UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

RANBAXY LABORATORIES, LTD, *et al.*, Plaintiffs, v. SYLVIA MATHEWS BURWELL, *Secretary, United States Department of Health and Human Services, et al.*, Defendants, v. DR. REDDY'S LABORATORIES, INC., ENDO PHARMACEUTICALS, INC., IVAX PHARMACEUTICALS, INC, TEVA PHARMACEUTICALS USA, Inc. Defendant-Intervenors.	Civil Action No. 14-1923 (BAH) Judge Beryl A. Howell

MEMORANDUM OPINION

A subsidiary of the plaintiffs, Ranbaxy Laboratories, Ltd. and Ranbaxy, Inc. (collectively, "Ranbaxy" or the "plaintiffs"), paid, in 2013, what was then the "largest drug safety settlement" in history, amounting to $500 million, in connection with criminal charges for falsifying data and manufacturing adulterated drugs at two of its facilities in India. U.S. Dep't of Justice, "Generic Drug Manufacturer Ranbaxy Pleads Guilty and Agrees to Pay $500 Million to Resolve False Claims Allegations, cGMP Violations and False Statements to the FDA," May 13, 2013, *available at* http://www.justice.gov/opa/pr/generic-drug-manufacturer-ranbaxy-pleads-guilty-and-agrees-pay-500-million-resolve-false. During the course of the investigation into the plaintiffs' (now) admitted wrongdoing, the Federal defendants in this case—the Secretary of Health and Human Services, the Commissioner of the U.S. Food and Drug Administration

("FDA"), and the FDA—granted "tentative approval" to five Abbreviated New Drug Applications ("ANDAs") submitted by the plaintiffs for the manufacture of certain generic drugs at the same facilities involved in the plaintiffs' subsidiary's criminal case. *See* Defs.' Mem. Opp'n Pls.' Mot. Prelim. Inj. and Supp. Defs.' Mot. Summ. J. ("Defs.' Mem.") at 10–17, ECF No. 52.

Years after the grant of those ANDAs, when two of these tentative approvals were preventing other drug manufacturers from coming to market with generic versions of costly medications, the FDA reexamined and revoked two of those five tentative approvals, for esomeprazole and valganciclovir, stating the approvals had been granted "erroneously." Defs.' Mem. at 3; Compl. ¶ 38, ECF No. 1; Administrative Record ("AR") at 1 (Letter from FDA to plaintiffs regarding esomeprazole and valganciclovir ANDAs, Nov. 4, 2014 (the "Rescission Letter")). This agency action prompted the plaintiffs to file the instant suit, contending that the Federal defendants had no authority, statutory or otherwise, to correct their egregious error and rescind the tentative approvals. *See generally* Compl. Now pending before the Court is the plaintiffs' Motion for Preliminary Injunction (the "Pls.' Mot."), ECF No. 41; the Federal defendants' Motion for Summary Judgment (the "Defs.' Mot."), ECF No. 51; and the Motions for Summary Judgment from four other generic drug manufacturers, Dr. Reddy's Laboratories ("Dr. Reddy's"), Endo Pharmaceuticals, Inc. ("Endo"), Ivax Pharmaceuticals, Inc. ("Ivax"), and Teva Pharmaceuticals USA, Inc. ("Teva"),[1] which have each been granted leave to intervene in this matter as defendants, ECF Nos. 53 and 73.[2] Although the FDA's practices, which

[1] Ivax is a subsidiary of Teva, *see* FRCP 7.1 Statement and Certificate Req. by LCvR 7.1 for Ivax and Teva at 1, ECF No. 72, and, although the two companies each intervened individually, the two defendant-intervenors moved jointly for summary judgment, Mot. of Ivax and Teva for Summ. J. at 1, ECF No. 73.

[2] The Court consolidated the hearing on the plaintiffs' Motion for Preliminary Injunction with its consideration of the merits of the plaintiffs' claims. Minute Order, Nov. 21, 2014; *see* FED. R. CIV. P. 65(a)(2).

apparently led to these errors, raise grave concerns, the Federal defendants' interpretation of the relevant portions of the Food, Drug, and Cosmetics Act (the "FDCA") as permitting the rescission of the erroneously issued tentative approvals is reasonable. Consequently, the Federal defendants' and defendant-intervenors' motions are granted and the plaintiffs' motion is denied.[3]

I. BACKGROUND[4]

The statutory regime under which generic drug applications, such as those at issue here, are approved, is complex. Thus, a brief summary of the regulations governing ANDAs and their approval is provided before turning to the history of the plaintiffs' applications, the concurrent investigations into the plaintiffs' manufacturing processes by the FDA, and the procedural background of the instant matter.

A. The Statutory Regime

All pharmaceutical manufacturers wishing to sell their products in interstate commerce must first seek approval from the FDA in compliance with 21 U.S.C. § 355. New drug applications ("NDAs") are subject to rigorous application protocols under which the applicant must prove the drug is safe and effective. *See* 21 U.S.C. § 355(b); Defs.' Opp'n Pls.' Mot. Temp. Restraining Order ("Defs.' TRO Opp'n") at 5, ECF No. 22-1. The applicant must also provide information about patents used in the drug, or for using the drug, "to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(c)(2).

[3] Portions of the AR in this matter contain confidential or sensitive information, which portions are unavailable to the public and, in some cases, to one or more of the parties to this case. The Federal defendants and plaintiffs refer to some of those portions in their submissions, which have been filed under seal with redacted versions publicly available. Consequently, this Memorandum Opinion will be filed under seal for a limited period to allow, first, the Federal defendants, and then the plaintiffs, the opportunity to propose any redactions necessary to protect such confidential or otherwise sensitive information.

[4] Although the defendant-intervenors have submitted extensive legal memoranda and exhibits, resolution of the pending motions is predicated entirely upon the administrative record submitted and the arguments raised by the plaintiffs and the Federal defendants.

1. *The Hatch-Waxman Amendments*

Between 1962 and 1984, companies wishing to manufacture generic versions of drugs already approved for use had to follow the same rigorous steps as in a new drug application before the drug could be approved and sold, even though the generic equivalent was effectively identical to a brand name drug.[5] H.R Rep. No. 98-857, pt. 1, (Report of the House Committee on Energy and Commerce on Drug Price Competition and Patent Term Restoration Act) at 14–15 (1984). In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act, codified in 21 U.S.C. § 355. Colloquially known as the "Hatch-Waxman Amendments," the amendments created a process by which generic drugs could be approved on the basis of an "abbreviated" new drug application, an ANDA, by "piggy-back[ing]" on the studies already completed by the pioneer drug manufacturer. *FTC v. Actavis, Inc.* (*Actavis*), 133 S. Ct. 2223, 2228 (2013); *see Mylan Labs, Inc. v. Thompson*, 389 F.3d 1272, 1274–75 (D.C. Cir. 2004).

This statutory change removed a major expense for generic drug manufacturers, since "[u]nlike an NDA, an ANDA need not contain clinical evidence of the safety or efficacy of the drug." *See Teva Pharm. Indus. Ltd. v. Crawford*, 410 F.3d 51, 52 (D.C. Cir. 2005). Its purpose is "to speed the introduction of low-cost generic drugs to market," *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S* (*Caraco*), 132 S. Ct. 1670, 1676 (2012), thus increasing competition and, theoretically, lowering prices, *Teva Pharms. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1305 (D.C. Cir. 2010). To further this goal, the Hatch-Waxman Amendments included the "so-called paragraph IV certification." *Caraco*, 132 S. Ct. at 1677. Since "the FDA cannot authorize a generic drug that would infringe a patent," *id.* at 1676, Congress required ANDA applicants, in

[5] The FDA had created "its own abbreviated procedures for generic copies of pioneer drugs," *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1316 n.1 (D.C. Cir. 1998), but did not apply those procedures to drugs approved after 1962, H.R. 98-857 pt. 1 at 16. In other words, the FDA's administrative abbreviated procedures applied only to pioneer drugs approved prior to 1962. *See id.*

21 U.S.C. § 355(j)(2)(A)(vii), to certify that the generic drug would not infringe upon any valid patents.

2. *Paragraph IV Certification*

Relevant to the instant matter, one of the bases on which an ANDA applicant may certify that its product will not infringe any valid patents is by certifying that some or all of the patents used in the making of the pioneer drug are invalid. 21 U.S.C. § 355(j)(2)(A)(vii)(IV). Known as a paragraph IV certification, this course of action entails significant risk since it will almost inevitably "provok[e] litigation" and, indeed, the mere filing of a paragraph IV certification is deemed to be "an act of infringement, which gives the [pioneer drug manufacturer] an immediate right to sue." *Caraco*, 132 S. Ct. at 1677; *see* 35 U.S.C. § 271(e)(2)(A). Assuming the pioneer drug manufacturer timely files suit, the FDA may not approve the ANDA, "usually for a 30-month period," while the patent dispute is litigated. *Actavis*, 133 S. Ct. at 2228.

To incentivize manufacturers to take advantage of paragraph IV certifications, despite the considerable expense and difficulties, the Hatch-Waxman Amendments included a provision allowing the first generic manufacturer to file an ANDA predicated on this certification to "enjoy a period of 180 days exclusivity (from the first commercial marketing of its drug)." *Id.* at 2228–29 (citing 21 U.S.C. § 355(j)(5)(B)(iv)); *Teva Pharms. USA, Inc.*, 595 F.3d at 1305 (noting exclusivity provision designed to "compensate [generic] manufacturers for research and development costs as well as the risk of litigation from patent holders" (internal quotation marks and citation omitted; alteration in original)). This exclusivity functions as a mini-generic monopoly for the generic drug manufacturer, providing a 180-day period in which only the first generic manufacturer may compete with the pioneer drug. *Actavis*, 133 S. Ct. at 2229. This incentive can be worth "several hundred million dollars," but it can "belong only to the first generic to file." *Id.* (citations omitted).

3. *Forfeiture Triggers*

While the 180-day exclusivity period holds out the promise of substantial monetary compensation for first-to-file generic manufacturers, it is not guaranteed. The exclusivity is forfeited if any statutorily defined "forfeiture event" occurs. 21 U.S.C. § 355(j)(5)(D)(i). An applicant forfeits any 180-day exclusivity by (1) failing timely to market the drug after certain specified events have occurred, *id.* § 355(j)(5)(D)(i)(I); (2) withdrawing the ANDA, either itself or constructively by the agency, "as a result of a determination by the Secretary that the application does not meet the requirements for approval under [21 U.S.C. § 355(j)(4)]," *id.* § 355(j)(5)(D)(i)(II); (3) amending or withdrawing the applicant's paragraph IV certifications, *id.* § 355(j)(5)(D)(i)(III); (4) failing to obtain tentative approval "within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed," *id.* § 355(j)(5)(D)(i)(IV); (5) entering into an agreement "with another applicant, the listed drug application holder, or a patent owner" found to be in violation of antitrust laws, *id.* § 355(j)(5)(D)(i)(V); or (6) expiration of the valid patents that would otherwise be infringed if the ANDA applicant marketed its drug, *id.* § 355(j)(5)(D)(i)(VI).

The forfeiture triggers were added to § 355(j) as an amendment to the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the "MMA"). 108 Pub. L. 173, 117 Stat. 2066, 2448–64. One of the amendment's primary sponsors noted during the final floor debate that the forfeiture triggers' purpose was to "ensure that the 180-day exclusivity period enjoyed by the first generic to challenge a patent cannot be used as a bottleneck to prevent additional generic competition." 149 Cong. Rec. S15746 (daily ed. Nov. 24, 2003) (statement of Sen. Schumer). The amendment was prompted by some "brand and generic companies . . . abusing this [180-day] exclusivity period-both through collusive agreements and use of other

tactics" that prevented the timely appearance of generic drugs in the marketplace. *Id.* The amendments were intended to "end this abuse because the generic company forfeits its exclusivity if it doesn't go to market in a timely manner." *Id.* In short, the amendments were viewed as "important, pro-consumer cost containment provisions." *Id.*; *see also id.* at 15761 (statement of Sen. Frist) ("The [amendments] also take[] additional steps to reduce or eliminate the delays in the movement of generic drugs to the marketplace.").

Although Congress' stated goal with the 1984 and 2003 amendments to the FDCA was to bring generic drug products to market faster, the Act still requires ANDA applicants to fulfill myriad statutory requirements before receiving approval to market a generic version of a pioneer drug. This approval process is discussed below, since the transition from one stage to the next, and whether those transitions are irrevocable, are the key questions at issue in the instant matter.

B. The ANDA Approval Process

The Federal defendants describe three significant "milestones" in the ANDA process: (1) when the ANDA may be "received" by the FDA because it is "substantially complete" such that the agency may conduct a "substantive review," Defs.' Mem. at 5; (2) when an ANDA receives "tentative approval," *id.* at 6; and (3) when an ANDA receives final, or "effective," approval, *id.* Each milestone is described in further detail below.

1. *Substantially Complete*

An ANDA does not require the submission of the results of human clinical trials, as is required for NDAs, but the application materials are substantial and governed by statute. *See* 21 U.S.C. § 355(j)(2)(A). An ANDA must contain, *inter alia*, "information to show" the bioequivalence of the proposed generic drug to the pioneer drug, *id.* § 355(j)(2)(A)(ii), *id.* § 355(j)(2)(A)(iv); a certification regarding any potential patent infringement, including, if applicable, the aforementioned paragraph IV certification, *id.* § 355(j)(2)(A)(vii); and "the items

specified in clauses (B) through (F) of" 21 U.S.C. § 355(b)(1), which is the section of the FDCA governing the contents of NDAs, 21 U.S.C. § 355(j)(2)(A)(vi). By cross-referencing and incorporating certain clauses of § 355(b)(1), Congress required ANDAs to contain

> (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug.

21 U.S.C. § 355(b)(1). Thus, ANDAs must contain all the elements required for NDAs under § 355(b)(1) except for "full reports and investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective for use" and "assessments required under [21 U.S.C. § 355c]."[6] *Id.* The agency "may not require that an abbreviated application contain information in addition to that required by" the statute. *Id.* § 355(j)(2)(A). The Federal defendants summarize that § 355(j)(2)(A) requires, in essence, that the ANDA applicant "demonstrate that its proposed generic drug product is the same as the previously approved-innovator drug in several respects and that the ANDA sponsor can reliably manufacture the drug product." Defs.' Mem. at 4.

FDA regulations mandate that "within 60 days after FDA receives an application, the agency will determine whether the application may be filed." 21 C.F.R. § 314.101(a)(1). In reviewing the application, the FDA determines if the ANDA complies with the terms of § 355(j)(2)(A) and any applicable agency regulations so that the "application is sufficiently complete to permit a substantive review." *Id.* § 314.101(b)(1). The same regulation lists the acceptable reasons for the agency to refuse to "receive[]" an ANDA and the procedure to perfect

[6] 21 U.S.C. § 355c pertains to certain special assessments and other requirements for pediatric uses of new drugs and biological products.

the application. *Id.* § 314.101(d), (e). Once this "threshold determination" has been made, the ANDA proceeds to the next phase of its review.

2. *Tentative Approval*

The substantive review of an ANDA "involves reviews by many disciplines of various aspects of an application, including bioequivalence, chemistry, labeling, and manufacturing," and, according to the Federal defendants, "often requires multiple 'review cycles' before an application is ready for approval." Defs.' Mem. at 5; *see* Admin. Rec. ("AR") at 312–14 (routing slip for tentative approval of generic ANDA, showing review by at least twelve FDA employees).[7] The purpose of this review is to determine whether an ANDA meets the statutory requirements for approval such that the drug can be sold in interstate commerce. *See* 21 U.S.C. § 355(j). Since an ANDA is, by definition, based on a drug that has already been approved for marketing and, consequently, has been found to be safe and effective, an ANDA "shall" be approved by the FDA unless the ANDA fails to meet certain conditions, including if "the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity." *Id.* § 355(j)(4)(A).

As the Federal defendants point out, however, "[t]he timing for ANDA approval depends, in part, on statutory patent protections afforded to the innovator drug." Defs.' Mem. at 6. In other words, an ANDA may meet all the requirements for approval, but the FDA may be barred by statute from approving the application until such time as certain patents for elements of the pioneer drug expire; in such cases, the agency may grant the ANDA "tentative approval."

[7] Per the Court's order, the entire AR has been submitted for *in camera* review. Minute Order, Jan. 6, 2015; *see* LCvR 7(n)(1). Citations to page numbers in the AR refer to the "bates" stamp number in the lower right corner of each page. All page numbers in the AR are preceded by the letters "FDA."

21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA). "Tentative approval," according to the statute, "means notification to an applicant by the Secretary that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the application does not meet the requirements of this subparagraph . . . ."[8] *Id.*

Tentative approval is often an intermediate step between the submission of a substantially complete application and "effective approval" allowing the marketing of a generic drug, but the practical importance of tentative approval is limited. "A drug that is granted tentative approval . . . is not an approved drug and shall not have an effective approval until the Secretary issues an approval after any necessary additional review of the application." 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(BB); 21 C.F.R. § 314.107(b)(3)(v) ("Tentative approval of an application does not constitute 'approval' of an application and cannot, absent a final approval letter from the agency, result in an effective approval . . . ."). Nevertheless, tentative approval does affect the eligibility of an ANDA applicant for the 180-day exclusivity period provided in 21 U.S.C. § 355(j)(5)(B)(iv).

As previously noted, the first ANDA applicant to file an ANDA with a paragraph IV certification is eligible for the 180-day exclusivity period, so long as none of the forfeiture triggers added to the law in 2003 apply. *Supra* Part I.A.3. One of those six forfeiture triggers, described as "forfeiture events" in the statute, is the failure of the ANDA applicant "to obtain tentative approval of the application within 30 months after the date on which the application is filed . . . ." 21 U.S.C. § 355(j)(5)(D)(i)(IV). Thus, while tentative approval, standing alone, does not provide any tangible benefit to the ANDA applicant, if an ANDA applicant becomes eligible

[8] Tentative approval also may be granted on the grounds that effective approval cannot be granted because "there is a period of exclusivity for the listed drug under subparagraph (F) or [21 U.S.C. § 355a] . . . or there is a 7-year period of exclusivity for the listed drug under [21 U.S.C. § 360cc]." 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA).

for the 180-day generic marketing exclusivity, the securing of tentative approval is necessary within a set time period in order to avoid forfeiting that exclusivity. *Id.*[9]

Importantly for the present dispute, the FDA maintains that its "policy . . . has always been, and remains, that an ANDA is not eligible for tentative approval absent a satisfactory showing of CGMP compliance." Defs.' Mem. at 29.

3. *Final Approval*

The eleven reasons allowed by statute for declining to provide final approval to an ANDA are set forth in 21 U.S.C. § 355(j)(4). Among these multiple reasons for the FDA to deny approval of an ANDA are that (1) the agency finds a drug's manufacturing process to be "inadequate to assure and preserve [a drug's] identity, strength, quality, and purity," *id.* § 355(j)(4)(A); (2) the generic drug is not shown to be sufficiently similar to the pioneer drug, *id.* § 355(j)(4)(C); *id.* § 355(j)(4)(F); (3) the drug's inactive ingredients "are unsafe for use under the conditions prescribed," *id.* § 355(j)(4)(H); (4) the approval of the pioneer drug has been revoked, *id.* § 355(j)(4)(I); (5) "the application does not meet any other requirement of paragraph (2)(A)," *id.* § 355(j)(4)(J); and (6) "the application contains an untrue statement of material fact," *id.* § 355(j)(4)(K).

Final approval does not follow by operation of law from a tentative approval letter. *See Ranbaxy Labs Ltd. v. FDA*, 30 F. Supp. 2d 15, 21 (D.D.C. 2004) (noting tentative approval does not convert to final approval "automatically" upon the cessation of patent litigation and

[9] Under the President's Emergency Plan for AIDS Relief ("PEPFAR"), drugs that have received tentative approval but are barred from sale in the United States because of patent or other exclusivity protection may be purchased by the United States Agency for International Development ("USAID") for distribution outside the United States, under certain circumstances. AR at 128. This tangible benefit does accrue for certain generic drugs used to treat AIDS based on tentative approval alone, but is a limited exception to the general rule. *See id.* Notably, the FDA states in its description of the PEPFAR program that tentative approval "signifies that the product meets all safety, efficacy, and manufacturing quality standards for marketing in the U.S." *Id.* Neither of the ANDAs at issue in this litigation are on the list of approved drugs for the PEPFAR program. *See id.* at 128–64 (listing all "Antiretrovirals Approved and Tentatively Approved in Association with the President's Emergency Plan Expedited Review Process").

expiration of a patent that previously prevented final approval). Rather, as expressly contemplated in § 355(j)(5)(B)(iv)(II)(dd)(BB), final approval accrues only after "any necessary additional review of the application" by the FDA after the impediments to final approval that necessitated a grant of tentative approval have been removed.[10] Once final approval is requested, the agency once again reviews the ANDA and determines whether final approval should issue. *See* Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338, 50,352 (Oct. 3, 1994) (stating the "agency will examine the application to determine whether there have been any changes in the conditions under which the application was tentatively approved" before sending notice of final approval).

Once an ANDA has been granted final approval, the manufacturer may begin selling the drug in interstate commerce. *See* 21 U.S.C. § 355(a). Even after a drug has been marketed, however, the agency retains the ability to revoke that final approval. *Id.* § 355(e). The agency "shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section," when it makes one or more of five findings: (1) that "such drug is unsafe for use under the conditions of use upon the basis of which the application was approved;" (2) that "new evidence of clinical experience," indicates the drug is no longer safe for use; (3) that new evidence indicates the drug is not effective; (4) that appropriate patent information was not filed in a timely manner; or (5) "that the application contains any untrue statement of a material fact." *Id.* If the Secretary determines that "there is an imminent hazard to the public health," the application may be suspended "immediately," with an expedited hearing to be held after such suspension. *Id.*

[10] The agency requires applicants whose ANDAs are tentatively approved to "reactivate" the applications "prior to final approval" by submitting a "'Minor Amendment – Final Approval Requested'" letter "90 days prior to the date [the applicant] believe[s] that [its] ANDA will be eligible for final approval." *E.g.*, AR at 233 (tentative approval letter for ANDA 77-830 (esomeprazole)).

The agency "may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application" if the Secretary finds that (1) "the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records . . .;" (2) that new information "evaluated together with the evidence before him when the application was approved, [shows that] the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity;" or (3) that new information combined with knowledge previously available to the Secretary shows that "the labeling of such a drug . . . is false or misleading." *Id.*

* * *

To sum up, an ANDA typically passes through three distinct phases of FDA review on the generic drug's way to the marketplace. A generic drug manufacturer must first perfect an application before that application is reviewed on the merits. If the ANDA could be approved, except for the presence of blocking patents or other periods of exclusivity, the ANDA may be tentatively approved, which approval does not allow the marketing of the drug but may serve to preserve eligibility for a 180-day generic marketing exclusivity period by eliminating a potential forfeiture event. After any patent impediments are removed, the ANDA may be granted final approval, at which point the drug may be marketed in interstate commerce. Post-final approval, an ANDA's approval must be revoked, after due notice and hearing, pursuant to certain statutory requirements, and may be revoked in certain other circumstances. As context for the treatment of the ANDAs at issue in this litigation, the Court turns next to a review of the recent history of enforcement actions against the plaintiffs as a result of rampant compliance problems at the

plaintiffs' production facilities in India where the generic drugs at issue were to be manufactured.

C. The Plaintiffs' Repeated Compliance Failures

The history of the plaintiffs' compliance—or lack thereof—with Current Good Manufacturing Practice (CGMP) at their facilities in India, where the plaintiffs planned to manufacture the generic drugs at issue in this litigation, is extensive. These compliance problems were apparently ongoing before, during, and even after the Federal defendants gave tentative approval to the ANDAs at issue. The Federal defendants now admit that granting tentative approval to these ANDAs was egregious error, which the FDA rectified, in November 2014, by rescinding the tentative approvals. These are the agency actions challenged by the plaintiffs in this lawsuit.

1. *The 2006 Inspection*

The plaintiffs' manufacturing facility in Simour District, Himanchal Pradesh, India ("Paonta Sahib"), was inspected by the FDA between February 20 and 25, 2006 in connection with certain of the plaintiffs' pending NDAs and ANDAs, including for antiretroviral drugs on the list of PEPFAR approved medications that were manufactured at the facility. AR at 1488 (Establishment Inspection Report, Ranbaxy Laboratories, Ltd. Simour District, India facility for inspection beginning Feb. 20, 2006 and ending Feb. 25, 2006 (the "2006 Inspection Report")). At the time of the 2006 Inspection Report, the plaintiffs [redacted] *Id.* at 1491.[11]

[11] [redacted] AR at 1491.

As reported in the 2006 Inspection Report, [redacted][12] *id.* at 1498–1506; [redacted] *id.* at 1507; [redacted] *id.*; [redacted] *id.*; [redacted], *id.* at 1507–08; [redacted] *id.* at 1508–09; [redacted] *id.* at 1509; and [redacted], *id.*

The plaintiffs discounted these observations in three letters filed with the FDA. AR at 1478–83 (Letter from plaintiffs to FDA, Mar. 20, 2006); *id.* at 1475–77 (Letter from plaintiffs to FDA, Apr. 20, 2006); *id.* at 1469–74 (Letter from plaintiffs to FDA, May 25, 2006). In each letter, the plaintiffs addressed one or more of the FDA's observations, either offering an explanation for the observation, *see, e.g.*, *id.* at 1481 (noting [redacted]), or noting that the plaintiffs had adopted new practices in response to the observations, *see, e.g.*, *id.* at 1477 (noting new [redacted]).

[12] Testing a drug's stability determines the amount of time the drug remains safe and effective for use, with the results of such tests determining the expiration date for the tested drug. *See United States v. Baxter Healthcare Corp.*, 901 F.2d 1401, 1414–15 (7th Cir. 1990).

2. *The 2006 Warning Letter*

Despite these explanations and implemented changes, the FDA issued a "Warning Letter" to the plaintiff on June 15, 2006, noting that the inspection of the Paonta Sahib facility "revealed significant deviations from U.S. Current Good Manufacturing Practice (CGMP) Regulations . . . in the manufacture of drug products." *Id.* at 1462 (Letter from FDA to plaintiff, June 15, 2006 (the "2006 Warning Letter")). The 2006 Warning Letter acknowledged the plaintiffs' "actions to restructure the stability group and institute a Management Review Committee to oversee the stability program," but noted that the agency "still [had] concerns regarding the observations." *Id.* Even with the changes, the FDA stated that "[t]here is no assurance that the stability sample test intervals for each attribute examined have been met to assure valid estimates of stability." *Id.* at 1463.

Perhaps foreshadowing later problems that would develop with the plaintiffs' reports to the FDA, the agency noted that the plaintiffs had averred that "a hard copy handwritten master list . . . identifies all the samples placed in each of the stability chambers" at the facility. *Id.* at 1464. The FDA investigators, however, did not see any such master list, "nor was it mentioned or provided to the investigative team when they initially requested the sample logbook or throughout the inspection." *Id.* The 2006 Warning Letter required the plaintiffs to submit a print-out of another log pertaining to stability sampling that the FDA investigators also failed to observe on their inspection, and further noted that certain of the plaintiffs' explanations were self-contradictory. *See id.* (noting "samples cannot be for both 'investigational purposes' only and 'impurity profile trending/deviations' because impurity testing is part of the drug product stability program"); *id.* at 1466 ("the purpose of these 'stand-by' samples remains unclear . . . . [p]lease clarify if these samples are for 'investigational' purposes, 'impurity profile' trending, or

for 'regulatory global filings' and explain the rationale for storage of these samples at [redacted] for up to [redacted] months.").

Additionally, the 2006 Warning Letter contained details of the FDA's own studies finding that certain drugs from the Paonta Sahib facility "show much lower potencies in these batches within approximately three to six months of release, and well before their expiration dates," as well as findings of "several abnormalities" among antiretroviral drugs shipped by the plaintiff to African nations under the PEPFAR program. *See id.* at 1467. As a result, the 2006 Warning Letter advised the plaintiffs that "[u]ntil FDA has confirmed correction of the deficiencies observed during the most recent inspection and compliance with CGMPs, this office will recommend withholding approval of any new applications listing your Paonta Sahib facility as the manufacturer of finished pharmaceutical drug products." *Id.*

In late August 2006, the plaintiffs responded to the 2006 Warning Letter by reaffirming their intention "to improve our quality programs and to enhance [their] operational performance at the Paonta Sahib facility." *Id.* at 1436 (Letter from plaintiffs to FDA, Aug. 29, 2006). As part of that commitment, the plaintiffs advised that they had retained a consulting firm "to verify that [their] stability laboratory program improvements are effective and systemic, and to verify the effectiveness of [their] commitments made in response to the Warning Letter." *Id.* This consulting team's assessment began in early July 2006 and was still ongoing as of August 29. *Id.* The plaintiffs also included a detailed response to the 2006 Warning Letter, identifying changes made to their policies and procedures in response to the FDA's observations, including some additional documentation. *See id.* at 1438–59. A month later, and of particular importance for the instant ANDAs, the agency requested [redacted]

[redacted]

Id. at 1434 (Letter from FDA to plaintiffs, Sept. 27, 2006).

The promised audit results proved to be a sticking point between the agency and the plaintiffs. In response to the FDA's request, the plaintiffs noted that "it was our and PAREXEL's understanding that it is FDA's policy not to review or copy any reports or records that result from such audits" and, consequently, the plaintiffs believed that turning over the report would "affect the candor with which personnel would approach future audits, and make them a far less valuable tool for senior management and for the company as a whole." *Id.* at 1431 (Letter from plaintiffs to FDA, Oct. 13, 2006). The plaintiffs offered to work with the agency to provide "other relevant materials" while stopping short of producing the audit report. *Id.*

On November 29, 2006, a team from the plaintiffs, including the plaintiffs' CEO, President, counsel, and a Vice-President from the plaintiffs' consulting firm, met with twelve FDA staff regarding the 2006 Warning Letter. *Id.* at 1424 (FDA's Meeting Minutes, Nov. 29, 2006). The agency expressed concern at the meeting "that there appeared to be a lack of global corrective actions" in response to the 2006 Warning Letter and peppered the plaintiffs' representatives with questions. *See id.* at 1425–28. In response to at least one of the concerns, the plaintiffs' consultant noted that certain "information was not provided" to the consultant "when requested" and believed that certain discrepancies between the plaintiffs' recollection of certain events and the inspectors' memories was "due mainly to communication barriers." *Id.* at 1427.[13]

[13] The plaintiffs' minutes of the meeting indicate that the outside consultant vouched for the plaintiffs' efforts and good intentions, stating [redacted]

The PAREXEL audit report was a specific topic of discussion. "The Agency clarified that FDA's policy of not requesting company audits does not apply to third party audits," such as that conducted by the plaintiffs' consultant. *See id.* at 1428. The plaintiffs' consultant averred that "disclosing results of audits to the Agency would be destructive to the company's audit program and be destructive to [the plaintiffs'] quality improvement goals for fear of disclosure of audits to the FDA." *Id.* The agency dismissed those concerns, noting that "audits are routinely received and reviewed by [the agency], and requested to see any information that could be provided by Parexel." *Id.* The plaintiffs agreed to "consider the request." *Id.* As to the scope of the audit, the plaintiffs' consultant stated that the consultant was "doing a retrospective verification of stability samples" and that a review of the accuracy of "all current and future ANDA filings" and that the results for the pending ANDAs "will be completed . . . and provided to the Agency in December, 2006." *Id.*

Finally, the FDA reiterated to the plaintiffs that the "hold on Ranbaxy's application[s]" instituted as part of the 2006 Warning Letter "would not be removed until the facility is re-inspected to ensure that updated procedures have been implemented and global issues have been addressed." *Id.* Although the plaintiffs appeared to push for a re-inspection as soon as possible, the agency noted that it "would be difficult to schedule a re-inspection in January, 2007, as this does not allow for sufficient preparation time." *Id.* Nevertheless, the FDA agreed to "work to schedule the re-inspection as soon as it is possible" after the additional information the plaintiffs' promised the agency in December 2006 was received. *Id.* at 1429.

[redacted] AR at 1416 (Plaintiffs' Minutes of Ranbaxy/FDA Meeting, Nov. 29, 2006).

The FDA conducted its re-inspection between January 26 and February 1, 2007, finding the Paonta Sahib "site acceptable for APIs."[14] AR at 1374 (Memo of Teleconference between FDA and plaintiffs' counsel, Apr. 5, 2007). The plaintiffs admitted in an April 2007 teleconference with the FDA that "Ranbaxy had not yet addressed all of [the FDA's] concerns from the June 2006 Warning Letter," and that the audit of "stability raw laboratory data" was still ongoing. *Id.* at 1375. The FDA informed plaintiffs that until they "reviewed the audit report," which the FDA had requested during the November 2006 meeting, "FDA could not complete its CGMP compliance assessment" necessary to lift the hold on processing the plaintiffs' ANDAs. *See id.*

3. *The Plaintiffs Seek Withdrawal Of FDA's Compliance Hold*

Two days before the plaintiffs' would lose their 180-day generic marketing exclusivity for a drug, tamsulosin hydrochloride—which is not at issue in this litigation—due to the plaintiffs' failure to obtain tentative approval within thirty months of the ANDA's submission, the plaintiffs notified the agency that "the retrospective stability verification promised during the November 29, 2006 meeting between Ranbaxy and FDA has been completed, and that the company's ANDA submissions are being updated today to reflect changes identified in the course of the review." *Id.* at 1371 (Letter from plaintiffs to FDA, June 18, 2007). The plaintiffs averred that with the completion of this retrospective review, the agency should be able to "lift the application hold related to Ranbaxy's finished dosage facility at Paonta Sahib, India" in time to grant tentative approval to the plaintiffs' tamsulosin ANDA so as to preserve the potential for 180-day exclusivity. *Id.* The plaintiffs summarized the review's findings, noting that three categories of errors were found and updates made to correct those errors, but, significantly, "in

[14] "API" stands for "active pharmaceutical ingredients."

no case did the corrections affect the previous conclusions about the stability of the sample." *Id.* at 1373.

Shortly after the submission of the corrections occasioned by the retrospective review, the FDA requested further information, including access to the plaintiffs' consultant's stability verification audit reports. *See id.* at 1366 (Letter from plaintiffs' counsel to FDA, July 27, 2007 referring to "meeting with FDA on June 26, 2007"). In late July 2007, the plaintiffs' counsel provided the reports due to "the importance of resolving the hold," even though they "were initially prepared under privilege." *Id.* The plaintiffs' counsel summarized the reports as showing a tiny proportion of errors discovered during a review of a sample of the plaintiffs' stability tests, and averred that the plaintiffs had "taken exhaustive steps to assure the accuracy of data contained in its stability reports and ANDA submissions." *Id.* at 1370.

At the same time that the plaintiffs were advocating for the FDA to lift the compliance hold on products manufactured at Paonta Sahib, a Federal criminal investigation into the plaintiffs was ongoing. *See id.* at 1362 (Email chain between plaintiffs' counsel and FDA, Dec. 27–28, 2007, referring to "implications for the criminal case of providing the audits"). Despite the FDA's persistent requests to review the audit reports from PAREXEL, the plaintiffs insisted that these audits were privileged and would not be produced. *See id.* The failure to submit the audits resulted in the withdrawal of an ANDA for clarithromycin, a drug for which the plaintiffs did not have 180-day exclusivity but would otherwise have been able to market at the beginning of 2008. *See id.* at 1365. The compliance hold continued. *See id.*

4. *The 2008 Inspection*

Between March 3 and March 7, 2008, FDA inspectors returned to the plaintiffs' facilities in India, this time to inspect a "new" plant, called "the Batamandi plant," which was [redacted]

[redacted] *See* AR at 1316 (Establishment Inspection Report, issued Apr. 16, 2008). The inspection had three goals: (1) [redacted] (2) [redacted] and (3) [redacted][15] *Id.* at 1314. The inspection revealed [redacted] (1) [redacted] (2) [redacted] (3) [redacted]. *Id.* at 1314–15.

In the course of the inspection, the FDA personnel discovered [redacted]. *See id.* at 1336–49. [redacted]. *See id.* at 1349.

Regarding the relationship between the Batamandi plant and the Paonta Sahib plant, the inspectors discovered that [redacted]

[15] The FDA initiated the investigation [redacted] AR at 1307.

[redacted]

Id. at 1351. The inspectors noted that [redacted]

[redacted] *Id.* at 1351. As one inspector was leaving, [redacted] *Id.* at 1353.

In response to the damaging findings from this inspection, the plaintiffs [redacted] *See* AR at 1275 (Letter from plaintiffs to FDA, May 1, 2008); *but see id.* at 1356 (noting that [redacted]). The plaintiffs also admitted that [redacted] *Id.* at 1273. [redacted] *See id.* at 1277.

5. *The 2008 Warning Letter*

Following the 2008 inspection and after reviewing the plaintiffs' response to the inspectors' observations, the FDA issued another Warning Letter to the plaintiffs. AR at 1266 (FDA Warning Letter to plaintiffs, Sept. 16, 2008 (the "2008 Warning Letter")). Similarly to the 2006 Warning Letter, the 2008 Warning Letter alerted the plaintiffs to "significant deviations from U.S. Current Good Manufacturing Practice" at both parts of the Paonta Sahib plant, and that "[t]hese CGMP deviations cause [the plaintiffs'] drug products to be adulterated within the meaning of" the FDCA. *Id.* Since the Batamandi plant was determined to be a mere extension

of the Paonta Sahib facility, not a new, separate facility as the plaintiffs had claimed, "the violations observed during the March 2008 inspection [were] indications of continuing CGMP deficiencies in the quality systems at the Paonta Sahib facility, including the failure of production and quality management to prevent such deficiencies." *Id.*

By 2008, the FDA's inspectors were "concerned that these instances of discrepancies observed during the March 2008 inspection, are indications of continuing, systemic CGMP deficiencies at the Paonta Sahib facility." *Id.* at 1267. For instance, the 2008 Warning Letter opines that the plaintiffs' "response regarding Employee I [who signed off on operations for which he was not present] demonstrates a lack of knowledge by the employee regarding the fundamental purpose of independent verification under CGMP, and the failure of [the plaintiffs] to ensure that employees conducting and recording these checks understood these essential requirements." *Id.* at 1268. Such independent checks are "an essential part of U.S. CGMP regulations" and the failure to perform the checks was cited as an "important example of the necessary steps [the plaintiffs] need to implement to ensure product quality." *Id.*

After detailing multiple instances of deficiencies in the plaintiffs' Paonta Sahib plant's quality systems, the 2008 Warning Letter stated in no uncertain terms that if the plaintiffs "wish to continue to ship [their] products to the United States, it is the responsibility of [the plaintiffs] to assure compliance with all U.S. standards for Current Good Manufacturing Practices." *Id.* at 1270. While the 2006 Warning Letter indicated that the FDA would recommend denial of any applications for drugs manufactured at Paonta Sahib, the 2008 Warning Letter enhanced this sanction by instituting a "refusal of admission" prohibiting the plaintiffs from exporting drugs manufactured at Paonta Sahib to the United states because "the methods and controls used in

their manufacture do not appear to conform to current good manufacturing practice." *Id.* at 1271.[16]

6. *The 2009 Letter*

By 2009, with the criminal investigation proceeding and the FDA's Center for Drug Evaluation and Research ("CDER") still concerned with the plaintiffs' practices, the FDA issued a letter informing the plaintiffs that it had "determined that Ranbaxy Laboratories Limited . . . submitted untrue statements of material fact in abbreviated and new drug applications filed with the Agency." AR at 1254 (Letter from FDA to plaintiffs, Feb. 25, 2009 (the "2009 Letter")). Citing the observations at Paonta Sahib in 2006 and 2008 as well as the responses given by the plaintiffs to those inspections, the agency determined that "[t]hese and other findings indicate a pattern and practice of submitting untrue statements of material fact and other wrongful conduct, which raise significant questions regarding the reliability of the data and information contained in applications (pending and approved) . . . filed with the Agency." *Id.* at 1258. Consequently, the FDA informed the plaintiffs that, pursuant to FDA policy, the agency would begin assessing "the validity of the data and information in all of Ranbaxy's affected applications" and that the FDA did "not intend ordinarily to conduct or to continue its normal substantive scientific review (including review of data and labeling) of any such pending application or supplement, or of any new application or supplemental applications" until the review was complete. *Id.* Among the applications affected by the 2009 Letter were the two ANDAs at issue here: ANDA 77830 (for esomeprazole magnesium) and ANDA 78078 (for valganciclovir hydrochloride). *Id.* at 1263. In

[16] The FDA made an exception for one drug, ganciclovir, because the plaintiffs were "the sole source supplier of Ganciclovir oral capsules" and "FDA considers it important to maintain a sufficient supply of this drug product." AR at 1271. Nevertheless, the plaintiffs were warned that a new arrangement would have to be reached regarding this drug, "which would likely include third-party supervision and verification of each batch prior to release" in order to allow the drug to be exported to the United States. *Id.*

essence, as of February 25, 2009, the FDA had frozen all of the plaintiffs' applications containing data from Paonta Sahib and would take no further steps toward approving those applications until the review of the plaintiffs' data was complete.

7. *The Consent Decree And Criminal Plea*

Three years later, the United States filed a Complaint for Permanent Injunction against the plaintiffs in the U.S. District Court for the District of Maryland. AR at 1232 (Complaint for Permanent Injunction, Case No. 12-cv-250 (JFM), Jan. 25, 2012). On the same date, the plaintiffs and the government filed a consent decree requiring the plaintiffs to, *inter alia*, establish new practices and offices to ensure compliance, AR at 1180–81 (Consent Decree of Permanent Injunction, Case No. 12-cv-250 (JFM), Jan. 25, 2012); withdraw certain ANDAs, *id.* at 1185; submit other ANDAs to new audits, *id.* at 1187–89; and ensure compliance with CGMP at the plaintiffs' Paonta Sahib and Dewas, India facilities, *id.* at 1189–90.[17] The extensive requirements in the Consent Decree supplanted the 2009 Letter's requirements, such that "the provisions of [the] Decree with respect to [the Paonta Sahib] facilities constitute the full requirements that [the plaintiffs] must satisfy to address FDA's concerns." *Id.* at 1224.

Sixteen months later, one of the plaintiffs' subsidiaries, Ranbaxy USA, Inc., pleaded guilty to seven criminal counts of fraud and introduction of adulterated drugs into interstate commerce. *See* Pls.' TRO Reply at 18, ECF No. 28 (referring to guilty plea and stating plaintiffs "paid a very heavy price from which it will take years to recover"). The combination of criminal fines, criminal forfeitures, and a civil settlement levied against the plaintiffs' subsidiary amounted to $500,000,000. U.S. Dep't of Justice, "Generic Drug Manufacturer Ranbaxy Pleads

[17] The agency issued a Warning Letter for the plaintiffs' manufacturing facility at Dewas, India that was similar to one for Paonta Sahib, based on extensive CGMP violations at the former facility. AR at 1513 (FDA Warning Letter to plaintiffs, Sept. 16, 2008).

Guilty and Agrees to Pay $500 Million to Resolve False Claims Allegations, cGMP Violations and False Statements to the FDA," May 13, 2013, *available at* http://www.justice.gov/opa/pr/generic-drug-manufacturer-ranbaxy-pleads-guilty-and-agrees-pay-500-million-resolve-false. As previously noted, this guilty plea was touted as the "largest drug safety settlement" in history. *Id.*

Yet, even this massive fine and the Consent Decree do not appear to have resolved the plaintiffs' compliance problems. Due to newly observed CGMP deficiencies at two of the plaintiffs' other plants in India, the Consent Decree has been expanded and currently "prohibits Ranbaxy from distributing in interstate commerce drug products, including APIs, manufactured at the Paonta Sahib, Dewas, Mohali, and Toansa facilities until Ranbaxy demonstrates its CGMP compliance at those facilities." Defs.' TRO Opp'n at 17.

Having provided context for the FDA's evolving understanding of the breadth and depth of the plaintiffs' compliance failures, culminating in a criminal conviction, an import ban, and hundreds of millions of dollars in fines, the Court now turns to the two ANDAs at issue in this litigation and the errors by the FDA that led to their tentative approval.

D. The Plaintiffs' ANDAs

Five of the plaintiffs' ANDAs affected by the problems at Paonta Sahib are of particular relevance to the instant litigation, including three ANDAs approved in 2007 and 2008, immediately prior to the tentative approval of ANDA 77830 for esomeprazole magnesium, and ANDA 78078 for valganciclovir hydrochloride tablets, which are the two ANDAs at issue here. The three prior ANDAs are addressed first before turning to the two ANDAs at issue in the instant litigation.

1. *Tentative Approval For Three Of The Plaintiffs' ANDAs Despite Compliance Problems At Paonta Sahib*

The AR shows that the plaintiffs received five tentative approvals despite their Paonta Sahib facility failing to comply with CGMP. The first of these ANDA exceptions was the application for tamsulosin, for which the plaintiffs would have forfeited any claim to 180-day exclusivity if they did not obtain tentative approval by June 20, 2007. *See supra* Part I.C.3. Despite the compliance hold preventing any tentative approvals for generic products manufactured as the Paonta Sahib facility, the plaintiffs launched a multi-pronged initiative to get this ANDA approved by approaching two FDA components, CDER and Office of Generic Drugs ("OGD"), with different arguments. *See* AR at 1371. In one approach, the plaintiffs alerted the FDA's CDER component that the stability verification audits the FDA had requested were complete and showed Paonta Sahib was following CGMP, thus negating the need for the compliance hold. *See* AR at 1371. As a second approach, the plaintiffs' counsel threatened the FDA's OGD component with a lawsuit if the agency did not immediately "confirm[] that Ranbaxy will not forfeit on June 20, 2007 its right to 180-day exclusivity." AR at 1868 (Letter from plaintiffs' counsel to FDA's OGD, June 18, 2007).

In a June 18, 2007 letter to the OGD, plaintiffs' counsel raised the same argument the plaintiffs press here: that 21 U.S.C. § 355(j) "does not authorize FDA to withhold tentative approval, and thereby deprive an ANDA applicant of its 180-day exclusivity, based on the adequacy of the methods, facilities, or controls used for the manufacture of the drug product." *Id.* at 1873. The letter left no doubt that if OGD did not grant tentative approval by June 20, 2007, just two days after the date of the letter from the plaintiffs' counsel, the FDA would find itself embroiled in lawsuit because, in the plaintiffs' view, failure to do so "would be arbitrary

and capricious," and because "there is no factual basis" to conclude that the conditions of the 2006 Warning Letter had not been resolved. *See id.* at 1874.

Under this threat of litigation and while CDER was processing the results of the stability studies submitted by the plaintiffs, though without the oft-requested independent audit reports from PAREXEL, *see supra* Part I.C.3, the OGD tentatively approved the plaintiffs' ANDA for tamsulosin. AR at 1858 (OGD Approval Routing Summary). Included in the routing summary for the tentative approval is an email chain from CDER employees to OGD, noting that, [redacted] In other words, the agency's compliance staff apparently believed, [redacted] *See id.* CDER noted that [redacted] *Id.*[18] With this caveat, CDER [redacted] OGD's grant of tentative approval. *Id.* at 1860.

[18] [redacted]

The process by which the FDA considered four more of the plaintiffs' other ANDAs for tentative approval is reminiscent of a child's game of telephone, where the initial message becomes distorted upon repetition. A second ANDA from the plaintiffs, for valsartan, was reactivated by agency staff the day after tentative approval was granted to the tamsulosin ANDA because the plaintiffs were [redacted] AR at 1856 (email chain between FDA employees, June 21–July 10, 2007). Review of this ANDA was, similarly to the ANDA for tamsulosin, urgent, since the plaintiffs would lose their eligibility for the 180-day generic marketing exclusivity if the ANDA were not tentatively approved in short order. An intervening change in the drug's monograph, however, resulted in a several month delay from the OGD's resuming review of the ANDA to its tentative approval. *See id.* at 1854–55.

[redacted] *Id.* at 1858. The defendants have not disputed the plaintiffs' attribution of these titles and others noted by the plaintiff, *see* Pls.' Mem. at 35, with the exception of Ms. Dickinson's title at the time being "Associate Chief Counsel," not "Deputy Chief Counsel," Defs.' Mem. at 8 n.4.

[redacted]

By October 2007, OGD asserted that the [redacted]" *Id.* at 1838 (email chain between Edwin Rivera Martinez and William P. Rickman, Oct. 25, 2007). This rationale never appeared in communications from CDER prior to October 2007 and, indeed, [redacted]. *See generally* AR. Nevertheless, the valsartan ANDA was given tentative approval shortly thereafter. *See id.* at 1834–35 (OGD Approval Routing Summary).

Thus, by late 2007, the FDA had violated its own policy not to grant tentative approval to ANDAs when a compliance hold was in place three times, for the plaintiffs' tamsulosin, galantamine, and valsartan ANDAs. Also, by late 2007, the CDER and OGD employees involved in making these decisions were apparently no longer considering why an exception to the plaintiffs' compliance hold should be granted, but were merely cutting-and-pasting language from previous emails pertaining to other ANDAs recommending that OGD issue tentative approval despite the compliance hold. [redacted]

[redacted]

[redacted] The two ANDAs at issue in this litigation, for esomeprazole and valganciclovir, were issued after this game of telephone had progressed for six months.

2. *The Plaintiffs' Esomeprazole ANDA*

The plaintiffs filed their ANDA for esomeprazole, including their paragraph IV certification, by letter dated August 4, 2005. AR at 1792 (ANDA Checklist for Completeness and Acceptability of an Application). The ANDA was noted as the first generic product application received and was approved for filing as substantially complete on September 30, 2005 by personnel in OGD. *Id.*

[redacted]

[redacted] Based on CDER's recommendation, OGD granted tentative approval for the plaintiff's esomeprazole ANDA 77830, on February 5, 2008, noting [redacted] *Id.* at 1771–72 (OGD Approval Routing Summary).

[19] "OAI" stands for "Official Action Indicated," meaning an intervention from the FDA.

As part of the 2012 Consent Decree, the plaintiffs were required to [redacted] *Id.* at 1768 (letter from FDA to plaintiffs, May 4, 2012 (internal quotation marks omitted)). CDER notified the plaintiffs that the esomeprazole ANDA [redacted] when it was initially filed, allowing the FDA, under the terms of the consent decree, to proceed in its audit of the esomeprazole ANDA. *Id.* at 1769. This audit was designed to determine if the application contained any "untrue statements of material fact" or "a pattern or practice of data irregularities affecting approval," as provided for in the Consent Decree. AR at 1766 (letter from FDA to plaintiffs, Nov. 4, 2014). The plaintiffs were notified on November 4, 2014, that there did not appear to be any "untrue statements of material fact" or "data irregularities" preventing the FDA from resuming its review of the ANDA. *Id.* Since the 2009 Letter and the Consent Decree had frozen all action on any of the plaintiffs' NDAs or ANDAs, completing this audit did not guarantee final approval, but rather allowed the FDA to resume *considering* whether the ANDA was eligible for such approval. *See id.*

3. *The Plaintiffs' Valganciclovir ANDA*

The plaintiffs filed their ANDA for valganciclovir, including their paragraph IV certification, by letter dated December 22, 2005. AR at 1820 (ANDA Checklist for Completeness and Acceptability of an Application). This ANDA, number 78078, was the first generic product application received for this drug and was approved for filing as substantially complete on February 27, 2006. *Id.*

[redacted]

[redacted] *Id.*

[redacted] Based in part on this recommendation, OGD granted the plaintiffs tentative approval for valganciclovir on June 20, 2008. *Id.* at 1807 (OGD Approval Routing Summary).

Pursuant to the 2012 Consent Decree, the ANDA was reviewed and found to have been substantially complete when submitted. *Id.* at 1802–03 (letter from FDA to plaintiffs, May 15,

2012). Also pursuant to the consent decree, the ANDA was audited and found not to "appear to contain any untrue statements of material fact . . . nor does it appear to contain a pattern or practice of data irregularities affecting approval," thus allowing FDA to resume reviewing the ANDA on August 10, 2012. *Id.* at 1798–99 (letter from FDA to plaintiffs, Aug. 10, 2012).

E. The Instant Litigation

Despite the intensive investigation the FDA conducted of the plaintiffs' manufacturing facilities—and the parallel criminal investigation—the FDA did not revisit any of the ANDAs tentatively approved in 2007 and 2008, including the valganciclovir and esomeprazole ANDAs, until 2014. Defs.' Mem. at 37. The Federal defendants explain that "[i]t was only in 2014, when applications from two other sponsors were ready for approval, that FDA had reason to determine whether Ranbaxy was entitled to exclusivity for this drug and, at that time, the agency recognized that Ranbaxy's claim to exclusivity was predicated on an erroneous decision." *Id.* When two other generic drug manufacturers, defendant-intervenors Dr. Reddy's and Endo, sought final approval for their own ANDAs for valganciclovir, the FDA reexamined the two ANDAs at issue here. *See id.* After review, the agency "determined that FDA erred in tentatively approving" the plaintiffs' two ANDAs because tentative approval was granted "while the compliance status of one or more of the facilities referenced in the applications was unacceptable to support tentative approval." Rescission Letter at 1. Consequently, the FDA revoked the tentative approval for the plaintiffs' valganciclovir and esomeprazole ANDAs and determined that the rescission meant the plaintiffs had forfeited any eligibility for 180-day exclusivity for the valganciclovir ANDA by failing to obtain tentative approval within thirty months of the date of the ANDA's submission. *Id.* at 1–2. The same day, November 4, 2014, the agency granted final approval to defendant-intervenors Dr. Reddy's and Endo for their own valganciclovir ANDAs. Compl. ¶ 41.

Ten days later, the plaintiffs filed the instant suit for declaratory and injunctive relief, Compl. at 1, and a motion for a temporary restraining order, ECF No. 2. A hearing on the TRO was held on November 19, 2014, by which time defendant-intervenors Dr. Reddy's and Endo had moved for and been granted leave to intervene. Minute Order, Nov. 17, 2014 (setting hearing date); Minute Order Nov. 17, 2014 (granting defendant-intervenor Endo's Motion to Intervene); Minute Order, Nov. 17, 2014 (granting defendant-intervenor Dr. Reddy's Motion to Intervene).

After oral argument at the November 19, 2014 hearing, the Court denied the plaintiffs' motion for a temporary restraining order "because the plaintiffs have not made a clear showing that this Court has subject matter jurisdiction over this matter or a likelihood of irreparable harm . . . let alone satisfy the other factors for the extraordinary relief of a TRO." Hrg. Tr. 91:20-25, ECF No. 61. Specifically, the plaintiffs had not shown at the time of the November 19, 2014 hearing that the plaintiffs "can take advantage of that [180-day] exclusivity" for valganciclovir that had been rescinded, "or that they will suffer any imminent harm as a result of the loss of that exclusivity." *Id.* 92:21-24. As for the plaintiffs' esomeprazole ANDA, the plaintiffs failed to show "that the FDA has taken any final agency action regarding the plaintiffs' eligibility for 180-day exclusivity," since the Rescission Letter stated that the FDA, "consistent with its longstanding policy . . . 'has not made any determination regarding Ranbaxy's eligibility for 180-day exclusivity for this ANDA.'" *Id.* 93:6-16 (quoting Rescission Letter at 1 n.3).

In light of the plaintiffs' stated intention to move for a preliminary injunction and the proposed briefing schedule submitted by the parties, consideration of the plaintiffs' preliminary injunction motion and the defendants' and defendant-intervenors' motions for summary judgment was consolidated. Minute Order, Nov. 21, 2014 (citing FED. R. CIV. P. 65(a)(2)).

After receiving extensive briefing from the parties, the preliminary injunction hearing was vacated "to conserve the parties' and judicial resources." Minute Order, Jan. 7, 2015 (citing LCvR 7(f)).

After the motions were fully briefed, the defendants notified the Court that FDA had "forfeited its eligibility for 180-day exclusivity for esomeprazole because it failed to obtain tentative approval of its ANDA within 30 months after the date on which the ANDA was submitted" and approved an ANDA filed by defendant-intervenor Ivax for the same medication. Defs.' Not. Admin. Action at 1, ECF No. 67. Three days later, defendant-intervenors Ivax and Teva moved for and were granted leave to intervene. Minute Order, Jan. 30, 2015. Defendant-intervenors Ivax and Teva moved for summary judgment on February 2, 2015, which motion became ripe for decision on February 5, 2015.

II. LEGAL STANDARD[20]

A. Summary Judgment

Pursuant to Federal Rule of Civil Procedure 56, summary judgment may be granted when the court finds, based upon the pleadings, depositions, affidavits, and other factual materials in the record, "that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." FED. R. CIV. P. 56(a), (c); *see Tolan v. Cotton*, 134 S. Ct. 1861, 1866 (2014) (per curiam); *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247 (1986). "A

[20] Although the plaintiffs' motion is one for preliminary injunction, since the Court consolidated consideration of the preliminary injunction motion with the defendants' and defendant-intervenors' motions for summary judgment on the merits, the motions are all properly considered as motions for summary judgment. Pls.' Reply Defs.' Opp'n Pls. Mot. ("Pls. Reply") at 23 n.8, ECF No. 60; *Teva Pharms. USA, Inc. v. FDA*, 441 F.3d 1, 3 (D.C. Cir. 2006) (accepting without comment district court's consideration of consolidated preliminary injunction and summary judgment motions as motions for summary judgment); *Ass'n. of Flight Attendants v. USAir, Inc.*, 24 F.3d 1432, 1436 (D.C. Cir. 1994) (same); *Takeda Pharms., USA v. Burwell*, No. 14-1850, 2015 WL 252806, at *2 n.1 (D.D.C. Jan. 13, 2015) (consolidating consideration of preliminary injunction motion with summary judgment motions and evaluating all motions under summary judgment standard). Thus, the familiar four part test for issuing a preliminary injunction is irrelevant to the resolution of the instant motions.

genuine issue of material fact exists if the evidence, 'viewed in a light most favorable to the nonmoving party,' could support a reasonable jury's verdict for the non-moving party." *Muwekma Ohlone Tribe v. Salazar*, 708 F.3d 209, 215 (D.C. Cir. 2013) (quoting *McCready v. Nicholson*, 465 F.3d 1, 7 (D.C. Cir. 2006)).

In APA cases such as this one, "the district judge sits as an appellate tribunal. The 'entire case' on review is a question of law." *Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1083 (D.C. Cir. 2001) (collecting cases). Accordingly, this Court need not and ought not engage in lengthy fact finding, since "[g]enerally speaking, district courts reviewing agency action under the APA's arbitrary and capricious standard do not resolve factual issues, but operate instead as appellate courts resolving legal questions." *James Madison Ltd. by Hecht v. Ludwig*, 82 F.3d 1085, 1096 (D.C. Cir. 1996); *see also Sierra Club v. Mainella*, 459 F. Supp. 2d 76, 90 (D.D.C. 2006) ("Under the APA . . . 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.") (quotation marks and citation omitted)); *accord McDonough v. Mabus*, 907 F. Supp. 2d 33, 42 (D.D.C. 2012); *Wilson v. McHugh*, 842 F. Supp. 2d 310, 315 (D.D.C. 2012). Judicial review is limited to the administrative record, since it "is black-letter administrative law that in an [Administrative Procedure Act] case, a reviewing court should have before it neither more nor less information than did the agency when it made its decision." *CTS Corp. v. EPA*, 759 F.3d 52, 64 (D.C. Cir. 2014) (internal citations and quotation marks omitted; alteration in original); *see* 5 U.S.C. § 706(2)(F) ("[T]he court shall review the whole record or those parts of it cited by a party . . . ."); *Fla. Power & Light Co. v. Lorion*, 470 U.S. 729, 743 (1985) (in applying the arbitrary and capricious standard under the APA, "[t]he focal point for judicial review should

be the administrative record already in existence . . . ." (quoting *Camp v. Pitts*, 411 U.S. 138, 142 (1973)).

B. *Chevron* Framework

The familiar two-step process set out in *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.* (*Chevron*), 467 U.S. 837, 845 (1984), applies to judicial review of claims that an agency has acted "in excess of statutory jurisdiction, authority or limitations, or short of statutory right" under the APA. *See Am. Fed'n of Gov't Emps. Local 3669 v. Shinseki*, 709 F.3d 29, 33 (D.C. Cir. 2013) (internal quotation marks omitted). At the first step of the inquiry, a court must "ask whether Congress has directly addressed the precise question at issue." *Mayo Found. for Med. Educ. & Research v. United States*, 131 S. Ct. 704, 711 (2011) (internal quotation marks omitted). "'If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress.'" *City of Arlington, Tex. v. FCC*, 133 S. Ct. 1863, 1868 (2013) (quoting *Chevron*, 467 U.S. at 842–43).

On the other hand, if "'Congress has not directly addressed the precise [interpretative] question at issue' . . . the agency is charged with filling the 'gap left open' by the ambiguity." *EPA v. EME Homer City Generation, L.P.* (*EME Homer*), 134 S. Ct. 1584, 1603 (2014) (quoting *Chevron*, 467 U.S. at 843, 866) (first alteration in original). Thus, if the statute is silent or ambiguous with respect to the specific issue under consideration, the analysis shifts to *Chevron* step two, where "the question for the court is whether the agency's answer is based on a permissible construction of the statute." *City of Arlington, Tex.*, 133 S. Ct. at 1868 (internal quotation marks omitted); *see CSX Transp., Inc. v. Nat'l Surface Transp. Bd.*, 754 F.3d 1056, 1063 (D.C. Cir. 2014) (same). The job of the courts is not to engage in "their own interstitial lawmaking" and "mak[e] public policy by prescribing the meaning of ambiguous statutory

commands." *City of Arlington, Tex.*, 133 S. Ct. at 1873 (quoting *Ford Motor Credit Co. v. Milhollin*, 444 U.S. 555, 568 (1980)). Rather, the "archetypal *Chevron* questions, about how best to construe an ambiguous term in light of competing policy interests" belong to the "agencies that administer the statutes." *See id.*

When Congress has delegated to the agency authority to make rules carrying the force of law, and the challenged agency interpretation was promulgated in the exercise of that authority, then the agency's rule is entitled to deference "as long as it is a permissible construction of the statute, even if it differs from how the court would have interpreted the statute in the absence of an agency regulation." *Sebelius v. Auburn Reg'l Med. Ctr.*, 133 S. Ct. 817, 826 (2013); *see also EME Homer*, 134 S. Ct. at 1606 (determining if agency's interpretation of ambiguous phrase is "permissible construction of statute" as second step of *Chevron* analysis); *Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs.* (*Brand X*), 545 U.S. 967, 980 (2005) ("If a statute is ambiguous, and if the implementing agency's construction is reasonable, *Chevron* requires a federal court to accept the agency's construction of the statute, even if the agency's reading differs from what the court believes is the best statutory interpretation."). Courts "routinely accord dispositive effect to an agency's reasonable interpretation of ambiguous statutory language." *EME Homer*, 134 S. Ct. at 1603 (citation omitted). "Deference is appropriate even if the agency's interpretation first appears during litigation, unless the interpretation conflicts with prior interpretations or amounts to nothing more than a convenient litigating position." *Shieldalloy Metallurgical Corp. v. Nuclear Regulatory Comm'n*, 768 F.3d 1205, 1208–09 (D.C. Cir. 2014) (internal quotation marks and citations omitted). A court "need not conclude that the [agency's] interpretation of the [s]tatute is the only one it permissibly could have adopted, or even the interpretation deemed *most* reasonable by the courts," so long as it is reasonable. *Nat'l*

Treasury Emps. Union v. Fed. Labor Relations Auth. (*NTEU*), 754 F.3d 1031, 1042 (D.C. Cir. 2014) (internal quotation marks and citations omitted; emphasis in original).

C. Administrative Procedure Act

Under the APA, a reviewing court shall "hold unlawful and set aside agency action, findings, and conclusions found to be . . . arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," 5 U.S.C. § 706(2)(A), "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right," *id.* § 706(2)(C), or "without observance of procedure required by law," *id.* § 706(2)(D); *see Otis Elevator Co. v. Sec'y of Labor*, 762 F.3d 116, 120–21 (D.C. Cir. 2014) (citing *Fabi Constr. Co. v. Sec'y of Labor*, 370 F.3d 29, 33 (D.C. Cir. 2004)).

In evaluating agency actions under the "arbitrary and capricious" standard, courts "must consider whether the [agency's] decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment." *Marsh v. Ore. Natural Res. Council*, 490 U.S. 360, 378 (1989) (citation and internal quotation marks omitted); *Citizens to Preserve Overton Park, Inc. v. Volpe* (*Overton Park*), 401 U.S. 402, 416 (1971), *overruled on unrelated grounds by Califano v. Sanders*, 430 U.S. 99, 105 (1977); *Blue Ridge Envtl. Def. League v. Nuclear Regulatory Comm'n*, 716 F.3d 183, 195 (D.C. Cir. 2013). The scope of review under this 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.* (*State Farm*), 463 U.S. 29, 43 (1983); *see also Fogo De Chao (Holdings) Inc. v. U.S. Dep't of Homeland Sec.*, 769 F.3d 1127, 1135 (D.C. Cir. 2014) (same) (quoting *Judulang v. Holder*, 132 S. Ct. 476, 483 (2011)); *Agape Church, Inc. v. FCC*, 738 F.3d 397, 408 (D.C. Cir. 2013) (same) (quoting *Cablevision Sys. Corp. v. FCC*, 597 F.3d 1306, 1311 (D.C. Cir. 2010)).

"[T]he arbitrary and capricious standard is 'highly deferential' and 'presumes agency action to be valid[.]'" *Am. Trucking Ass'ns, Inc. v. Fed. Motor Carrier Safety Admin.*, 724 F.3d 243, 245 (D.C. Cir. 2013) (quoting *Am. Wildlands v. Kempthorne*, 530 F.3d 991, 997 (D.C. Cir. 2008)); *Envtl. Def. Fund, Inc. v. Costle*, 657 F.2d 275, 283 (D.C. Cir. 1981) (same). If an agency, however, "failed to provide a reasoned explanation, or where the record belies the agency's conclusion, [the court] must undo its action." *Cnty. of Los Angeles v. Shalala*, 192 F.3d 1005, 1021 (D.C. Cir. 1999) (quoting *BellSouth Corp. v. FCC*, 162 F.3d 1215, 1222 (D.C. Cir. 1999)); *see Select Specialty Hosp.-Bloomington, Inc. v. Burwell*, 757 F.3d 308, 312 (D.C. Cir. 2014) ("[T]here are cases where an agency's failure to state its reasoning or to adopt an intelligible decisional standard is so glaring that we can declare with confidence that the agency action was arbitrary and capricious." (quoting *Checkosky v. SEC*, 23 F.3d 452, 463 (D.C. Cir. 1994) (internal quotation marks omitted; alteration in original)). At the very least, the agency must have reviewed relevant data and articulated a satisfactory explanation establishing a "rational connection between the facts found and the choice made." *State Farm*, 463 U.S. at 43 (internal quotation marks and citation omitted); *EME Homer*, 134 S. Ct. at 1602 (holding that agency "retained discretion to alter its course [under a regulation] provided it gave a reasonable explanation for doing so"); *see also Amerijet Int'l, Inc. v. Pistole*, 753 F.3d 1343, 1350 (D.C. Cir. 2014) ("[A] fundamental requirement of administrative law is that an agency set forth its reasons for decision; an agency's failure to do so constitutes arbitrary and capricious agency action." (internal quotation marks and citation omitted)). "[C]onclusory statements will not do; an agency's statement must be one of *reasoning*." *Amerijet Int'l Inc.*, 753 F.3d at 1350 (internal quotation marks omitted; emphasis in original).

An agency's action is arbitrary and capricious if that action "has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise." *Am. Wildlands*, 530 F.3d at 997–98 (internal quotation marks omitted). While the agency's explanation cannot "run[ ] counter to the evidence," *State Farm*, 463 U.S. at 43, courts should "uphold a decision of less than ideal clarity if the agency's path may reasonably be discerned," *Bowman Transp., Inc. v. Ark.–Best Freight Sys., Inc.*, 419 U.S. 281, 286 (1974).

Furthermore, when "an agency has acted in an area in which it has 'special expertise,' the court must be particularly deferential to [the agency's] determinations." *Sara Lee Corp. v. Am. Bakers Ass'n Ret. Plan*, 512 F. Supp. 2d 32, 37 (D.D.C. 2007) (quoting *Bldg. & Constr. Trades Dep't, AFL–CIO v. Brock*, 838 F.2d 1258, 1266 (D.C. Cir. 1988)). "Deferring as appropriate to the agency's expertise and looking only for 'a rational connection between the facts found and the choice made,'" *Am. Trucking Ass'ns, Inc.*, 724 F.3d at 249 (quoting *State Farm*, 463 U.S. at 43), "we remain ever mindful that in performing 'a searching and careful inquiry into the facts, we do not look at the [agency's] decision as would a scientist, but as a reviewing court exercising our narrowly defined duty of holding agencies to certain minimal standards of rationality.'" *Id.* (quoting *Nat'l Envtl. Dev. Ass'ns Clean Air Project v. EPA*, 686 F.3d 803, 810 (D.C. Cir. 2012)).

III. DISCUSSION

The plaintiffs assert four grounds to invalidate the Federal defendants' decision to rescind the tentative approvals for the plaintiffs' ANDAs for esomeprazole and valganciclovir. First, the plaintiffs argue that the FDA's decision is contrary to the plain text of 21 U.S.C. § 355, which, in the plaintiffs' view, does not authorize the FDA to decline to issue tentative approval for an

ANDA because the facility in which the drug is to be manufactured is out of compliance with CGMP. Pls.' Mem. at 1. Second, the plaintiffs contend that, contrary to the FDA's assertions about making an "error," the agency "consciously adopted [the plaintiffs'] interpretation of the statute when it considered" whether to issue tentative approval to the ANDAs at issue and has now changed its policy. *Id.* at 2. Third, the plaintiffs contend that the FDA has no authority to rescind an ANDA's tentative approval. *Id.* at 3. Finally, the plaintiffs argue that the agency's interpretation of the forfeiture trigger at issue here is contrary to the plain text of the statute. *Id.* at 31. None of these arguments is persuasive for the reasons explained below.[21]

A. The FDA May Condition Tentative Approval On Compliance With CGMP

First, the plaintiffs assert that the Federal defendants' interpretation of the FDCA as allowing them to condition tentative approval of ANDAs on compliance with CGMP is not in accordance with law, and thus violates the APA. *See* Pls.' Mem. at 1. Under the APA, the agency's interpretation of a statute that the agency is tasked with enforcing is subject to the familiar two-step *Chevron* inquiry. *See Chevron*, 467 U.S. at 845. Under the first step, the statute under which the agency purports to act must be examined for ambiguity. *Id.* If Congress has not spoken with clarity as to the precise question at issue in the matter at issue, the analysis moves to *Chevron* step two. Under the second step, assuming the statute is ambiguous, a court must determine if the agency's interpretation of the statute is reasonable. *Id.* In the instant matter, the statutory provision at issue is ambiguous as to whether the agency may condition

[21] The FDA issued its final decision regarding the plaintiffs' eligibility for 180-day exclusivity for the plaintiffs' esomeprazole ANDA on January 26, 2015, after briefing on the instant motions was complete. Defs.' Not. Admin. Action ("Defs.' Not.") at 1, ECF No. 67. The Federal defendants now concede that the plaintiffs' claim regarding the esomeprazole ANDA is ripe for judicial review, and the Court concurs. *Id.* By contrast to the posture of the plaintiffs' claim regarding the esomeprazole ANDA at the time of the TRO hearing, the Court finds that the plaintiffs have alleged a concrete and particularized injury stemming from the agency's rescission of tentative approval for this ANDA and the resulting loss of 180-day exclusivity eligibility, that is both fairly traceable to the defendants' actions and redressable by the relief sought. Accordingly, the plaintiffs have standing to challenge the agency's action. *See Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560-61 (1992).

tentative approval on compliance with CGMP, and the agency's interpretation of the statute is reasonable.

1. *21 U.S.C. § 355(j) Is Ambiguous Regarding CGMP Compliance*

The plaintiffs' submissions fail to make clear whether they are challenging the FDA's position under the first or second step of the *Chevron* analysis. Nevertheless, the arguments raised by the plaintiffs acknowledge the agency's alternative interpretation of 21 U.S.C. § 355(j) and thereby recognize that this provision is ambiguous as to whether the agency may condition the granting of tentative approval on compliance with CGMP at the facility identified in an ANDA for manufacture of the generic drug product. *See, e.g.*, Pls.' Mem. at 25 ("FDA's Letter Decision misinterprets the statutory requirements for obtaining TA"); *id.* at 28 ("FDA's position effectively rewrites the statute"); Pls.' Reply at 4 ("The problem for the defendants is that only Ranbaxy's statutory interpretation fulfills that duty" to "give meaning to every clause and word" (internal quotation marks omitted)). *But see* Pls.' Mem. at 27–28 ("the statute's plain text and structure make clear that FDA cannot lawfully condition the award of [tentative approval] on substantive compliance with ultimate . . . standards for final approval.").

As previously noted, the statutory provision at issue, 21 U.S.C. § 355(j), describes the process by which an ANDA is approved, including the information an ANDA "shall contain," 21 U.S.C. § 355(j)(2)(A), under what circumstances "an application for a drug" may be denied, *id.* § 355(j)(4), and the circumstances under which an applicant's 180-day exclusivity eligibility may be revoked, *id.* § 355(j)(5). The term "tentative approval" appears three times in § 355(j): in § 355(j)(5)(B)(iv)(II)(dd), where the term is defined, in relevant part, as "notification to an applicant . . . that an application under this subsection meets the requirements of paragraph (2)(A), but cannot receive effective approval because the application does not meet the requirements of this subparagraph;" in § 355(j)(5)(D)(i)(I)(bb), where the term appears in the

"failure to market" forfeiture provision to start the clock running on the applicant's duty to obtain final approval; and in § 355(j)(5)(D)(i)(IV), where the term appears in the "failure to obtain tentative approval" within thirty months of the filing of the ANDA.

None of the three subsections that contain the words "tentative approval" expressly state that tentative approval may be conditioned on a manufacturing facility's compliance with CGMP. Only the definition of "tentative approval," in § 355(j)(5)(B)(iv)(II)(dd), references the requirements for granting tentative approval, and that section describes a "notification" to an ANDA applicant that the ANDA "meets the requirements of paragraph [355(j)](2)(A)," which lists the items an ANDA must contain. The statute does not define or describe the precise steps for fulfillment of "meets the requirements."

The only subsection addressing the conditions under which any approval may be denied is 21 U.S.C. § 355(j)(4), which describes eleven conditions that would prevent final approval of an ANDA. The first such finding is that "the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity." 21 U.S.C. § 355(j)(4)(A). This subsection does not reference tentative approval. In short, the statute is utterly silent as to the relationship between CGMP compliance at manufacturing facilities where generic drug products are to be produced and tentative approval, but the statute clearly requires such compliance before final approval may be granted. *See id.*

This conspicuous silence weighs heavily in favor of finding the statute ambiguous as to the circumstances upon which the FDA may condition tentative approval, since absent a specific Congressional command, "silence suggests, instead, that the [agency] has the discretion to fill the consequent statutory gap." *Brand X*, 545 U.S. at 997. Indeed, the D.C. Circuit has held that

Congress' "decision to leave 'a gap for an agency to fill . . . is a delegation of authority to the agency to give meaning to a specific provision of the statute by regulation.'" *Nat'l Mining Ass'n v. Kempthorne*, 512 F.3d 702, 709 (D.C. Cir. 2008) (quoting *Michigan v. EPA*, 268 F.3d 1075, 1082 (D.C. Cir. 2001)) (alteration in original).

This silence does not, as the plaintiffs argue, mean that the statutory text must be read as barring the conditioning of tentative approval on CGMP compliance. Pls.' Mem. at 1; Pls.' Reply at 1. To the contrary, absent any statutory language describing the circumstances under which the agency may decline to issue tentative approval, under the first step of the *Chevron* analysis, the statute is ambiguous. Therefore, the Court moves on to the second step of the *Chevron* analysis, to consider whether the agency's interpretation of the statute is reasonable.

2. *The Agency's Interpretation Is Reasonable*

By regulation, the FDA clearly conditions tentative approval on a finding of compliance with CGMP. Specifically, the regulations require the agency to notify an ANDA applicant that its application is approved "if none of the reasons in [21 C.F.R.] § 314.127 for refusing to approve the [ANDA] applies. The approval becomes effective on the date of the issuance of the agency's approval letter unless the approval letter provides for a delayed effective date." 21 C.F.R. § 314.105(d). Approval letters with "delayed effective date[s are] tentative." *Id.* The cross-referenced section of the agency's regulations lists as a reason for refusing to approve an ANDA that "[t]he methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug product are inadequate to ensure and preserve its identity, strength, quality, and purity." 21 C.F.R. § 314.127(a)(1). Together, these two regulations at 21 C.F.R. §§ 314.105(d) and 314.127(a)(i), require the FDA to reject an ANDA for tentative or final approval if the agency finds that the facility in which the ANDA drug is to be manufactured is not in compliance with CGMP. *See* 21 C.F.R. §§ 314.105(d), § 314.127(a)(1).

The parties do not dispute that the FDA may condition *final* approval of an ANDA on demonstrated compliance with CGMP, nor could they: 21 U.S.C. § 355(j)(4)(A) prohibits the agency from approving an ANDA if the drug is to be manufactured in a facility out of compliance with CGMP. The plaintiffs contend, however, that after the 2003 MMA Amendment to 21 U.S.C. §§ 355(j)(4) and (5), which added the circumstances under which an applicant forfeits its 180-day exclusivity eligibility, Congress implicitly overturned the longstanding FDA practice of requiring demonstrated compliance with CGMP for *tentative* approval, requiring instead only that the ANDA applicant present a plan for a facility where the drug could be manufactured. *See* Pls.' Mem. at 25-26. The plaintiffs root this contention in the alleged difference between two three word phrases, "information to show," and "full description of." *Id.* at 26. Indeed, plaintiffs' counsel even highlighted these two phrases in a Powerpoint slide presented at the TRO hearing to ensure that the Court saw them. *See* Pls.' Resp. to Minute Order Attach. 1 (Pls.' Powerpoint Presentation) at 8, ECF No. 31-1. Even without the visual aids, however, the Court can see that the statutory language the plaintiffs highlight is not the silver bullet the plaintiffs believe it to be.

The plaintiffs' reasoning is that the phrase "information to show" imposes more of a burden on an applicant than the phrase "full description of." In the plaintiffs' view, the statute's use of the phrase "information to show" signals that the requirement is "proof-based," meaning "mere disclosure" is insufficient to satisfy the requirements of § 355(j)(2). Pls.' Mem. at 26. In contrast, the plaintiffs contend that the phrase "full description of" is not "proof-based." *Id.* Thus, for example, when the phrase "information to show" is used, such as in § 355(j)(2)(A)(ii)(I)—which requires ANDA applicants to submit, as part of their applications, "information to show that the active ingredient of the new drug is the same as that of the listed

drug"—the FDA may condition granting tentative approval on the fulfillment of that condition. *Id.* By contrast, when the statute uses the phrase "full description of," such as in § 355(b)(1)(D)—which requires NDA and ANDA applicants to submit, as part of their applications, "a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug"—the plaintiffs contend that the FDA may not condition granting tentative approval on actual compliance with that statutory provision. *See id.*

At the outset, neither phrase "information to show" nor "full description of" is defined in the FDCA. The plaintiffs cite a canon of statutory interpretation that "when the legislature uses certain language in one part of the statute and different language in another, the court assumes different meanings were intended," as support for their contention that conditioning tentative approval on actual compliance with, or fulfillment of, items for which a "full description of" is required in the ANDA is contrary to the statute. Pls.' Mem. at 27 (quoting *Roberts v. Sea-Land Servs., Inc.*, 132 S. Ct. 1350, 1357 n.5 (2012)). Without any support from the statute's legislative history or case law, the plaintiffs baldly assert that any other interpretation "impermissibly conflates the distinctions Congress drew" between the language in § 355(j)(2), the conditions that must be met for the grant of tentative approval, and § 355(j)(4), the conditions that must be met for final approval. Pls.' Mem. at 28.

In essence, the plaintiffs argue that the cross-reference in the definition of tentative approval, in § 355(j)(5)(B)(iv)(II)(dd), to § 355(j)(2)(A), means that the FDA may only condition tentative approval on "the requirements of" that subparagraph. *See* Pls.' Mem. at 26–27. Section 355(j)(4), which describes the eleven findings that would prohibit the FDA from granting final approval, specifically mentions failure to comply with CGMP as a condition that

would prohibit granting such approval. Ergo, in the plaintiffs' view, since § 355(j)(2)(A) requires only "information to show" compliance with CGMP, instead of the actual compliance required by § 355(j)(4), the FDA may not condition a grant of tentative approval on compliance with CGMP at the facility identified as the one where the generic drug will be manufactured. *See id.* at 27-28. The plaintiffs' interpretation would, quite simply, lead to absurd results in at least two ways.

First, the plaintiffs' contention that tentative approval of an ANDA must be granted so long as the ANDA applicant includes *any* description of the methods, facilities, and controls used at the facility where the ANDA drug is to be manufactured cannot be squared with the statutory purpose or text. By the plaintiffs' logic, an applicant could state in its ANDA that it planned to manufacture a generic drug in an outhouse behind the applicant's house using a child's chemistry set, and the FDA would have no power to deny tentative approval to that application on the grounds that the applicant could *never*, as submitted, be granted final approval since the application does not comply with CGMP.

Second, the plaintiffs' argument that tentative approval cannot be conditioned on any circumstance required for final approval, as outlined in § 355(j)(4), unless that circumstance is also contained in § 355(j)(2), which is cross referenced in the definition of tentative approval, would lead to equally absurd results. For example, § 355(j)(4) prohibits the awarding of final approval where the approval of the pioneer drug has been withdrawn, 21 U.S.C. § 355(j)(4)(I), or where the application contains an untrue statement of material fact, *id.* § 355(j)(4)(K). Section 355(j)(2) does not require "information to show" or a "full description of" the reasons why the ANDA does not run afoul of those conditions. *See* 21 U.S.C. § 355(j)(2). By the plaintiffs' logic, therefore, the FDA could not withhold tentative approval of an ANDA even if the FDA

knew it had withdrawn approval for the pioneer drug or that the ANDA contained an untrue statement of material fact. Such a reading of the statute is patently absurd: the plaintiffs cannot argue seriously that the FDA is prevented from denying tentative approval to an ANDA in such circumstances. Yet the interpretation proposed by the plaintiffs would lead inexorably to such a result.

Despite the untenable nature of the plaintiffs' interpretation, they vigorously contend that their interpretation is superior to the FDA's. *See* Pls.' Mem. at 28 ("Any other approach impermissibly conflates the distinctions Congress drew . . ."); Pls.' Reply at 4 (contending that "only Ranbaxy's statutory interpretation fulfills that duty" to "give meaning to every clause and word" in a statute (internal quotation marks omitted)). The Court's role, however, is not to determine if the FDA's interpretation is the *best* interpretation, but rather whether the FDA's interpretation is *reasonable*. *NTEU*, 754 F.3d at 1042 ("We need not conclude that the [agency's] interpretation of the [s]tatute is the only one it permissibly could have adopted or even the interpretation deemed *most* reasonable by the courts. On the contrary, we defer to an agency's interpretation of a statute so long as it is reasonable.") (internal quotation marks and citations omitted; emphasis in original); *see also Novartis Pharm. Corp. v. Leavitt*, 435 F.3d 344, 349 (D.C. Cir. 2006) ("We have held on a number of occasions that FDA interpretations of the FDCA receive deference, as do its interpretations of its own regulations unless plainly erroneous or inconsistent with the regulations."). The FDA's interpretation of § 355(j) as allowing it to withhold tentative approval based on non-compliance with CGMP is a reasonable one. *See* Defs.' Mem. at 1.

The FDA relies on four interrelated subsections of the FDCA to show that the agency's interpretation follows directly from the text of the FDCA: 21 U.S.C.

§ 355(j)(5)(B)(iv)(II)(dd)(AA); 21 U.S.C. § 355(j)(2)(A); 21 U.S.C. § 355(b)(1)(D); and 21 U.S.C. § 355(j)(4). *See* Defs.' Mem. at 24-26. In 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA), the FDCA defines tentative approval as "notification to an applicant by the Secretary that an application under this subsection meets the requirements of [21 U.S.C. § 355(j)(2)(A)], but cannot receive effective approval because the application does not meet the requirements of this subparagraph," referring to the FDCA's section regarding 180-day exclusivity eligibility based on paragraph IV certification. The FDA interprets this clause, including the use of the word "because," as requiring the agency to grant *tentative* approval, instead of *final* approval, to an ANDA when the only reasons preventing final approval from being granted is "a stay, some form of exclusivity, or existing patents." Defs.' Mem. at 26. The FDA interprets § 355(j)(2) as containing all of the requirements for an application to be substantially complete and § 355(j)(4) as the requirements for an application to be granted final approval. *See id.* at 24. In other words, in the FDA's view, the requirements for tentative and final approval are identical, except that tentative approval does not require a showing that the ANDA will not infringe upon any valid patent. Thus, the FDA must withhold tentative approval for the same reasons it must withhold final approval, including a lack of CGMP compliance. *See* 21 U.S.C. § 355(j)(4)(A). This is a reasonable interpretation of the statutory text.[22]

[22] The plaintiffs contend that the Federal defendants should be estopped from arguing that the FDCA's use of the word "because" in 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA) denotes an exhaustive list of conditions. Pls.' Reply at 4–5. According to the plaintiffs, the FDA "has taken—and prevailed in court on—precisely the opposite position with respect to the FDCA's other causation requirement, which arises in this same context." *Id*. at 5. The plaintiffs cite *Mylan Laboratories Ltd. v. U.S. Food and Drug Administration* (*Mylan Labs*), 910 F. Supp. 2d 299 (D.D.C. 2012) for this contention, Pls.' Reply at 5, but the position taken by the Federal defendants in that case is the same as the Federal defendants' position in this one. In *Mylan Labs*, the clause at issue provides for the forfeiture of 180-day exclusivity eligibility when an ANDA applicant fails to obtain tentative approval within thirty months of filing the ANDA "unless the failure is *caused by* a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed." 21 U.S.C. § 355(j)(5)(D)(i)(IV) (emphasis supplied); *Mylan Labs*, 910 F. Supp. 2d at 302. The FDA's interpretation of this clause, as explained in *Mylan Labs*, was that an applicant must "show that one or more issues holding up tentative approval at the 30 month date [was] causally connected to approval requirements that FDA reviewed or changed." *Mylan Labs.* 910 F. Supp. 2d at 302 (internal quotation marks and citation omitted). The FDA stated in *Mylan Labs*, however, that "[b]ut-for causation is not

Consequently, under step two of the *Chevron* analysis, the FDA's interpretation of the FDCA as allowing the agency to condition tentative approval on a showing that the facility in which the drug is slated for manufacture complies with CGMP is a reasonable one and entitled to deference. This does not, however, end the inquiry. In addition to challenging the FDA's interpretation of the FDCA, the plaintiffs also challenge whether the FDA changed its policy of conditioning tentative approval on compliance with CGMP at the facility where the drug was to be manufactured after the plaintiffs raised a challenged to the policy in its letter of June 18, 2007. *See* Pls.' Mem. at 33.

B. The FDA Did Not Change Its Policy Regarding Tentative Approval

The parties do not dispute that at the time the FDA granted tentative approval to the plaintiffs' two ANDAs, for esomeprazole and valganciclovir, the facilities in India where those generic drug products were to be manufactured were out of compliance with CGMP. Pls.' Mem. at 33 ("[T]he Agency was fully aware of, and indeed carefully considered, [the plaintiffs'] compliance problems before it issued these [tentative approvals] in 2008"); Defs.' Mem. at 16-17. As a consequence, the FDA admits that granting tentative approval to the two ANDAs at

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required to meet this exception," meaning that the "applicant need only show that acceptability of one aspect of the ANDA (e.g. chemistry) was delayed due to a change in or review of the requirements for approval, irrespective of what other elements may have been outstanding at the 30-month date." *Id.* The plaintiffs argue that the phrase "is caused by," in 21 U.S.C. § 355(j)(5)(D)(i)(IV), is "materially indistinguishable" from the word "because" in the definition of tentative approval and, therefore, the use of "because" in 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA) similarly does not limit the listed reasons for tentative approval. Pls.' Reply at 5. The Court agrees that the word "because" and the phrase "caused by" are "materially indistinguishable" in this context, but disagrees with the plaintiffs' conclusion that the Federal defendants' positions are inconsistent. The FDA interprets the language in both statutory provisions as setting forth necessary and sufficient conditions. In 21 U.S.C. § 355(j)(5)(D)(i)(IV), the FDA interprets the 30-month forfeiture trigger as being tolled if (1) there is "a change in . . . requirements for approval of the application," and (2) tentative approval could not be granted as a result of that change. *See Mylan Labs*, 910 F. Supp. 2d at 302. In 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA), the FDA interprets the statute to require an ANDA (1) meet all the requirements for final approval and (2) be ineligible for final approval by virtue of a blocking patent or other statutory bar. Defs.' Mem. at 26. In both instances, the circumstance listed in the statute immediately after "because" or "caused by," i.e., the presence of a blocking patent or a change in requirements, must be present and must be sufficient, standing alone, to prevent the preceding statutory clause from taking effect, i.e., forfeiture of 180-day exclusivity eligibility or the 30-month forfeiture trigger. Thus, the FDA's reading of both statutory provisions is consistent.

issue was an error, which the Federal defendants attribute to a breakdown in communications between CDER, the compliance inspection component of the FDA, and OGD, the approval component of the FDA. Defs.' Mem. at 14-16. The plaintiffs dispute this characterization, contending that the FDA consciously changed its policy as a result of the plaintiffs' legal arguments. Pls.' Mem. at 34.

At the TRO hearing, before the filing of the AR, the Court observed that "the record is decidedly cloudy on this assertion." Hrg. Tr. 101:21-22. The plaintiffs stress that whether the FDA erred or changed a long-standing policy matters, noting that "the power to correct inadvertent ministerial errors may not be used as a guise for changing previous decisions because the wisdom of those decisions appears doubtful in light of changing policies." Pls.' Mem. at 36 (quoting *Am. Trucking Ass'ns v. Frisco Transp. Co.*, 358 U.S. 133, 146 (1958)). The Court concurs with the long-standing principle articulated by the plaintiffs but, upon review of the full administrative record, concludes that documentation of intra-agency communications supports the Federal defendants' view that miscommunication and, bluntly, a rushed and ill-considered process, led to the erroneous issuance of tentative approval to the ANDAs in dispute *despite* the existence of a clear policy against such issuance.

First, the circumstances under which the OGD granted tentative approval to the plaintiffs' ANDAs in 2007 and 2008 belies the plaintiffs' assertion that a policy change had occurred. The AR contains documentary evidence of personnel within OGD, specifically OGD Deputy Director Robert West,[23] asking CDER for a recommendation to grant tentative approval to each of the plaintiffs' ANDAs even though the plaintiffs had failed to address the FDA's concerns in the 2006 Warning Letter. AR at 1786; *id.* at 1814; *id.* at 1847; *id.* at 1856; *id.* at 1859. These

[23] As previously noted, due to the lack of clarity in the AR, the titles for individual FDA employees at the relevant time period are derived from the plaintiffs' memorandum in support of its preliminary injunction. Pls.' Mem. at 35.

documented requests to deviate from policy and grant tentative approval to the plaintiffs'ANDAs is a clear indication that no policy change had occurred to cease requiring CGMP compliance before granting tentative approval. Had such a policy change occurred, there would have been no need for Mr. West to seek CDER recommendations each time.

Second, although the plaintiffs assert that "***at least*** 21 different officials," including high-level FDA officials, "personally were involved in the decision to issue these TAs despite their awareness of [the plaintiffs'] compliance issues," Pls.' Mem. at 34 (emphasis in original), that assertion is not supported by the AR. For instance, the plaintiffs contend that Elizabeth Dickinson, the Associate Chief Counsel in the Office of the FDA Commissioner, was one of those FDA leaders "personally . . . involved" in the decision to grant the plaintiff tentative approval for an ANDA despite non-compliance with CGMP. Pls.' Mem. at 35. As grounds for this contention the plaintiffs rely upon their former counsel's declaration stating that she had explained the plaintiffs' "situation and [the plaintiffs'] interpretation of the MMA's new definition of TA. [Ms. Dickinson] asked [the plaintiffs' counsel] to memorialize [the plaintiffs'] legal position in a letter to Gary Buehler, the Director of OGD, with a copy to her." Decl. of Kate C. Beardsley ("Beardsley Decl.") ¶ 10, ECF No. 40-4.

The AR contains no record of this phone call, although a letter from the plaintiffs' former counsel to Mr. Buehler, with a copy to Ms. Dickinson, does appear in the AR. AR at 1868-75. The presence of this letter in the AR, listing Ms. Dickinson as the recipient of a copy, may indicate that Ms. Dickinson may have received the letter, but falls far short of demonstrating that she accepted the rationale outlined in it. As another example, the plaintiffs list every official appearing in the "cc" line of an email chain between FDA employees as having participated in this alleged policy change, even though many of those employees authored no part of the email

chain. *See* Pls.' Mem. at 35 (listing, *inter alia*, John Dietrick, Shawnte Adams and Theresa Liu as among the officials to "personally" review the decision to issue tentative approval, citing AR 1782-87); AR 1782-87 (showing John Dietrick, Shawnte Adams and Theresa Liu in "cc" line of email without authoring any portion of email chain). The AR simply does not contain evidence of extensive, substantive discussion among more than twenty high-ranking FDA officials, as the plaintiffs characterize the record, *see* Pls.' Mem. at 34, regarding the plaintiffs' ANDAs. The AR also does not contain any indication that the FDA ever adopted the plaintiffs' argument expressed in June 2007 that the FDA could not condition tentative approval on CGMP, nor do the plaintiffs point to any portion of the AR aside from its own letter to the agency as support for this contention.

[redacted] After this initial determination—which was made on an accelerated basis under the threat of litigation from the plaintiffs—the record is bare that any further analysis was undertaken by the FDA regarding whether CGMP compliance was an appropriate condition for tentative approval. *See generally* AR. [redacted]

[redacted]

The slipshod nature of this approval process, especially considering the long-existing policy in place designed to prevent approval of applications for drugs manufactured in non-CGMP compliant facilities, is disturbing. *See* Tr. 45:17-21 (questioning from the Court regarding what steps, if any, had been taken to hold accountable the FDA staff responsible for the errors). Yet, despite the plaintiffs' contrary interpretation, the fact that the officials involved consistently had to ask recommendations to deviate from established policy; the lack of evidence in the record of any other generic drug manufacturer receiving tentative approval absent a showing of compliance with CGMP; and the obvious confusion within CDER regarding why it was deviating from policy make clear that the FDA did not change its policy. Instead, a rushed and confused approval process, conducted with lackadaisical regard for an important public health policy, contributed to an error that took the FDA more than six years to discover. Such a consistent failure of policies and procedures is stunning, but it does not indicate a change in policy. The Court finds that the FDA did not alter its policy regarding conditioning tentative approval on CGMP compliance and, instead, clearly erred when it tentatively approved the plaintiffs' ANDAs for esomeprazole and valganciclovir.

C. The FDA's Rescission Of Tentative Approval For Plaintiffs' ANDAs Was An Appropriate Exercise Of The FDA's Inherent Authority

Even assuming an error had been made, the plaintiffs nevertheless contend that the FDA's rescission of tentative approval for the plaintiffs' ANDAs was contrary to law in violation of the APA for two reasons. First, the plaintiffs argue that the FDA lacks *any* authority to

rescind tentative approval. Pls.' Reply at 12. Second, the plaintiffs posit that if the FDA has such authority, its exercise of that authority regarding the plaintiffs' ANDAs was unauthorized. *Id.* at 13. Neither argument is persuasive.

1. *The FDA Has The Inherent Authority To Rescind Tentative Approval*

The plaintiffs' contention that the FDA cannot rescind tentative approval at all rests on a statutory construction that elevates form over substance to the detriment of the statutory scheme and purpose. Initially, the plaintiffs contend that because the statute provides for the rescission of *final* approval in a number of circumstances, *see* 21 U.S.C. § 355(e), the absence of a specific mechanism for the rescission of tentative approval indicates that Congress did not intend to provide for one, Pls.' Reply at 12.[24] The plaintiffs cobble together this interpretation from two inapposite court decisions.

First, the plaintiffs rely on *New York v. FERC*, 535 U.S. 1, 18 (2002), for the proposition that "an agency literally has no power to act . . . unless and until Congress confers power upon

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[24] Section 355(e) provides, in pertinent part, that "[t]he Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds" one of five conditions to have occurred. 21 U.S.C. § 355(e). The subsection further provides that the Secretary "may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) of this section" when certain other conditions are found, including

> that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

Id. The D.C. Circuit has described this subsection as applying to tentative approvals as well as final approvals by mentioning more than one form of approval to which § 355(e) applies. *See Mylan Labs. v. Thompson*, 389 F.3d 1272, 1281 (D.C. Cir. 2004) ("[S]ection 355(e) simply sets out specific, not necessarily exclusive, circumstances under which the FDA must withdraw any ANDA approval (*whether final or otherwise*) after notice and hearing." (emphasis supplied)). The parties are unanimous in asserting that the Circuit's discussion of this subsection is *dicta* and that the reference to "approval" in § 355(e) means only final approval. *See* Pls.' Mem. at 38 ("Every party to this case . . . agrees that section 355(e) applies only to final approvals"); Defs.' Mem. at 35 ("Section 355(e) does not apply to rescission of tentative approvals"). Absent an assertion from any party that the agency's interpretation of § 355(e) is in error, and the briefing that would accompany such an assertion, the Court assumes, without deciding, that the provisions in § 355(e) do not apply to the agency's ability to rescind tentative approval.

it." Pls. Mem. at 40. That case addressed a federal agency's power to preempt state regulations, as is evident from the full quotation cherry-picked by the plaintiffs: "*[A] federal agency may pre-empt state law only when and if it is acting within the scope of its congressionally delegated authority . . . [for]* an agency literally has no power to act, *let alone pre-empt the validly enacted legislation of a sovereign State*, unless and until Congress confers power upon it." 535 U.S. at 18 (emphasis indicates words omitted in plaintiffs' brief). In context, *New York v. FERC* stands for the unsurprising principle that federal agencies may not preempt state law unless Congress has explicitly authorized them to do so. *See id.* Preemption is simply not at issue here and, consequently, the FERC has no bearing on whether the FDA has inherent authority to rectify regulatory errors in furtherance of the FDCA's comprehensive scheme for the federal government to ensure the safety of drugs in interstate commerce and to "supplement the protection for consumers already provided by state regulation and common-law liability." *Wyeth v. Levine*, 555 U.S. 555, 566 (2009).

The other case relied upon by the plaintiffs, *North Carolina v. EPA*, 531 F.3d 896, 922 (D.C. Cir. 2008), is similarly inapposite. The plaintiffs quote *North Carolina* for the proposition that the EPA "is 'a creature of statute,' and has 'only those authorities conferred upon it by Congress'; 'if there is no statute conferring authority, a federal agency has none.'" Pls.' Mem. at 40; Pls.' Reply at 12. *North Carolina* involved the EPA's attempt to redistribute emissions credits among states under the Clean Air Act. *North Carolina*, 531 F.3d at 920. In that case, the D.C. Circuit found that the agency's exercise of inherent authority was contrary to the statute's limited goals since the agency purported to create an entirely new emissions control scheme. *See id.* *North Carolina* said nothing about an agency's ability to correct its own errors. Rather, *North Carolina* stands for the principle that an agency cannot unilaterally expand the scope of a

limited statute. *See id.* In the instant matter, the FDA is not expanding the scope of the FDCA, but exercising its inherent authority to ensure the FDCA's statutory purpose is followed by correcting its own admitted error. In sum, the two primary cases cited by the plaintiffs for the assertion that the FDA has no power to correct its mistakes are inapposite and the Court rejects the argument.[25]

Indeed, the D.C. Circuit recently reaffirmed federal agencies' inherent authority to reconsider and correct their own mistakes in *Ivy Sports Medicine, LLC v. Burwell* (*Ivy Sports*), 767 F.3d 81, 86 (D.C. Cir. 2014). In that case, the D.C. Circuit recognized its long held principle that "administrative agencies are assumed to possess at least some inherent authority to revisit their prior decisions, at least if done in a timely fashion." *Id.* The D.C. Circuit found, however, that the FDA lacked the authority to rescind a previous classification of a medical device—in order to reclassify the device—since Congress had established a statutory mechanism for reclassifying such devices that would be subverted by the mechanism employed by the agency. *See id.* at 87. In the instant matter, the parties do not dispute that Congress has not provided an exclusive statutory mechanism for the rescission of tentative approval, such as that provided for final approvals. 21 U.S.C. § 355(e); Pls.' Reply at 12 n.4 ("All parties, however, agree that

[25] In a string of citations, the plaintiffs also assert that *United States v. Seatrain Lines, Inc.*, 329 U.S. 424, 432–33 (1947), and *Civil Aeronautics Board v. Delta Air Lines, Inc.*, 367 U.S. 316, 333–34 (1961), support their contention that an agency may not revoke a prior decision unless explicitly authorized to do so by statute. Pls.' Mem. at 40–41. In *Seatrain Lines, Inc.*, the Supreme Court found that the agency's decision was a change in policy, not an inadvertent error, and, consequently, the Commission could not reopen proceedings to "correct a mere clerical error," 329 U.S. at 428–29, a situation that is decidedly not present here, *see supra* Part III.B. Additionally, in *Seatrain Lines, Inc.*, the agency had a specific statutory mechanism to review and revise certain decisions within a set period of time. *Seatrain Lines, Inc.* at 432–33. Unsurprisingly, the Supreme Court found that when Congress has set forth a specific mechanism to review and revoke previous decisions, the agency may not rely on its inherent authority to act outside of the authority Congress has inferred. *Id.* Similarly, in *Delta Air Lines, Inc.*, the Supreme Court reiterated that an agency "must follow the procedures 'specifically authorized' by Congress and cannot rely on their own notions of implied powers." *Delta Air Lines, Inc.*, 367 U.S. at 334. In the instant matter, the parties agree that the statute does not contain any set procedure for revoking tentative approval. *See supra* note 24. Consequently, *Seatrain Lines, Inc.* and *Delta Air Lines, Inc.* are inapposite.

section 355(e) applies only to final approvals.").[26] Thus, the FDA has the inherent authority to revisit its own decisions, since "the power to reconsider is inherent in the power to decide." *Ivy Sports*, 767 F.3d at 86 (internal quotation marks omitted).

2. *The Rescission Of The Plaintiffs' Tentative Approvals Was A Reasonable Exercise Of The FDA's Inherent Authority*

The plaintiffs' fallback position—that the FDA exceeded its inherent authority by failing to rescind the tentative approvals at issue in a timely manner, Pls.' Mem. at 37-38—is more troubling, but still does not save the plaintiffs' case. At first glance, the FDA's description as "timely" of its reconsideration and rescission of tentative approvals more than six years after those approvals were granted strains credulity. Yet, the unique circumstances of this case render the FDA's lengthy delay in correcting its error by rescinding tentative approval for the ANDAs at issue is more understandable, even if the delay is extraordinary.

The FDA was stymied at nearly every turn by the plaintiffs in the agency's attempt to discover the extent of CGMP violations at the Paonta Sahib facility. As previously noted, it took over a year for the plaintiffs to turn over audit reports that the FDA had made clear were needed to complete a review of the plaintiffs' compliance with CGMP. *See supra* Part I.C.3. The initial summaries the plaintiffs did turn over deceived the FDA into believing that all of the issues identified in the 2006 Warning Letter were resolved. AR at 1859 [redacted] The compliance hold was not lifted, however, and, in 2008, the FDA discovered the problems at Paonta Sahib were unresolved and systemic. *See generally* 2008 Warning Letter.

[26] As previously noted, the parties' position that § 355(e) applies only to final approvals is open to dispute, *supra* note 24, but the parties' failure to engage this issue despite the Court's invitation, *see* Pls. Reply at 12 n.4, renders a decision on this point unnecessary to resolve the instant motions.

By 2009, the FDA had stopped processing the plaintiffs' applications, including the two ANDAs at issue here, as a penalty for the plaintiffs' failure to address the problems at Paonta Sahib and Dewas. *See* 2009 Letter at 1258 ("[T]he Agency does not intend ordinarily to conduct or to continue its normal substantive scientific review (including review of data and labeling) of any such pending application or supplement, or of any new application or supplemental applications . . . that contain data developed at the Paonta Sahib site . . . .").

The FDA froze all of the plaintiffs' applications, including the ANDAs at issue in this suit, until 2014, first as a result of the plaintiffs' own recalcitrance in providing audit reports, then as a result of the 2009 Letter, the subsequent consent decree and criminal charges, and additional reviews. When the FDA finally resumed reviewing the plaintiffs' ANDAs, the FDA did so with the information unavailable when the tentative approvals were issued in 2008—namely, the full picture of the plaintiffs' compliance problems developed over the intervening years.

The plaintiffs argue that an agency's inherent authority to correct its own errors is fleeting, and must be exercised "in weeks, not years." Pls.' Mem. at 37 (quoting *Mazaleski v. Treusdell*, 562 F.2d 701, 720 (D.C. Cir. 1977)). *Mazaleski* does state that the time in which an agency could reconsider its decision and rescind it "would be measured in weeks, not years," but the D.C. Circuit acknowledged that such a time period was appropriate "absent unusual circumstances." *Mazaleski*, 562 F.2d at 720. The agency error considered in *Mazaleski* was the agency's failure to provide the specific reasons for an employee's termination, as required by applicable procedures. *Id*. at 718. After the terminated employee filed suit in federal court, the agency provided those reasons and sought to excuse the belated compliance with procedures because the lapse "was fully rectified by this corrective action." *Id.* The D.C. Circuit did not

accept this excuse, insisting that the agency "afford [the employee] the opportunity of prosecuting his administrative appeal once again. In the event that this appeal ultimately proves unsuccessful, [the employee] must be permitted his day in court . . . ." *Id.* at 722. Thus, the D.C. Circuit's rationale for remanding *Mazaleski* to the agency was rooted in a desire to ensure adequate consideration at the administrative level before judicial review. *See id.*

The instant case differs from *Mazaleski* in at least two crucial respects. First, no evidence was presented in *Mazaleski* that the employee affirmatively interfered with the agency's ability to recognize and rectify its error. By contrast, in the instant case, the plaintiffs failed to provide the requested audit reports to the FDA and also concealed the extent of their non-compliance with CGMP to such an extent that the plaintiffs were eventually held criminally liable. Hence, although the D.C. Circuit did not detail the type of "unusual circumstances" that would excuse a corrective action occurring more than a period of "weeks" after the original decision, this Court believes that the instant matter qualifies for such an exception, particularly in light of the public safety risks presented by disallowing the FDA from correcting its mistakes in approving a generic drug product.

Second, in *Mazaleski*, the terminated employee's circumstances had changed dramatically by the time the agency attempted to rectify its error: he had been terminated and filed suit in federal court. *See Mazaleski*, 562 F.2d at 718. By contrast, the plaintiffs in this case were in the identical position when the tentative approvals at issue were granted as when they were rescinded: the blocking patents had not expired. Indeed, even if the tentative approvals had remained in place, the plaintiffs would have been unable to obtain final approval to market the drugs due to the compliance holds that persist on the plaintiffs' manufacturing facilities in India. Defs.' TRO Opp'n at 17. The plaintiffs contend that they are harmed by the rescissions even

though they are not able to market the generic drug products at issue because they should be able to monetize their 180-day exclusivity rights by receiving payment from their potential competitors, including the pioneer drug maker, to abstain from exercising that right. *See* Pls.' Mem. at 5. This argument bolsters the Federal defendants' position and undermines that of the plaintiffs.

The plaintiffs' asserted harm—that the rescission of tentative approval for their ANDAs prevents them from excluding generic competitors from the market, *see id.*—is the exact situation the MMA Amendment was designed to prevent, *see supra* Part I.A.3. Indeed, the Hatch-Waxman framework and its subsequent amendments were designed to *prevent* first ANDA applicants from creating a "bottleneck" and stop low-cost generic drugs from reaching the market. *See id.* In particular, the MMA Amendment was designed to eliminate "parking" exclusivity rights and to speed generic drugs' progress to market. *See id.* The plaintiffs' interpretation of the FDCA as supporting the plaintiffs' "right" to exclude competitors and keep a generic drug off the market is directly contrary to the intent of Congress and, as such, is rejected. Consequently, since the plaintiffs were not able to market their drugs when the tentative approvals were rescinded, the plaintiffs' position had not materially changed.

* * *

In sum, the FDA should have recognized its errors earlier, but its failure to do so was caused in substantial part by the plaintiffs' own malfeasance to which they eventually pleaded guilty criminally and paid $500 million in fines. Such a set of circumstances qualifies as "unusual" within the meaning of *Mazaleski*, since following that case's "weeks, not years" maxim in this case would lead to the incongruous result of allowing the plaintiffs to benefit from

their own misdeeds. Such a result is not mandated by case law or the statute. The FDA acted within its inherent authority to rescind its tentative approval of the plaintiffs' ANDAs.

D. The FDA's Interpretation Of The 30-Month Forfeiture Trigger Is Reasonable

The plaintiffs' final argument is that the FDA's interpretation of the 30-month forfeiture trigger for a first ANDA applicant's 180-day exclusivity eligibility is contrary to law since tentative approval is an "historical fact . . . established for all time" and, therefore, cannot be rescinded. Pls.' Mem. at 33. Since the question is one of interpretation of the forfeiture trigger found in 21 U.S.C. § 355(j)(5)(D)(i)(IV), the FDA's interpretation is due deference under *Chevron* so long as the statute is ambiguous and the FDA's interpretation is reasonable. The FDA has no trouble meeting both prongs of the *Chevron* test here.

1. *The Forfeiture Trigger Is Ambiguous*

21 U.S.C. § 355(j)(5)(D)(i)(IV) defines one of the six forfeiture triggers as the failure of an ANDA applicant otherwise eligible for 180-day exclusivity "to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed." As previously noted, "tentative approval" is defined as "notification to an applicant by the Secretary that an application under this subsection meets the requirements of" § 355(j)(2)(A), but "cannot receive effective approval" because of blocking patents or statutory exclusivity.
21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA). The statute does not define "notification," *id.*, nor does the statute say anything about whether a "notification," once given, may never be withdrawn by the agency or whether the rescission of tentative approval nullifies a previous notification and causes a retroactive forfeiture of 180-day exclusivity. *See* generally 21 U.S.C.

§ 355. Indeed, although the plaintiffs state that "the statute's plain language and structure foreclose FDA's assertion that [the plaintiffs'] constructively failed to obtain [tentative approval] within the statutory deadline," Pls.' Mem. at 33, the plaintiffs rely only on statutory silence regarding the possible retroactive effect of tentative approval rescission for their contention that the statute is unambiguous, *see id.* at 32. As previously noted, statutory silence weighs strongly *in favor* of finding that a statute is ambiguous and the Court, consequently, finds the FDCA ambiguous here. Thus, the Court must move on to *Chevron*'s second step.

2. *FDA's Interpretation Is Reasonable*

The plaintiffs interpret "notification" of tentative approval as a one-time matter of historical fact. Pls.' Mem. at 32-33. The plaintiffs contrast tentative approval with final approval, which the plaintiffs contend "is a continuing status" that may be revoked "[i]f its requirements cease to be met . . . that is why Congress empowered FDA to rescind it." *Id.* at 32. In other words, according to the plaintiffs, the FDA's sending of a letter notifying the applicant that an ANDA was tentatively approved prior to the 30 month deadline imposed by the forfeiture trigger is sufficient to preserve potential 180-day exclusivity rights, no matter what happens subsequently. The FDA asserts an alternative interpretation that "forfeiture under section 355(j)(5)(D)(i)(IV) is avoided only when a tentative approval is valid," and the issuance of an invalid notification does not prevent forfeiture. Defs.' Mem. at 40.

The two interpretations may both be colorable, but the FDA's interpretation will be credited so long as it is reasonable. *NTEU*, 754 F.3d at 1042. The FDA's interpretation here does not, as the plaintiffs assert, add a "gloss on the statute that is not found in the text." Pls.' Reply at 10 (quoting *Kloeckner v. Solis*, 133 S. Ct. 596, 606 (2012)). Instead, the agency merely reads the forfeiture trigger in the context of the larger statute and interprets the forfeiture trigger accordingly. *See FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000) ("It is a

'fundamental canon of statutory construction that the words of a statute must be read in their context and with a view to their place in the overall statutory scheme.'" (quoting *Davis v. Mich. Dep't of Treasury*, 489 U.S. 803, 809 (1989)).

The Hatch-Waxman Amendments, in general, and the MMA Amendment, in particular, are designed to speed generic drugs to market. *See supra* Part I.A. The forfeiture triggers were written into the statute to prevent first applicants from "parking" their rights by failing to act on their applications, either due to a monetary "pay-to-delay" settlement or for other reasons. *See* 149 Cong. Rec. S15746 (Statement of Sen. Schumer) (noting purpose of amendments was to "ensure that the 180-day exclusivity period enjoyed by the first generic to challenge a patent cannot be used as a bottleneck to prevent additional generic competition."). The FDA's interpretation of the statute as allowing the retroactive forfeiture of exclusivity if tentative approval is later rescinded is entirely in keeping with this Congressional goal and the larger Hatch-Waxman goal of streamlining generic drug approvals to allow safe, effective generic drugs to reach the market sooner.

As the Court noted at the temporary restraining order hearing, reading the forfeiture trigger as the plaintiffs' suggest "elevates form over substance and would lead to absurd results." Hrg. Tr. 106:6-7. If forfeiture for failure to obtain tentative approval could not be triggered retroactively, any ANDA later discovered to be deficient would still prevent other manufacturers from entering the market, even though, as is the case in the instant matter, the ANDA should never have been granted tentative approval in the first instance. Such a scheme would create a perverse incentive to pharmaceutical companies to conceal any deficiencies in an ANDA until tentative approval is granted, relying on the often lengthy time period between tentative approval and final approval to fix any problems. Since the plaintiffs' argument to the contrary is rooted

entirely in an alternative interpretation of the statute that does not show the FDA's interpretation to be unreasonable, either exclusively based on the statutory text or in the context of the statute as a whole and its purposes, the Court credits the FDA's interpretation that the forfeiture trigger in 21 U.S.C. § 355(j)(5)(D)(i)(IV) may be applied retroactively under *Chevron* step two.

IV. CONCLUSION

A series of agency errors combined with the plaintiffs' malfeasance led to the tentative approval of the plaintiffs' ANDAs for generic drug products for esomeprazole and valganciclovir. The patented forms of these drugs, Nexium© and Valcyte©, are used by hundreds of thousands of Americans to treat maladies both minor and severe. Even though the plaintiffs have no realistic chance at entering the market in the near future, they nonetheless argue that they should be allowed to keep their competitors from entering the generic market for these drugs because they managed to deceive and pressure the FDA into erroneously granting tentative approval to the plaintiffs' ANDAs. For its part, the FDA has demonstrated that its internal system of checks and balances failed to prevent serious errors with at least five of the plaintiffs' ANDAs, including the two at issue in this lawsuit, and the very employees who were tasked with carefully reviewing manufacturers' applications to ensure compliance with the industry's best practices were granting approval without knowing why, using language they did not understand.

In the final analysis, neither the plaintiffs nor the Federal defendants should be satisfied with their actions during the processing of the two ANDAs at issue. Nevertheless, the Federal defendants' interpretation of the FDCA and the agency's implementing regulations is due substantial deference. Since the FDA is authorized to condition tentative approval on a showing of CGMP compliance at the facility where a generic drug is to be manufactured, the FDA erred in granting tentative approval to the plaintiffs' ANDAs for esomeprazole and valganciclovir. Even though that error was belatedly corrected, the agency has the inherent authority to correct its mistakes. The FDA's interpretation of the statutory provision requiring forfeiture of 180-day generic marketing exclusivity rights if the first ANDA applicant is found not to have met the

requirements for tentative approval within thirty months of an ANDA's submission is reasonable. Consequently, the Federal defendants' motion for summary judgment and the defendant-intervenors' motions for summary judgment are granted and the plaintiffs' motion for a preliminary injunction is denied.

An Order consistent with this Memorandum Opinion will issue contemporaneously.

First Issued: February 27, 2015

Interim Redacted Opinion Issued: March 11, 2015

Digitally signed by Judge Beryl A. Howell
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BERYL A. HOWELL
United States District Judge