribed, recommended, or suggested in the proposed labeling."[2] 21 U.S.C. § 355(d)(1), (2), (5).

If FDA approves a supplement, it will send the sponsor a letter informing it of the approval, noting that the approval is effective "*for use as recommended in the enclosed, agreed-upon labeling text*." *See, e.g.*, Administrative Record-To-Date ("AR") at 001, 185 (emphasis added). Thus, the letter makes clear that the scope of the approval is defined by the text in the approved labeling. The scope of a drug's approval for an indication is not governed by language in an FDA approval letter.

B. Abbreviated New Drug Applications

The Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Amendments), codified at 21 U.S.C. § 355 and 35 U.S.C. §§ 156, 271, and 282, permits a manufacturer to submit an ANDA requesting approval of a generic version of an approved drug product. 21 U.S.C. § 355(j). ANDA applicants need not submit clinical data to demonstrate the safety and efficacy of the generic product, as with an NDA. *See id*. Rather, an ANDA relies on FDA's previous findings that the product approved under the NDA is safe and effective. Among other information, an ANDA must include data showing that the generic drug

[2] The FDCA defines "labeling" as "all labels and other written, printed or graphic matter (1) upon any article or any of its components or wrappers, or (2) accompanying such article." 21 U.S.C. § 321(m). "Label," a narrow category of "labeling," is defined as a display of written, printed, or graphic matter upon the immediate container of any article. 21 U.S.C. § 321(k).

product is bioequivalent[3] to the innovator product. 21 U.S.C. § 355(j)(2)(A)(iv), (j)(4)(F); 21 C.F.R. § 314.127(a)(6)(i), 314.94(a)(7).

In order to limit the ability of brand-name companies to delay generic approvals, Congress passed 21 U.S.C. § 355(q)(1)(A), which requires a company that raises issues that would effectively delay the approval of ANDAs to raise them in a special form of petition, known as a citizen petition, which FDA is required to answer within 150 days.[4] *See* 21 U.S.C. § 355(q)(1)(F); *Hospira, Inc. v. Burwell*, Case No. 8:14-cv-02662-GJH, 2014 WL 4406901, *7 (D. Md. Sept. 05, 2014) (citing § 355(q) with approval).

C. Marketing Exclusivity

As noted, the timing for approval of ANDAs may depend, in part, on some form of marketing exclusivity afforded to the innovator drug. For instance, pioneer drugs may be eligible for three years of exclusivity under the Hatch-Waxman Amendments ("three-year Hatch-Waxman exclusivity") for a change approved in a sNDA if that sNDA "contains reports of new clinical investigations (other than bioavailability studies)[5] essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement." 21 U.S.C. § 355(j)(5)(F)(iv).

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[3] Two drugs are considered bioequivalent if, in general, the rate and extent of absorption of the generic drug do not show a significant difference from the rate and extent of absorption of the listed drug. 21 U.S.C. § 355(j)(8)(B).

[4] Although plaintiffs are clearly seeking to delay the entry of intervenor-defendants into this market, plaintiffs have not filed a citizen petition pursuant to 21 U.S.C. § 355(q)(1)(F).

[5] FDA's implementing regulation (21 C.F.R. § 314.108(a)) defines "new clinical investigation" as "an investigation in humans the results of which have not been relied on by FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety for a new patient population and do not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness or safety in a new patient population of a previously approved drug product."

In addition, pioneer drugs may be eligible for seven years of exclusivity for orphan indications. Congress enacted the Orphan Drug Act (Public Law 97-414) in 1983, to provide incentives to develop drugs to treat rare diseases and conditions. *See* 21 U.S.C. § 360aa *et seq*. As defined in 21 U.S.C. § 360bb, a rare disease or condition includes any disease or condition that affects fewer than 200,000 persons in the United States. To obtain orphan exclusivity, a sponsor must first request and obtain from FDA orphan designation for the drug for the proposed orphan indication. 21 U.S.C. § 360bb. The statute generally grants seven-year orphan exclusivity to designated drugs for specific indications upon approval for those indications. 21 U.S.C. § 360cc.

Although the FDCA generally mandates that generic drug labeling be the same as the reference listed drug's labeling, *see* 21 U.S.C. § 355(j)(2)(A)(v)[6], it allows for exceptions if "the new [ANDA] drug and the listed drug are produced or distributed by different manufacturers." *See also* 21 C.F.R. § 314.94(a)(8)(iv). In such cases, ANDA applicants may, for example, "carve out" indications protected by marketing exclusivity in certain circumstances. The implementing FDA regulation, 21 C.F.R. § 314.94(a)(8)(iv), provides examples of permissible labeling differences that may result because the generic drug product and reference listed drug are produced or distributed by different manufacturers, including omission of an indication or other aspect of labeling protected by patent or accorded exclusivity. *Id*. In order to approve an ANDA containing proposed labeling that omits such protected information, FDA must find that the "differences do not render the proposed drug product less safe or effective than the listed drug for all remaining, non-protected conditions of use." 21 C.F.R. § 314.127(a)(7).

[6] Section § 355(j)(2)(A)(v) requires that an ANDA contain "information to show that the labeling proposed for the new [generic] drug is the same as the labeling approved for the listed drug."

Courts have confirmed an ANDA applicant's ability to carve out labeling protected by exclusivity. *See, e.g., Sigma-Tau Pharms., Inc. v. Schwetz*, 288 F.3d 141, 147-48 (4th Cir. 2002) (upholding ANDA applicant's ability to carve out an indication protected by orphan exclusivity and noting dangers of extending exclusivity beyond what Congress intended); *Bristol-Myers Squibb v. Shalala*, 91 F.3d 1493, 1500 (D.C. Cir. 1996) (noting that the FDCA "expresses the legislature's concern that the new generic be safe and effective for each indication that will appear on its label; whether the label for the new generic lists every indication approved for use of the pioneer is a matter of indifference"); *cf. Hospira, Inc.*, 2014 WL 4406901 at *17 (upholding FDA's carve out of information protected by patent exclusivity).

III. FACTUAL BACKGROUND

A. FDA's December 12, 2014, Approval Letter for Abilify

Otsuka holds several NDAs (Nos. 21436, 21713, 21729, 21866) for various forms and strengths of aripiprazole, which the company markets under the proprietary name Abilify.[7] Abilify currently has six different approved indications for use, all psychiatric in nature.[8] FDA first approved Abilify on November 15, 2002, and it has been marketed without generic competition since that time.[9]

On December 12, 2014, FDA's Center for Drug Evaluation and Research, Division of Psychiatry Products approved Otsuka's sNDA for Abilify for a new indication, treatment of Tourette's Disorder. AR 001-096. As noted, *see supra* section II.A, the scope of FDA's

[7] *See* drugs@fda, *available at* http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm (search for "Abilify") (last accessed Apr. 7, 2015).

[8] *Id.*

[9] *See* Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, *available at* http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=021436&TABLE1=OB_Rx (search for "Abilify") (last accessed Apr. 7, 2015).

approval for a particular indication for use, including the Tourette's Disorder indication, is reflected in Abilify's labeling. FDA's December 12, 2014, approval letter made this clear, stating that Otsuka's sNDA was "approved, effective on the date of this letter, *for use as recommended in the enclosed, agreed-upon labeling text*." AR 001 (emphasis added); *see also* AR 005-095 (the enclosed, agreed-upon labeling text).

B. FDA's February 24, 2015 Letter Correcting Housekeeping Error in FDA's December 12, 2014, Approval Letter

As noted, *see supra* section II.A, while FDA approval letters generally inform a sponsor that a drug is approved for a particular indication, they do not attempt to include all of the labeling language that fully describes the scope of approval. FDA's Division of Psychiatry Products typically only includes the basic indication information from the Indications and Usage statement in a drug's labeling in the text of its approval letters.[10]

When FDA issued its approval letter on December 12, 2014, the letter did not track the Indications and Usage statement in Abilify's approved labeling (enclosed with the December letter) and, instead, listed "pediatric patients with Tourette's Disorder," AR 001, while the Indications and Usage statement in Abilify's enclosed, approved labeling listed "Treatment of Tourette's Disorder." AR 007. When FDA noticed that its December 12, 2014 approval letter failed to track the Indications and Usage statement, it issued a corrected approval letter on February 24, 2015, to correct this housekeeping error and mirror the existing Indications and Usage statement. AR 184-272; *see also* AR 284 (FDA General Advice Letter explaining that the

[10] The Indications and Usage statement in the Full Prescribing Information of drug labeling often includes only a concise statement of the disease or disorder to be treated, without identifying specific age ranges. *See* 21 C.F.R. § 201.57(a)(6); *see also* AR 283.

February 24, 2015, "correction was a housekeeping matter" to "harmonize[] the [approval] letter with the [Indications and Usage] statement in the [Full Prescribing Information]").[11]

However, the corrected approval letter expressly noted that the "labeling is *unchanged*." AR 184 (emphasis added); *see also* AR 283 (explaining that "when the approval letter was corrected, the [Full Prescribing Information], which describes the scope of approval, was not amended"). Indeed, a comparison of the language in Abilify's current labeling regarding Tourette's Disorder and the labeling approved on December 12, 2014, regarding Tourette's Disorder confirms that such language is *identical*.[12] *Cf.* AR 007, to AR 190 (Indications and Usage statement listing indication for "Treatment of Tourette's Disorder"); AR 010, to AR 192-93 (Section 2.5 providing dosing and administration instructions for Tourette's Disorder in pediatric patients, ages 6-18)[13]; AR 038-41, to AR 217-19 (Section 6.1 describing adverse reactions in pediatric patients, ages 6-18 with Tourette's Disorder); AR 055 to AR 233 (Section 8.4 describing pediatric use of Abilify for Tourette's Disorder); and AR 079-81, to AR 254-57

[11] FDA issued a General Advice Letter on March 27, 2015, to clarify the effect, or, rather, lack thereof, of FDA's corrected approval letter issued on February 24, 2015. AR 283-285, *see also infra* section III.C.

[12] The only substantive change to Abilify's labeling since FDA's December 12, 2014 approval letter relates to a different indication. Specifically, on January 23, 2015, FDA agreed to Otsuka's proposed labeling, which "included pertinent information in section 8.4 (Pediatric Use) under the 'Irritability with Autistic Disorder' subsection that was inadvertently omitted." AR 097. Minor editorial changes suggested by Otsuka were also reflected in this labeling (*i.e.*, correcting the numbering of tables throughout; removing mg/day where repetitive; and numbering the Nervous System Disorders in one of the tables). AR 099-183. Although Otsuka submitted and FDA agreed to update labeling on January 23, 2015, Otsuka did not suggest that any changes to either the indication statement or to the description of the data regarding treatment of Tourette's Disorder were needed at that time.

[13] Although the labeling describes these patients as "pediatric" patients, under applicable FDA labeling regulations, patients 17 and older are no longer considered to be pediatric. *See* 21 C.F.R. § 201.80(f)(9) (pediatric populations and pediatric patients are defined as "the pediatric age group from birth to 16 years including age groups often called neonates, infants, children and adolescents").

(Section 14.5 describing clinical study data supporting the use of aripiprazole for the treatment of Tourette's Disorder in pediatric patients ages 6-18). In addition, there is no Limitation of Use[14] statement based on age in the current labeling or the labeling approved on December 12, 2014. *Cf.* AR 007, to AR 190; *see also* AR 283. Thus, the corrected approval letter did not change or broaden the scope of the approval or Abilify's indication for Tourette's Disorder. AR 284 (explaining that "the corrected approval letter did not broaden the indication or the scope of the underlying approval").

C. Subsequent Communications between Otsuka and FDA

On March 9, 2015, Otsuka emailed Captain William Bender, an FDA project manager in the Division of Psychiatry Products, and asked whether the Division considered the supplement approval to be for the treatment of Tourette's disorder in the general population, or limited to the pediatric population. AR 273. Capt. Bender replied on March 11, 2015, that the supplement approval was for the treatment of Tourette's disorder in the general population.[15] *Id*. Capt. Bender's email did not make any statements regarding FDA's corrected approval letter. *Id*.

Thereafter, on March 18, 2015, Otsuka sent another email to Capt. Bender, *see* AR 274-85, contending that FDA's corrected approval letter issued on February 24, 2015, had changed and broadened the approved indication for Tourette's Disorder "from an approval for use limited to pediatric patients . . . to an approval for use in all patients with Tourette's Disorder, both pediatric and adult patients." AR 274. Otsuka characterized the email as its "formal objection to

[14] "Major limitations of use (*e.g.*, lack of effect in particular subsets of the population, or second line therapy status) must be briefly noted" in the Indications and Usage statement. 21 C.F.R. § 201.57(a)(6).

[15] An individual employee cannot change the scope of an approval or indication through an informal email. Pursuant to 21 C.F.R. § 10.85(k), this email was, at most, an informal communication that represents the judgment of that particular FDA employee at that time. As noted above, the approved labeling remained unchanged.

the change." *Id*. However, the administrative process for parties such as Otsuka to object to FDA action is set forth in FDA regulations; for example, filing a citizen petition requesting that the Commissioner "take or refrain from taking any other form of administrative action." 21 C.F.R. § 10.25. Otsuka did not file a citizen petition.

On March 24, 2015, Otsuka filed its Complaint and contemporaneous Motion for Summary Judgment in this action (Dkt. Nos. 1 & 2). Thereafter, in an effort to clear up apparent confusion regarding FDA's housekeeping correction letter issued on February 24, 2015, FDA issued a General Advice Letter on March 27, 2015, to clarify the effect, or, rather, lack thereof, of FDA's corrected letter. AR 283-285. FDA explained that "the corrected approval letter did not broaden the indication or the scope of the underlying approval" and, instead, was a housekeeping matter" to "harmonize[] the [approval] letter with the [Indications and Usage] statement in the [Full Prescribing Information]" section of the labeling approved on December 12, 2014. AR 284.

D. FDA's Pending Review of Otsuka's Exclusivity and Generic Abilify Approval

FDA has not approved any generic version of Abilify and has made no final determination with respect to whether it will, or will not, approve any generic version of Abilify. Nor has FDA made any final determinations regarding whether or not exclusivities that Otsuka holds, including orphan drug exclusivity and three-year Hatch-Waxman exclusivity, preclude generic Abilify approval.

On January 21, 2015, Otsuka's counsel sent a letter to Elizabeth H. Dickinson, FDA's Chief Counsel, raising the argument that FDA cannot approve generic versions of Abilify for *any* indication, including those without patent or exclusivity protection, until the expiration of Otsuka's seven-year orphan exclusivity period for its Tourette's Disorder indication. AR 286-

88. Otsuka's seven-year orphan exclusivity period runs from the date of approval for the Tourette's Disorder indication, December 12, 2014, meaning, under Otsuka's position, that potential generic competitors would not be able to market Abilify for any indication until December 2021. *Id.*[16]

Otsuka arrives at this result by arguing that Abilify's Tourette's Disorder indication contains pediatric information that cannot be carved out of a generic drug's labeling by virtue of § 505A(o) of the FDCA (21 U.S.C. § 355A(o)). According to Otsuka, without the ability to permissibly carve out this pediatric information, a generic drug would violate the FDCA's general rule that generic drug labeling be the same as the referenced listed drug, *see* 21 U.S.C. § 355(j)(2)(A)(v). Under Otsuka's interpretation, while 21 U.S.C. § 355A(o) permits a generic label to carve out pediatric information protected by Hatch-Waxman exclusivity without running afoul of the general same labeling requirement, the provision does not allow a labeling carve out for pediatric information protected by orphan exclusivity because orphan exclusivity is not expressly enumerated in § 355A(o). AR 286-87.[17]

FDA has made no determination with respect to the issues raised in Otsuka's January 21, 2015 letter and, to the extent it ultimately finds it necessary to decide these issues, would only do so if, and when, it approves any generic versions of Abilify. In order to make any generic Abilify approval decisions, however, the agency may also need to consider other potentially important parts of the regulatory scheme, which Otsuka's letter does not take into account.

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[16] Despite the fact that Otsuka's letter seeks to delay the approval of ANDAs, Otsuka has not filed a citizen petition pursuant to 21 U.S.C. § 355(q)(1)(A), *see supra* section II.D, which would allow generic drug manufacturers and other potentially interested parties the opportunity to comment.

[17] To be clear, these are three separate but interrelated concepts. There are two types of exclusivity at play, Hatch-Waxman and orphan, the latter of which refers to the potential number of patients in need of the drug. Pediatric information is also a separate concept.

These may include the scope of the permissible difference to the same labeling requirement in the statute (*see* 21 U.S.C. § 355(j)(2)(A)(v)), regulations (*see* 21 C.F.R. § 314.94(a)(8)(iv)), and applicable case law, as well as the effect of 21 U.S.C. § 355A(o) on labeling that is protected by *both* Hatch-Waxman and orphan exclusivity. FDA may also deem it important to consider arguments potentially raised by generic drug sponsors.

In addition, even when FDA has tentatively approved an ANDA,[18] any number of events may nevertheless prevent or delay final approval (*e.g.*, a pre-approval inspection that reveals manufacturing deficiencies or a change in standards governing impurity are just two examples). FDA will consider all relevant factors, in making any future decisions on these matters. However, FDA will make these final determinations at the time that it approves any generic versions of Abilify (and not before).

E. Otsuka's Complaint

On March 24, 2015, Otsuka filed a Complaint against the defendants containing two counts. Count I alleges that "FDA's *reversal of its original approval decision* . . . was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law." Compl. ¶ 59 (emphasis added). With respect to Count I, Otsuka's requested relief consists of asking this Court to "declare that FDA's reversal of its original approval decision, approving a new indication for Abilify for treatment of pediatric patients with Tourette's Disorder, was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law and, accordingly, [to] . . . *vacate FDA's unlawful 'corrected' decision and reinstate or order FDA to reinstate*

[18] FDA grants "tentative approval" to an ANDA when all scientific and procedural conditions for approval have been met, but the application cannot be fully approved because approval is blocked by, among other things, some form of marketing exclusivity. *See* 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA); *see generally Barr Labs., Inc. v. Thompson*, 238 F. Supp. 2d 236, 245-50 (D.D.C. 2002). An application with a tentative approval has a delayed effective date, and will not become finally approved (and the drug may not be legally marketed) until the agency issues final approval. *See* 21 C.F.R. § 314.105(d); 21 C.F.R. § 314.107(b)(3)(v).

FDA's original lawful approval decision." Compl., Prayers For Relief ¶ (c) (emphasis added).[19] Count II assumes that "on April 20, 2015, FDA will approve generic versions of Abilify" and further assumes and alleges that, if FDA does approve generic versions of Abilify on that date, it will do so in a manner that "will be arbitrary, capricious, and contrary to law.'' Compl. ¶ 68. With respect to Count II, Otsuka requests that this Court issue injunctive and declaratory relief in advance of FDA's yet to be made decision regarding generic versions of Abilify. *See* Compl., Prayers For Relief ¶¶ (d) & (e).

IV. STANDARD OF REVIEW

A. Motion to Dismiss

This case should be dismissed pursuant Federal Rules of Civil Procedure 12(b)(1) and 12(b)(6) because this Court lacks jurisdiction and Otsuka has failed to state a claim upon which relief can be granted. For these same reasons, Otsuka's motion for summary judgment must be denied.

1. Federal Rule of Civil Procedure 12(b)(1)

A motion to dismiss pursuant to Rule 12(b)(1) "tests a court's subject matter jurisdiction to adjudicate a case." *FTC v. AmeriDebt, Inc.*, 343 F. Supp. 2d 451, 459 (D. Md. 2004). Such a motion is properly granted "where a claim fails to allege facts upon which the court may base jurisdiction." *Davis v. Thompson*, 367 F. Supp. 2d 792, 799 (D. Md. 2005) (citations omitted). Plaintiffs bear the burden of proving that subject matter jurisdiction properly exists in federal court. *See Evans v. B.F. Perkins Co., a Div. of Standex Int'l Corp.*, 166 F.3d 642, 647 (4th Cir. 1999). In considering a Rule 12(b)(1) motion, the court "may consider evidence outside the pleadings" to help determine whether it has jurisdiction over the

[19] In its recent Motion to Compel, Otsuka now ignores this and contends that it is challenging the original approval. *See* Pls.' Reply in Supp. of Mot. to Compel at 2-6 (Dkt. No. 50).

case before it. *Richmond, Fredericksburg & Potomac R.R. Co. v. United States*, 945 F.2d 765, 768 (4th Cir. 1991); *see also Evans*, 166 F.3d at 647.

Where, as here, plaintiffs seek to challenge agency action under the APA, jurisdiction will only lie if the challenged action is final; thus, absent a showing that FDA has taken final agency action in this case, Otsuka's complaint should be dismissed for lack of subject matter jurisdiction. *See Invention Submission Corp. v. Rogan*, 357 F.3d 452, 460 (4th Cir. 2004) (dismissing claim against federal agency under Rule 12(b)(1) where no final agency action was found to have occurred); *Wollman v. Geren*, 603 F. Supp. 2d 879, 883 (E.D. Va. 2009); *Shipbuilders Council of Am., Inc. v. U.S. Dep't of Homeland Sec.*, 481 F. Supp. 2d 550, 555-58 (E.D. Va. 2007) (dismissing claim under Rule 12(b)(1) where agency's letter regarding future regulatory consequences was held to not be final agency action).

B. Federal Rule of Civil Procedure 12(b)(6)

A motion to dismiss pursuant to Rule 12(b)(6) "tests the sufficiency of the complaint." *Vance v. CHF Int'l*, 914 F. Supp. 2d 669, 677 (D. Md. 2012). A complaint will survive a motion to dismiss only if it contains "sufficient factual matter, accepted as true, to state a claim to relief that is plausible on its face." *Id.* (quoting *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009) (internal quotation marks omitted)). Thus, in reviewing a Rule 12(b)(6) motion, "a court must determine whether it is plausible that the factual allegations in the complaint are enough to raise a right to relief above the speculative level.'" *Id.* (quoting *Monroe v. City of Charlottesville*, 579 F.3d 380, 386 (4th Cir. 2009) (internal quotation marks omitted)). Although for purposes of applying Rule 12(b)(6), the court must "accept[] all well-pled facts as true and construe[] these facts in the light most favorable to the plaintiff," *Nemet Chevrolet, Ltd. v. Consumeraffairs.com, Inc.*, 591 F.3d 250, 255 (4th Cir. 2009) (citations omitted), the court need not accept as true "a legal conclusion couched as a factual allegation," "conclusory allegations devoid of any reference to actual

events," or "allegations that are merely conclusory, unwarranted deductions of fact or unreasonable inferences." *Vance*, 914 F. Supp. 2d at 677.

C. Motion for Summary Judgment

On summary judgment, the moving party must demonstrate that there is no genuine issue of material fact and that it is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(c); *Celotex Corp. v. Catrett*, 477 U.S. 317, 325 (1986). As this Court correctly explained in *Hospira, Inc.*, "[i]n a case involving review of a final agency action under the APA, however, the standard set forth in Rule 56(a) does not apply because of the limited role of a court in reviewing the administrative record." 2014 WL 4406901 at *9 (citing *Roberts v. United States*, 883 F.Supp.2d 56, 62-63 (D.D.C. 2012); *Kaiser Found. Hosps. v. Sebelius*, 828 F.Supp.2d 193, 197-98 (D.D.C. 2011)).

In APA actions such as this, "[s]ummary judgment thus serves as a mechanism for deciding, as a matter of law, whether the agency action is supported by the administrative record and is otherwise consistent with the APA standard of review." *Id.* (citing *Richard v. INS*, 554 F.2d 1173, 1177, n.28 (D.C. Cir. 1977)). "Thus, 'the function of the district court is to determine whether or not as a matter of law the evidence in the administrative record permitted the agency to make the decision it did.'" *Id*. (quoting *Kaiser Found. Hosps.*, 828 F.Supp.2d at 198).

Moreover, under the APA, FDA's administrative decisions may be disturbed only if "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). This standard is highly deferential to the agency. *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 416 (1971). As recently explained by this Court:

> In evaluating agency decision making under the APA, the Court's only role is to determine whether "the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment." *Citizens of Overton Park v. Volpe*, 401 U.S. 402, 416 (1971), *abrogated on other grounds*,

> *Califano v. Sanders*, 430 U.S. 99 (1977). The scope of review "under the 'arbitrary and capricious' standard is narrow and a court is not to substitute its judgment for that of the agency." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 42–43 (1983). Furthermore, administrative actions are presumed valid; thus, a "court will not second guess an agency decision or question whether the decision made was the best one." *C & W Fish Co. v. Fox*, 931 F.2d 1556, 1565 (D.C. Cir. 1991). The APA only requires the Court to decide whether the agency "articulated a rational connection between the facts found and the choice made." *Baltimore Gas & Elec. Co. v. Natural Res. Def. Council*, 462 U.S. 87, 105 (1983) (citations omitted).

Hospira, Inc., 2014 WL 4406901 at *10.

V. ARGUMENT

A. Count I Must Be Dismissed

1. Count I Must Be Dismissed Because the Challenged Action – FDA's Corrected Approval Letter – Does Not Constitute Final Agency Action.

The APA only permits review of final agency action. Otsuka argues that FDA's corrected approval letter "reversed," "broadened," or "changed" the scope of Abilify's indication for Tourette's Disorder and that such action violated the APA.[20] This challenged action does not constitute final agency action for several reasons and, thus, Count I must be dismissed. First, since FDA did not initiate or undertake any re-review of Otsuka's sNDA for its Tourette's Disorder indication following the sNDA's approval on December 12, 2014; the corrected approval letter cannot be the consummation of an agency decision-making process that never took place. Second, as the terms of the corrected approval letter and FDA's March 27, 2015, letter of general advice make clear, FDA never intended the corrected letter to have any legal consequences and, instead, considered it a housekeeping matter. Finally, the scope of any

[20] Otsuka alleges that "FDA's *reversal of its original approval decision* . . . was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law." Compl. ¶ 59 (emphasis added); *see also* Pls.' Mot. for Summ. J. ("MSJ") at 17 (explaining that "[i]n count one of the complaint, Otsuka's claim is that FDA abused its discretion and acted arbitrarily, capriciously, and contrary to law *when it reversed its original approval decision* . . .").

particular indication is reflected in the approved labeling, *see supra* section II.A. Because the corrected letter did not modify the scope of the existing labeling regarding Tourette's Disorder, the scope of the indication approved on December 12, 2014, was unchanged, and Otsuka's rights and obligations were unaffected and the corrected letter carried no legal consequence.

To be reviewable under the APA, the agency conduct in question must (1) constitute "agency action" and (2) be "final." *Golden & Zimmerman, LLC v. Domenech*, 599 F.3d 426, 431 (4th Cir. 2010). Under the APA, an "agency action can be an agency rule, order, license, sanction, relief, or the equivalent or denial thereof, or failure to act, under 5 U.S.C. § 551(13), but an agency action is reviewable as final only if its impact is sufficiently direct and immediate." *Wollman*, 603 F. Supp. 2d at 884 (quoting *Franklin v. Massachusetts*, 505 U.S. 788, 796-97 (1992)). To be final, "the action must be one by which rights or obligations have been determined, or from which legal consequences will flow." *Bennett v. Spear*, 520 U.S. 154, 177 (1997) (internal citations omitted). The legal consequences of agency action are "'a function of the agency's intention to bind either itself or regulated parties.'" *Tozzi v. HHS*, 271 F.3d 301, 310 (D.C. Cir. 2002) (quoting *Kennecott Utah Copper Corp. v. United States Dept. of Interior*, 88 F.3d 1191, 1223 (D.C. Cir. 1996)). Agency action is considered final if it "mark[s] the consummation of the agency's decision making process" and defines parties' rights and obligations or carries other legal consequences. *Bennett v. Spear*, 520 U.S. at 177-78. Both conditions must be satisfied for agency action to be final. *Id.* The plaintiff bears the burden of identifying specific federal conduct and explaining how it qualifies as final agency action. *Lujan v. Nat'l Wildlife Fed'n*, 497 U.S. 871, 882 (1990). Otsuka has not met, and cannot meet, that burden here.

a. The Corrected Letter Is Not the Consummation of Agency Decision-Making.

As the undisputed facts in the administrative record-to-date establish, FDA never undertook a re-review of its sNDA for Tourette's Disorder following its approval on December 12, 2014. Otsuka recognizes that FDA "did not 'evaluate' the proposed indication and the supporting clinical data," MSJ at 22, after the December 12, 2014, approval and therefore concludes that FDA's purported "'reversal' is unlawful because it is without factual or evidentiary support," MSJ at 24. Otsuka is not far off the mark on the facts but strays inexplicably far afield in drawing the correct conclusion from those facts. The fact that FDA did not review the sNDA after December 12, 2014, does not mean that FDA acted unlawfully; it means that FDA did not approve a change to the indication at all.

There are clear processes for dealing with labeling changes. FDA had no basis to, and did not, initiate such processes after December 12, 2014. Nor did Otsuka trigger such processes by using avenues available to it to prompt such a change, *e.g.*, filing a citizen petition or labeling supplement. Thus, FDA did not consummate a decision regarding the scope of the approval or indication through the corrected approval letter or otherwise.

b. FDA Did Not Intend Its Corrected Approval Letter to Have Legal Consequences.

The legal consequences of agency action are "a function of the agency's intention to bind either itself or regulated parties." *Tozzi v. HHS*, 271 F.3d at 310. FDA's corrected approval letter issued on February 24, 2015, incorporated a ministerial change to the wording of the approval letter meant *only* to track language in the Indications and Usage statement in Abilify's December 12, 2014, approved labeling and not to broaden the scope of the indication or the approval. AR 184-272. As noted, *see supra* section II.A, the scope of any particular indication is reflected in the approved labeling. *See also* AR at 001 (explaining Otsuka's sNDA was

"approved, effective on the date of this letter, *for use as recommended in the enclosed, agreed-upon labeling text*."). The corrected letter issued on February 24, 2015, expressly noted that the "labeling is *unchanged*" from the December 12, 2014 approved labeling. AR 184 (emphasis added). Thus, the indication was unchanged when the approval letter was corrected.

On March 27, 2015, FDA issued a letter of general advice to Otsuka in order to clarify the effect, or lack thereof, of FDA's February 24, 2015, corrected approval letter. AR 283-85. That letter stated in part that "when the approval letter was corrected, the [Full Prescribing Information], which describes the scope of the approval, was not amended, and the [Indications and Use] statement has always listed 'Treatment of Tourette's Disorder' as the indication. As such, the correction was a housekeeping matter and not a change intended to alter the conditions of approval." *See* AR 283-84. Thus, in issuing the corrected approval letter, FDA clearly did *not* intend to make a decision that would affect the original scope of the approved sNDA labeling, and, thus, indication.

c. FDA's Corrected Letter Does Not, in Fact, Have Legal Consequences.

FDA's corrected approval letter does not confer any rights or obligations upon Otsuka, *see Bennett*, 520 U.S. at 178, and Otsuka cannot identify any legal consequences that flow from FDA's letter because there are none. The labeling for the Tourette's Disorder indication is the same today as it was when approved on December 12, 2014. Court after court has held that agency communications and publications with *greater* substantive content than the letter at issue here—including guidelines, reports, policy documents, classifications, and even advisory opinions—do not qualify as final agency action under the APA because they carry no legal consequences. Otsuka has not pointed to any court that has held that an agency's ministerial or housekeeping letter constitutes final agency action fit for review under the APA.

For instance, the Fourth Circuit's decision in *Flue-Cured Tobacco Cooperative v. EPA*, involved a challenge to a report prepared by the Environmental Protection Agency ("EPA") that analyzed the effects of secondhand smoke on human health. 313 F.3d 852, 855 (4th Cir. 2002). Notwithstanding the potential impact of the report on the plaintiffs' business, the Fourth Circuit concluded that the EPA's issuance of the report was not final agency action subject to judicial review because it carried no "direct and appreciable legal consequences." *Id*. at 859 (quoting *Bennett*, 520 U.S. at 178). Like the letter at issue here, the mere issuance of the EPA report in *Flue-Cured* did not "act as a permit or carry any comparable legal consequences." *Id.* at 858, 861.

To similar effect is *Golden & Zimmerman, L.L.C., v. Domenech*, in which the plaintiff claimed that a Bureau of Alcohol, Tobacco, Firearms and Explosives publication contained an erroneous interpretation of a statute. Nevertheless, the court found that the publication was not final agency action because it "neither announced a new interpretation of the law and regulations, nor effected a change in the law or regulations themselves. It 'was purely informational in nature; it imposed no obligations and denied no relief' [and] has no 'direct and appreciable legal consequences' for plaintiffs, nor does it 'alter the legal regime' to which they are subject." 599 F. Supp. 2d 702, 711-12 (E.D. Va. 2009) (quoting *Bennett*, 520 U.S. at 178)); *see also Pharm.l Manuf. Assoc. v. Kennedy*, 471 F. Supp. 1224, 1231 (D. Md. 1979) (court dismissed a suit challenging FDA's publication of therapeutic equivalence ratings because there was no judicially reviewable agency action under the APA because the ratings did not "order[] [plaintiff] to engage in or refrain from any action" nor did the agency "do[] anything which is binding on the parties") (internal citation omitted).

Other jurisdictions have reached similar conclusions. The D.C. Circuit, for instance, recently held that no final agency action occurred when the FDA posted company-specific warning letters on its website admonishing those manufacturers to comply with FDA regulations. *Holistic Candlers and Consumers Ass'n v. Food and Drug Admin.*, 664 F.3d 940, 944-45 (D.C. Cir. 2012). The letters expressed FDA's opinion that those manufacturers' products were misbranded and did not comply with regulations but, as in this case, did not compel the plaintiffs to take or refrain from taking any particular action. Similarly, in *Air Brake Sys., Inc., v. Mineta*, the court found an agency's opinion "with negative consequences for [plaintiff]'s business" expressed in letters posted on the agency's website did not constitute final agency action subject to review under the APA. 357 F.3d 632, 635, 641 (6th Cir. 2004). As the *Air Brake* court observed, "[a]n agency's determination of 'rights or obligations' generally stems from an agency action that is directly binding on the party seeking review, such as an administrative adjudication (like a recall proceeding) or legislative rulemaking . . . ." *Id.* at 641; *see also, e.g.*, *Aerosource, Inc. v. Slater*, 142 F.3d 572, 581 (3d Cir. 1998) (holding letter was not final agency action because it did not impose "legal consequences" on the contractor, which was not required to "comply with any directive"); *Industrial Safety Equipment Association v. EPA*, 837 F.2d 1115, 1121 (D.C. Cir. 1988) (holding that an advisory agency report stating that certain asbestos-protection respirators were recommended for use by employers, while others were not, did not have legal consequences because it "establishes no rule that the regulated industry must obey"); *Asbetec Constr. Servs. v. EPA*, 849 F.2d 765, 768-69 (2d Cir. 1988) (agency order was not final agency action even though it led to plaintiff's "diminished opportunities" and "stigma" in obtaining contracts since the order did not affect the plaintiff's duties or obligations).

As the above cases amply demonstrate, FDA's transmission of a corrected approval letter is simply not reviewable because it carries no "direct and appreciable legal consequences" and is therefore not final agency action. *Bennett*, 520 U.S. at 178. FDA's corrected approval letter does not propose to do anything or require plaintiff to do, or refrain from doing, anything. The corrected approval letter is not a permit, rule, penalty, or sanction, nor does it impose civil or criminal penalties. It does not modify the original labeling and, thus, does not modify the scope of the Tourette's Disorder indication approved on December 12, 2014. The letter does not even contain the FDA's guidance, advisory opinions, requests for compliance, or policies. And even assuming, *arguendo*, the corrected approval letter could affect FDA's exclusivity determination regarding Abilify, that exclusivity determination has yet to occur, *see infra* section V.B, and action is "final only if its impact is sufficiently direct and immediate." *See Wollman*, 603 F. Supp. 2d at 884.

2. Count I Must Be Dismissed Because Otsuka Lacks Standing to Challenge FDA's Corrected Approval Letter.

Plaintiff bears the burden of establishing subject matter jurisdiction, including the elements of standing. *Northeastern Fla. Chapter, Associated Gen. Contractors of Am. v. City of Jacksonville*, 508 U.S. 656, 663 (1993); *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560-61 (1992); *see also Strawn v. AT&T Mobility*, 530 F.3d 293, 296 (4th Cir. 2008). Standing cannot be "inferred argumentatively from averments in the pleading," but, rather, plaintiffs "must allege facts essential to show jurisdiction." *FW/PBS, Inc. v. City of Dallas*, 493 U.S. 215, 231 (1990) (citations omitted). A party must establish as a threshold matter the existence of a "justiciable controversy" with the defendant, that is, one that is "definite and concrete, touching the legal relations of parties having adverse legal interests." *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240-41 (1937).

To establish constitutional standing, a plaintiff must satisfy three requirements. First, a plaintiff must show an "injury-in-fact," which is defined as "an invasion of a legally protected interest which is (a) concrete and particularized [meaning that the injury must affect the plaintiff in a personal and individual way], and (b) actual or imminent, not conjectural or hypothetical." *Lujan*, 504 U.S. at 560 & n.1 (citations and quotation marks omitted); *see also Warth v. Seldin*, 422 U.S. 490, 508 (1975). Second, the plaintiff must demonstrate a "causal connection between the injury and the conduct complained of." *Lujan*, 504 U.S. at 560. This means that the injury has to be "fairly . . . trace[able] to the challenged action of the defendant, and not . . . th[e] result[] [of] the independent action of some third party not before the court." *Simon v. Eastern Ky. Welfare Rights Org.*, 426 U.S. 26, 41-42 (1976). Third, the injury in question must be redressable by the relief sought by the complaint. This means that it "must be 'likely,' as opposed to merely 'speculative,' that the injury will be 'redressed by a favorable decision.'" *Lujan*, 504 U.S. at 561 (quoting *Simon*, 426 U.S. at 38); *see also Allen v. Wright*, 468 U.S. 737, 750-51 (1984). Otsuka has clearly failed to meet these requirements here.

Otsuka makes much of FDA's purported actions allegedly in excess of the agency's authority or contrary to law in broadening the Tourette's Disorder indication, but the closest Otsuka comes to alleging an injury from those actions is to assert that "FDA sought to prevent Otsuka from receiving the market exclusivity to which it is entitled." Pls.' MSJ at 3. But Otsuka does not explain how it is unable to enjoy its exclusivity currently. As of this date, no generic versions of Abilify have been approved and Otsuka markets its product without competition.

The only way that a broadened indication could potentially injure Otsuka is if it affects Otsuka's exclusivity in a way that causes FDA to approve generic versions of Abilify. However, FDA has made no determination with respect to the exclusivity issues Otsuka raises, nor has the

agency made determinations with respect to other relevant factors that may bear on generic Abilify approval decisions, *see supra* section V.B. To the extent the agency ultimately finds it necessary to decide these issues, the agency would only do so if, and when, it approves any generic versions of Abilify. As discussed, no such generic approvals have occurred. FDA may decide not to approve generic versions of Abilify or, if it does, it may decide to do so without regard to the scope of the Tourette's Disorder indication—*e.g.*, may approve generic Abilify even assuming that the Tourette's Disorder indication is limited to pediatric population. Until FDA's decision is made, Otsuka's claim of injury for Count I is entirely hypothetical, speculative, and conjectural and manifestly insufficient to confer Article III standing. *See also infra* section V.B.2 (explaining Otsuka's lack of standing for Count II).

In addition, plaintiffs have also failed to show that Count I is redressable by the relief sought in its Complaint. Here, it is not likely that a favorable decision on Count I would provide Otsuka with any meaningful relief. *See Lujan*, 504 U.S. at 561 (explaining it must be likely that an injury will be "redressed by a favorable decision"), *see also Townes v. Jarvis*, 577 F.3d 543, 548 (4th Cir. 2009). With respect to Count I, Otsuka seeks an order to "reinstate FDA's original lawful approval decision." Compl., Prayers For Relief ¶ (c). But, as explained earlier, FDA's "original lawful approval decision" is already in place and has been since the approval went into effect on December 12, 2014. Thus, any such order from the Court would have no substantive effect or benefit Otsuka in any way, and Count I can be dismissed for this additional reason.

3. Otsuka's Improper Attempt to Amend Its Complaint by Filing a Motion to Compel Supplementation of the Administrative Record-To-Date Cannot Save Count I from Dismissal.

In apparent recognition of the fatal weakness in its Complaint, Otsuka is now attempting to amend its Complaint through the filing of a motion to compel the agency to supplement the administrative record-to-date. *See* Mot. to Compel, Dkt. 38. This motion rewrites Otsuka's

Complaint and seeks to punish FDA for failing to file the administrative record for a claim that is simply not present in Otsuka's Complaint. This Court should not allow Otsuka to expand the administrative record and obtain a *de facto* amendment of its Complaint in contravention of the Federal Rules of Civil Procedure, *see* Fed. R. Civ. P. 15, and in the midst of briefing on this Motion to Dismiss and Otsuka's current Motion Summary Judgment. *See* Defs.' Opp'n to Mot. to Compel, Dkt. No. 47.

In its motion to compel, Otsuka, in an effort to salvage its Complaint, attempts to shift the action it seeks to challenge in Count I from the corrected approval letter to FDA's December 12, 2014, decision to approve Otsuka's sNDA for the Tourette's Disorder indication. It is a fundamental concept of jurisprudence that defendants must be permitted an opportunity to be apprised of the claims against them and to respond. In its motion to compel and reply, Otsuka attempts to shift its cause of action by cherry picking a few hazy and imprecise introductory statements in its Complaint. However, the overall structure, substance, and content of plaintiffs' Complaint and, most importantly, the prayer for relief, leave no doubt plaintiffs' Complaint did not challenge the December 12, 2014 sNDA approval decision. *See* Compl., Prayers For Relief ¶ (c), (requesting that this Court "reinstate FDA's original lawful approval decision").[21] Indeed, the Fourth Circuit has rejected a similar request to construe a complaint liberally to ignore the prayer for relief, noting a plaintiffs' failure to amend the complaint, and stating that "we begin our analysis with the relief sought by Plaintiffs." *DIRECTV, Inc. v. Tolson*, 513 F.3d 119, 124-125 (4th Cir. 2008). Thus, the Court should reject Otsuka's invitation to rule on this new claim.

[21] Plaintiffs have performed a complete about face: Otsuka's Complaint states FDA's original sNDA approval was "lawful." Compl., Prayers For Relief ¶ (c), while its latest filing says it was "unlawful," *see* Reply in Supp. of Mot. to Compel at 2-6 (Dkt. No. 50). Otsuka cannot have it both ways.

Moreover, even if Otsuka did amend its Complaint to include this new claim, such an amendment would be fruitless, because Otsuka cannot show an injury for standing purposes with respect to its new claim and, it, like the original claim, would be subject to dismissal. As with its previous claim, the only potential injury of which Otsuka complains that would derive from FDA's allegedly improper approval of its sNDA for Tourette's Disorder for use in the general population is that such a broad approval may affect FDA's yet-to-be made decisions regarding Abilify's orphan exclusivity and generic Abilify approval. But, as discussed, *see supra* section III.D, FDA has not made either of those decisions and Otsuka currently enjoys marketing exclusivity. As noted, FDA may decide not to approve generic versions of Abilify or, if it does, it may decide to do so even if Abilify's Tourette's Disorder indication is limited to the pediatric population. Until FDA makes these decisions, Otsuka simply cannot know whether it will be injured by a broad indication and, thus, even if Otsuka's Complaint could be construed to challenge its own sNDA approval, Otsuka's injury for Count I is entirely hypothetical, speculative, and conjectural and, thus, insufficient for standing purposes.

Similarly, a favorable decision on a challenge to Otsuka's December 12, 2014, sNDA approval would not provide Otsuka with meaningful relief. *See Lujan*, 504 U.S. at 561, *Townes*, 577 F.3d at 548. Again, Otsuka seeks an order to "reinstate FDA's original lawful approval decision," Compl., Prayers For Relief ¶ (c), thus, any such order from the Court would not redress Otsuka's new claim that the original sNDA approval is infirm. Moreover, any remedy for Otsuka's new claim alleging that FDA unlawfully approved its sNDA could potentially jeopardize the sNDA approval for that indication and Otsuka's orphan drug exclusivity for that indication. Nonetheless, if Otsuka truly believes that FDA was wrong to approve its sNDA and that the current approval and labeling for the Tourette's indication has not been "proven to be

safe and effective by adequate and well-controlled clinical trials," Mot. to Compel at 2, there are numerous available administrative avenues for Otsuka to pursue the matter. Otsuka could file a citizen petition pursuant to 21 C.F.R. § 10.25, requesting that the agency withdrawal its approval of its sNDA, or take other appropriate relief. Or, Otsuka could submit a new labeling supplement to its sNDA requesting labeling changes regarding the Tourette's Disorder indication. 21 U.S.C. § 356A; 21 C.F.R. § 314.70(b)(2)(v)(A). Otsuka, however, has not availed itself of these available administrative remedies before seeking judicial intervention from this Court and, thus, the Court would be justified in dismissing this case on this additional basis as well.[22]

B. Count II Must Be Dismissed

1. Count II Must Be Dismissed Because It Is Not Ripe.

Count II of Otsuka's Complaint must be dismissed because it seeks an advisory decision from this Court, and is not ripe. In Count II, Otsuka alleges that "on April 20, 2015, FDA will approve generic versions of Abilify." Compl. ¶ 68. Otsuka further assumes and alleges that, if FDA does approve generic versions of Abilify at that future date, it will do so in a manner that "will be arbitrary, capricious, and contrary to law,'' *id*., and requests that this Court issue injunctive and declaratory relief in advance of FDA's yet to be made decision regarding generic versions of Abilify. *See* Compl., Prayers For Relief ¶¶ (d) & (e). Thus, Count II depends entirely on speculation that FDA's future decisions will be legally infirm. As of this date, FDA

[22] Even if this Court were to allow Otsuka's new claim and further assuming that Otsuka were successful on that claim, the only available remedy would be for the Court to remand to the agency to consider how to proceed and/or ask Otsuka to submit a new labeling supplement. *See Fla. Power & Light Co.*, 470 U.S. at 744 (explaining that the proper course for a court, except in very rare circumstances, is to remand to the agency for additional investigation or explanation); *see also Avoyelles Sportsmen's League, Inc. v*, 715 F.2d at 904. FDA has primary jurisdiction to review the proposed text of labeling for matters of safety and efficacy.

has not approved any generics or made any determinations with respect to Abilify's marketing exclusivity.

Indeed, Otsuka's requested relief would circumvent an FDA decision altogether. Rather than wait for FDA to make a decision and develop a record, Otsuka wants the Court to issue an advisory opinion on a complex generic drug approval issue, without the benefit of FDA's expertise or even a complete administrative record that would underlie any substantive decision. Under settled legal principles, however, Otsuka's claim is not ripe, and this Court should refrain from stepping into FDA's shoes and deciding the exclusivity issue. Indeed, if this Court were to grant Otsuka's requested relief, courts would be flooded with anticipatory lawsuits designed to obstruct orderly agency decision-making. Such an outcome runs counter to well-established administrative law.

The ripeness doctrine is rooted in both Article III limitations on judicial power and prudential reasons for declining to exercise jurisdiction. *Reno v. Catholic Soc. Servs., Inc.*, 509 U.S. 43, 58 n.18 (1993). As the Supreme Court explained in *Abbott Labs. v. Gardner*, 387 U.S. 136, 148 (1967), "injunctive and declaratory judgment remedies are discretionary, and courts traditionally have been reluctant to apply them to administrative determinations unless these arise in the context of a controversy 'ripe' for judicial resolution." The purpose of this doctrine is "to prevent the courts, through avoidance of premature adjudication, from entangling themselves in abstract disagreements over administrative policies, and also to protect the agencies from judicial interference until an administrative decision has been formalized and its effects felt in a concrete way by the challenging parties." *Id*. at 148-149. The APA likewise authorizes judicial review only with respect to "final agency action." 5 U.S.C. § 704. Thus, the requirement of final agency

action is both part of the ripeness inquiry, as well as an independent basis for dismissal under the APA.

Ripeness turns upon two primary considerations: (1) "the fitness of the issues for judicial decision"; and (2) "the hardship to the parties of withholding court consideration." *Abbott Labs.*, 387 U.S. at 149; *accord Toilet Goods Ass'n, Inc. v. Gardner*, 387 U.S. 158, 162 (1967). A case is fit for adjudication "when the issues are purely legal and when the action in controversy is final and not dependent on future uncertainties." *Landsdowne on the Potomac Homeowners Ass'n, Inc. v. OpenBand at Lansdowne, LLC*, 713 F. 3d 187, 198 (4th Cir. 2013). Conversely, "a claim is not ripe when 'it rests upon contingent future events that may not occur as anticipated.'" *Naranjo*, 768 F.3d at 347 (quoting *Scoggins v. Lee's Crossing Homeowners Ass'n*, 718 F. 3d 262, 270 (4th Cir. 2013)); *see also Ohio Forestry Ass'n v. Sierra Club*, 523 U.S. 726, 733 (1998) (issue not fit for judicial review where "the courts would benefit from further factual development of the issues presented"). In evaluating the hardship prong, the court considers the immediacy of the threat and burden imposed on parties. *Naranjo*, 768 F.3d at 347; *Potomac Homeowners Ass'n*, 713 F.3d at 198. There must be a "sufficiently direct and immediate" impact on the plaintiff's "day-to-day business," such that the plaintiff faces the dilemma of either complying with the challenged agency action or risking prosecution for failure to do so. *Abbott Labs.*, 387 U.S. at 152. A court must also consider "whether judicial intervention would inappropriately interfere with further administrative action." *Ohio Forestry Ass'n*, 523 U.S. at 733. In light of the above considerations, Count II is manifestly unripe for judicial review and should be dismissed.

a. Otsuka's Claim is Not Fit for Judicial Review.

Count II "rests upon contingent future events," ignores this Court's need for "further factual development of the issues," and asks this Court to "interfere with administrative action."

First, Count II is not fit for review because it raises complex exclusivity and generic approval issues, which fall squarely within FDA's primary jurisdiction to determine. Otsuka's arguments are entirely premised on assumptions and speculation about how FDA may decide issues of exclusivity and generic approval. Issues involving drug exclusivity and generic approval are complex, as this Court has recognized.[23] FDA, as the agency with the relevant scientific and technical expertise, and as the agency that is most familiar with the regulatory scheme, must be given the opportunity to review these issues, compile a record upon which to base its decision, and then make the decision in the first instance.

Indeed, the issue of whether pediatric information protected by orphan drug exclusivity can be carved out of a generic drug's labeling involves the complex intersection of law, facts, and science.[24] FDA has not made a decision with respect to that complex exclusivity issue, nor does it expect to do so until it decides whether to approve a generic version of Abilify, which will not occur until April 20, 2015, at the earliest. FDA's determination also may, or may not, ultimately turn on its yet to be made interpretation of statutory and regulatory provisions that FDA is charged with implementing, including 21 U.S.C. § 355A(o), 21 U.S.C. § 355(j)(2)(A)(v), and 21 C.F.R. § 314.94(a)(8)(iv), which interpretations would be entitled to deference. *See Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984), and its progeny.

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[23] *See Hospira, Inc.*, 2014 WL 4406901 at *1 (noting that the statutes at play in approving generic drugs are "complex"); *see also* MSJ at 11 (noting "complex statutory scheme").

[24] FDA has permitted generic drug sponsor's to carve out indications protected by orphan drug exclusivity and Hatch-Waxman exclusivity from their labeling, in other contexts, however. *See, e.g., Sigma-Tau Pharms., Inc.*, 288 F.3d at 148 n.3; *Bristol-Myers Squibb*, 91 F.3d at 1500; *cf. Hospira, Inc.*, 2014 WL 4406901 at *17 (upholding FDA's carve out of information protected by patent exclusivity).

b. Otsuka's Claim Is Not Ripe Under Applicable Caselaw.

The overwhelming weight of judicial authority supports awaiting an FDA decision on exclusivity and generic approvability issues. For instance, *Pfizer Inc. v. Shalala*, 182 F.3d 975, 980 (D.C. Cir. 1999), supports dismissal of this case as unripe. Pfizer filed a citizen petition seeking a determination that its product was a unique dosage form and that no other ANDA could be accepted or approved. *Id*. at 977. FDA denied the petition before any ANDA was approved. *Id*. at 979. The D.C. Circuit dismissed Pfizer's claim challenging the petition response as unripe, reasoning that "judicial intervention at this time could lead to 'piecemeal review which at the least is inefficient and upon completion of the agency process might prove to have been unnecessary.'" *Id*. at 980 (citing *FTC v. Standard Oil Co.*, 449 U.S. 232, 242 (1980)).

Similarly, in *Mylan Pharmaceuticals Inc. v. FDA*, 789 F. Supp. 2d 1 (D.D.C. 2011), the court held that a claim was "not ripe for adjudication if it rests upon contingent future events that may not occur as anticipated.'" *Id*. at 11-12. In *Mylan*, as in Pfizer, the court determined that uncertainties about the approvability of an ANDA presented "open factual questions that the FDA needs to determine. This Court should not prematurely intrude in that process, but rather afford 'the agency . . . the opportunity to apply its expertise.'" *Id*. at 12. *See also Hi-Tech Pharmacal Co., Inc. v. FDA*, 587 F. Supp. 2d 1, 10 (D.D.C. 2008) (denying plaintiff's motion for preliminary injunction regarding entitlement to generic exclusivity because the agency had not yet taken final agency action, and plaintiff's claims were not ripe).

Defendants are aware of only one case, *Teva Pharms. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1313 (D.C. Cir. 2010), in which a plaintiff has obtained judicial relief before FDA made an exclusivity decision. In *Teva*, the exclusivity decision was a purely legal issue, and the agency had previously interpreted the governing statute two times on that precise issue. 595 F.3d at 1308-09 ("[The issues] turn on questions of statutory construction . . . and the

interpretations chosen by the FDA and proposed by Teva both constitute bright-line rules, impervious, so far as appears, to factual variation.") (internal citations omitted). The court thus determined that the agency had effectively announced its policy, and that "an about-face seems extraordinarily unlikely." *Id.* In sharp contrast, in this case, FDA's determination regarding Abilify's orphan drug exclusivity and generic approval is affected by the complex facts of this case. Thus, there is no basis for an expectation about what the agency will decide in this case, as there was in *Teva*, nor does Otsuka cite any precedent that would dictate the decision it assumes FDA will make.

c. Withholding Judicial Review Will Not Cause Otsuka Hardship.

Nor has Otsuka demonstrated that withholding judicial review now will cause a direct and immediate impact on its day-to-day operations. Otsuka, like any other NDA or sNDA holder, would like the opportunity to effectively challenge an FDA decision before it has been made so that it need not face any generic competition (in the event it prevails in its judicial challenge) and so that approval of any potential competition is delayed (while its judicial challenge is being litigated regardless of ultimate outcome). But the APA only provides for judicial review of final agency actions, and FDA has not made any final, substantive decision about the issues regarding Otsuka's exclusivity or generic Abilify approval.

To be sure, judicial review of a merits decision after the agency has acted can be grueling for courts and the parties, but would not likely be any more onerous than the current schedule that Otsuka's suit has imposed. Indeed, the Court and parties would have the benefit of a complete administrative record and decision from FDA setting forth its thinking on these complex exclusivity and generic approval issues. Nothing prevents Otsuka from seeking judicial recourse if, and when, FDA approves an ANDA using reasoning that Otsuka deems insufficient. The burden of participating in such a proceeding at some future time "[does] not constitute

sufficient hardship for the purposes of ripeness." *See Fla. Power & Light v. EPA*, 145 F.3d 1414, 1421 (D.C. Cir. 1998); *see also Ohio Forestry Ass'n*, 523 U.S. at 735; *Biovail*, 448 F. Supp. 2d at 165. Otsuka will not suffer any hardship if judicial review is postponed until such time as FDA may take concrete action on a particular ANDA. Then, and only then, will FDA have analyzed the relevant facts and made the requisite scientific and administrative determinations to permit meaningful judicial review upon the record.[25]

Only after the agency has taken final agency action is judicial review appropriate. Otherwise, any decision will not be based on the actual facts and record and, instead, will be an advisory opinion based on Otsuka's guess-work about what the agency may do on April 20, 2015, and its speculation regarding the reasoning that the agency may use to reach that hypothetical result. Without any FDA decision, and corresponding record for that decision, the court has nothing to review under the APA.

This is in keeping with the principle that Courts are "loath to grant a motion for summary judgment in an APA proceeding where the entire record has not yet been filed." *Devlin v. Berry*, 26 F. Supp. 3d 74, 80 (D.D.C. 2014); *see also, e.g., Fla. Power & Light Co. v. Lorin*, 470 U.S. 729, 743-44 (1985) ("The task of the reviewing court is to apply the appropriate APA standard review . . . based on the record *the agency* presents to the reviewing court." (emphasis added)); *Camp v. Pitts*, 411 U.S. 138, 142 (1973) (stating that "focal point" of Court's review is the administrative record compiled by the agency). Until the administrative record is produced, the court is left unable to "ascertain whether the [agency] examined all the relevant data and articulated a satisfactory explanation for [its] chosen course of action," *Banner Health v.*

[25] If there is a material change in the relevant facts regarding the status of generic versions of Abilify while this litigation is pending, if the Court requested, the government will promptly provide notice to the Court and, to the extent permissible under its regulations, the parties.

Sebelius, 797 F. Supp. 2d 97, 113 (D.D.C. 2011), and the government cannot properly defend against a plaintiff's motion. *See Devlin*, 26 F. Supp. 3d at 80 ("[I]n cases involving review of an agency decision, the defendant cannot necessarily point to contrary evidence until the administrative record is filed."). *See Hospira, Inc.*, 2014 WL 4406901 at *15 (evaluating exclusivity, carve out and generic approval issues under APA *after* FDA made a determination on those issues as reflected in a fifteen page letter and granting FDA's summary judgment motion while denying drug manufacturer's motion for summary judgment).

2. Count II Must Be Dismissed Because Otsuka Lacks Standing

As discussed *supra* section V.A.2, a plaintiff bears the burden of establishing the elements of standing, including establishing that he has an injury in fact. *Northeastern Fla. Chapter, Associated Gen. Contractors of Am.*, 508 U.S. at 663; *Lujan*, 504 U.S. at 560-61; *see also Strawn*, 530 F.3d at 296. To establish injury in fact, a "plaintiff must allege that he has been or will in fact be perceptibly harmed by the challenged agency action, not that he can imagine circumstances in which he could be affected by the agency's action." *United States v. Students Challenging Regulatory Agency Procedures (SCRAP)*, 412 U.S. 669, 688-89 (1973); *see also Fla. Audubon Soc'y v. Bentsen*, 94 F.3d 658, 663 (D.C. Cir. 1996) (en banc) (plaintiff must show that a particularized injury is at least imminent). The requirement of injury in fact is not satisfied "simply because a chain of events can be hypothesized in which the action challenged eventually leads to actual injury." *Nw. Airlines, Inc. v. FAA*, 795 F.2d 195, 201 (D.C. Cir. 1986).

Here, Otsuka has not identified an injury sufficiently imminent and concrete for purposes of Article III standing. Otsuka currently enjoys marketing exclusivity for Abilify and can only speculate if, or on what basis, FDA may approve a generic version of Abilify. The agency has not made a determination with respect to either generic Abilify approval or Otsuka's arguments regarding orphan drug exclusivity. Thus, Otsuka cannot know or predict the outcome of these

matters. Therefore, no injury currently exists and Otsuka cannot show that any injury is imminent. *Workers Nat'l Union*, 442 U.S. 289, 298 (1979) (requiring a plaintiff to show that "the injury is certainly impending") (citation and quotation marks omitted). A plaintiff's unwillingness to wait for the appropriate time for review, *i.e.*, when injury becomes sufficiently imminent, does not confer standing. This Court should not reward Otsuka's impatience with an expansion of the standing doctrine.

C. Otsuka Is Not Entitled to Summary Judgment

1. Otsuka Is Not Entitled to Summary Judgment on Count I.

Even if the Court had jurisdiction to hear the case, the few actions FDA has taken here are amply supported by the administrative record-to-date and fully in accord with the APA standard of review. Because Otsuka cannot establish that FDA has acted arbitrarily and capriciously or otherwise contrary to law, it would not be entitled to summary judgment even if it could overcome the jurisdictional deficiencies of its Complaint. Indeed, Otsuka rests its entire motion on the faulty premise that "FDA approved a broader indication that that which Otsuka requested," MSJ at 17, which in turn presupposes that they somehow "requested" a particular indication and received something else instead. But the only indication approved in the Abilify sDNA is that embodied in the text of the labeling that was negotiated with FDA and agreed to by Otsuka before final approval. *See* AR 001 (noting that the December 12, 2014 labeling text was "agreed-upon" by FDA and Otsuka). Buyer's remorse is not a basis for a finding on the merits for Otsuka.

a. FDA Did Not Act in Excess of Statutory Authority or Without Factual Support.

Otsuka contends that FDA unlawfully reversed its original sNDA approval in excess of statutory authority, MSJ at 18, and without factual or evidentiary support, MSJ at 24. But Otsuka draws the wrong conclusion about the absence of evidentiary support for FDA's

purported "reversal" of its original approval decision. The fact that FDA did not review the submitted sNDA or other materials after December 12, 2014, does not mean that FDA acted unlawfully; it means that FDA did not approve a change to the indication at all. There are clear processes for dealing with labeling changes. FDA had no basis to, and did not, initiate such processes after December 12, 2014. Nor did Otsuka trigger such processes by using avenues available to it to prompt such a change, *e.g.*, the filing of a citizen petition or labeling supplement. The simple fact is that FDA approved Otsuka's sNDA on December 12, 2014, for the indication set forth in the approved labeling and nothing the agency did since then has altered that approval (or the approved indication) in any conceivable way. Thus, Otsuka's claim that FDA unlawfully "broadened" the approved indication without legal authority or evidentiary support must fail.

b. FDA Has Not Taken Action Based On An Impermissible Reason.

Nor can Otsuka establish that FDA took any action for an impermissible reason. Otsuka offers nothing beyond rank speculation to support its theory that FDA acted in bad faith. On December 12, 2014, FDA approved a sNDA that Otsuka itself submitted, for an indication Otsuka specifically sought, defined by proposed labeling that plaintiffs themselves, a group of sophisticated pharmaceutical companies represented by sophisticated counsel, agreed to, and that was supported by clinical trial data that Otsuka submitted to FDA. FDA's subsequent modification of the approval letter, undertaken purely as a housekeeping measure, had no bearing on the approved indication (set forth in the approved labeling) and no legal effect on Otsuka. However much Otsuka may speculate about FDA's unspoken motivation for issuing the corrected approval letter, its claim that the agency acted for "impermissible" reasons is unavailing where, as here, the action complained of had no adverse effect on Otsuka, nor any legal effect whatsoever.

2. Otsuka Is Not Entitled to Summary Judgment on Count II.

In Count II, Otsuka assumes and alleges that, if FDA does approve generic versions of Abilify in the future, it will do so in a way that violates the APA and requests that this Court issue injunctive and declaratory relief in advance of FDA's yet to be made decision regarding generic versions of Abilify. *See* Compl., Prayers For Relief ¶¶ (d) & (e). But as of this date, FDA has not approved any generics or made any determinations with respect to Abilify's marketing exclusivity. Otsuka's requested relief would circumvent an FDA decision altogether and ask the Court to issue an advisory opinion on a complex generic drug approval issue, without the benefit of FDA's expertise or even a complete administrative record that would underlie any future substantive decision. Because Otsuka's claim is utterly speculative and unripe, it should be rejected for all of the reasons discussed above. *See Abbott Labs. v. Gardner*, 387 U.S. at 148-149 (ripeness doctrine intended "to prevent the courts, through avoidance of premature adjudication, from entangling themselves in abstract disagreements over administrative policies, and also to protect the agencies from judicial interference until an administrative decision has been formalized and its effects felt in a concrete way by the challenging parties").

VI. CONCLUSION

For the foregoing reasons, this Court should grant Defendants' Motion to Dismiss and deny Otsuka's Motion for Summary Judgment.

Respectfully submitted,

Dated: April 7, 2015

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CERTIFICATE OF SERVICE

I hereby certify that, on this 7th day of April 2015, FEDERAL DEFENDANTS' MOTION TO DISMISS AND OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT was served on the following individuals through ECF who are counsel for the Plaintiffs, as well as all other attorneys of record registered with ECF:

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