Public Health Service

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993-0002

Docket No. FDA-2015-N-2713

SENT VIA EMAIL

Dear Cyclosporine Ophthalmic Emulsion ANDA Applicant:

This letter addresses two questions regarding certain 180-day exclusivity[1] issues posed in a letter sent to cyclosporine ophthalmic emulsion, 0.05% abbreviated new drug application (ANDA) applicants on July 28, 2015 and posted for public comment at www.regulations.gov in Docket No. FDA-2015-N-2713.

As explained below, we have concluded that the one or more applicants that submitted ANDAs or patent amendments containing paragraph IV certifications to U.S. Patent No. 5,474,979 (the '979 patent) during the period of time when the '979 patent was the only patent listed for Restasis (cyclosporine ophthalmic emulsion), 0.05% (i.e., after August 2, 2009 but before January 14, 2014) and that did not receive paragraph IV acknowledgment letters until after the '979 patent expired were a "first applicant" under section 505(j)(5)(B)(iv)(II)(bb) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). Additionally, we have concluded that the first applicant(s) (hereinafter the "Applicant" [2]) forfeited eligibility for any 180-day exclusivity period on May 17, 2014 when the '979 patent expired. Accordingly, there are no 180-day exclusivity barriers to approval of a subsequent applicant's ANDA that references Restasis as the RLD.

I. Statutory and Regulatory Background

The Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Amendments)[3] amended the FD&C Act to, among other things, add section 505(j), establishing a statutory abbreviated approval pathway for generic drugs. The Hatch-Waxman Amendments reflect Congress's efforts to balance the need to "make available more low cost generic drugs by establishing a generic drug approval procedure" with new incentives for drug development in the form of exclusivity and patent term extensions.[4]

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[1] 180-day exclusivity refers to the exclusivity provided for in section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act, which is commonly referred to as 180-day exclusivity.

[2] For simplicity, this letter will use singular nouns to refer to the one or more applicants that submitted a paragraph IV certification to the '979 patent with or to a substantially complete ANDA after August 2, 2009 but before January 14, 2014.

[3] Public Law 98-417, 98 Stat. 1585 (1984).

[4] See House Report No. 98-857, part 1, at 14-15 (1984), reprinted in 1984 U.S.C.C.A.N. 2647 at 2647-2648; see also *Abbott Labs. v. Young*, 920 F.2d 984, 985 (D.C. Cir. 1990).

A. Patent Submission, Certification, and Notice Requirements

Under the Hatch-Waxman Amendments, an applicant who submits a new drug application (NDA) under section 505(b) must submit information for each patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug, and that claims the drug for which the NDA applicant submitted the NDA and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent or that claims a method of using such drug for which approval is sought or has been granted in the application.[5] FDA publishes this patent information in its publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the "Orange Book").[6]

An ANDA is not required to contain independent evidence of the safety and effectiveness of the proposed generic drug.[7] Instead, an ANDA applicant relies on FDA's safety and effectiveness findings for a reference listed drug (RLD)[8] in seeking approval of its ANDA. For each patent that claims the listed drug or claims a method of using the listed drug for which the ANDA applicant seeks approval, an ANDA must contain one of the following certifications:

- that such patent information has not been submitted to FDA by the NDA holder (paragraph I certification);
- that such patent has expired (paragraph II certification);
- the date on which such patent will expire (paragraph III certification);
- that such patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted (paragraph IV certification).[9]

The timing of ANDA approval depends on, among other things, patent and exclusivity protections for the RLD.[10] A patent for which an ANDA applicant submits a paragraph I or paragraph II certification will not delay ANDA approval.[11] A patent for which an ANDA applicant submits a paragraph III certification may delay approval until the patent's expiration date.[12] A patent for which an ANDA applicant submits a paragraph IV certification (paragraph-IV certified patent) may also delay approval, depending on various factors, as discussed further below.

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[5] Section 505(b)(1)(A)(viii), (c)(2) of the FD&C Act; see also 21 CFR 314.53.
[6] The current annual edition and current cumulative supplement are available at https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm.
[7] E.g., section 505(j)(2)(A) of the FD&C Act.
[8] 21 CFR 314.3(b) (defining *reference listed drug* as "the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its ANDA"). RLDs are identified in the Orange Book. See Section 505(j)(2)(A), (4) of the FD&C Act; see also 21 CFR 314.94(a).
[9] Section 505(j)(2)(A)(vii) of the FD&C Act; see also 21 CFR 314.94(a)(12)(i)(A). If the patent listed in the Orange Book for the RLD is for a method of use for which the ANDA applicant does not seek approval in its ANDA, in lieu of a patent certification, the ANDA may instead contain what is commonly referred to as a "section viii statement." Section 505(j)(2)(A)(viii) of the FD&C Act; see also 21 CFR 314.94(a)(12)(iv).
[10] Section 505(j)(5) of the FD&C Act; see also 21 CFR 314.107.
[11] Section 505(j)(5)(B)(i) of the FD&C Act.
[12] Section 505(j)(5)(B)(ii) of the FD&C Act.

An ANDA applicant that submits an ANDA containing a paragraph IV certification must give notice of the paragraph IV certification to the NDA holder and patent owner, which includes "a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed" (notice).[13] The statute distinguishes between a paragraph IV certification submitted in an ANDA and a paragraph IV certification submitted in an amendment or supplement to an ANDA. "[I]f the [paragraph IV] certification is in the application," the applicant shall give notice "not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed."[14] "[I]f the [paragraph IV] certification is in an amendment or supplement to the application", the applicant shall give notice "at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application."[15] The regulations further specify that an applicant must send the notice on or after the date it receives the paragraph IV acknowledgement letter[16] from FDA; if an applicant sends the notice before it receives a paragraph IV acknowledgment letter, the notice is invalid.[17, 18]

If the patent information for the paragraph-IV certified patent was submitted to FDA before the ANDA was submitted, and the NDA holder or patent owner initiates a patent infringement action against the ANDA applicant within 45 days of receiving the notice, approval of the ANDA generally will be stayed for 30 months[19] (beginning on the later of the dates the patent owner and NDA holder receive the notice[20]), or such shorter or longer time as the court may order because either party to the action failed to reasonably cooperate in expediting the action.[21] If the patent information for the paragraph-IV certified patent was submitted after the ANDA was submitted but before it was approved, no 30-month stay of approval is available.[22]

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[13] Section 505(j)(2)(B) of the FD&C Act; 21 CFR 314.95. In this letter, the statutory and regulatory provisions pertaining to notice contained in section 505(j)(2)(B) of the FD&C Act and 21 CFR 314.95 will be collectively referred to as "the notice requirements."

[14] Section 505(j)(2)(B)(ii)(I) of the FD&C Act; 21 CFR 314.95(b).

[15] Section 505(j)(2)(B)(ii)(II) of the FD&C Act; 21 CFR 314.95(d).

[16] A paragraph IV acknowledgment letter "is a written, postmarked communication from FDA to an applicant stating that the Agency has determined that a 505(b)(2) application or ANDA containing a paragraph IV certification is sufficiently complete to permit a substantive review. A paragraph IV acknowledgment letter indicates that the 505(b)(2) application is regarded as filed or the ANDA is regarded as received." 21 CFR 314.3(b).

[17] 21 CFR 314.95(b), (d)(2). Thus, if an applicant submits an amendment containing a paragraph IV certification to its ANDA before the applicant has received a paragraph IV acknowledgement letter from FDA for a paragraph IV certification in its original ANDA, the applicant must wait to send notice until it receives the paragraph IV acknowledgement letter, rather than send notice of the paragraph IV certification in the amendment at the same time as the submission of its amendment. Id. Although 21 CFR 314.95(b)(2) was not finalized until October 6, 2016, it has been FDA's longstanding practice that notice of a paragraph IV certification may not be sent by an ANDA applicant unless and until FDA has notified the applicant that its application has been received in an acknowledgement letter or paragraph IV acknowledgement letter. *Abbreviated New Drug Applications and 505(b)(2) Applications, Proposed Rule*, 80 Fed. Reg. 6802, 6831-6833 (Feb. 6, 2015) (MMA Proposed Rule).

[18] Notice is also invalid if it is sent before the first working day after the day the patent is published in the Orange Book. 21 CFR 314.95(b)(2).

[19] If the RLD referenced by the ANDA has new chemical entity (NCE) exclusivity, the stay is extended to 7.5 years from date of the RLD's approval (7.5 year period). Section 505(j)(5)(F)(ii) of the FD&C Act.

[20] 21 CFR 314.107(b)(3)(i).

[21] Section 505(j)(5)(B)(iii) of the FD&C Act; 21 CFR 314.107(b)(3)(i)(A).

[22] Id.

B. 180-Day Exclusivity

As originally enacted in 1984, the Hatch-Waxman Amendments created an incentive to submit a paragraph IV certification, stating:

> [i]f the application contains a [paragraph IV] certification . . . and is for a drug for which a previous application has been submitted under this subsection continuing [sic] such a certification, the application shall be made effective not earlier than one hundred and eighty days after— . . . the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application . . . .[23]

This is commonly referred to as "180-day exclusivity."[24] In 1994, FDA issued regulations interpreting the 180-day exclusivity provisions, which provided that an applicant that (1) submits a substantially complete ANDA, (2) with a paragraph IV certification, (3) before the submission of any other substantially complete ANDA referencing the same listed drug with a paragraph IV certification to the same patent was eligible for 180 days of exclusivity (i.e., FDA would not approve during the exclusivity period any later-submitted ANDA for the same drug product containing a paragraph IV certification to the same patent).[25] Thus, at that time, under the Hatch-Waxman Amendments as originally enacted and implementing regulations, FDA recognized 180-day exclusivity on a patent-by-patent basis, meaning there could be multiple 180-day periods of exclusivity for ANDA drug products referencing the same listed drug if there were more than one listed patent, because there could be multiple occasions on which an applicant submitted the first substantially complete application containing a paragraph IV certification to one of the listed patents (the qualifying patent).[26]

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (Dec. 8, 2003) (the MMA) revised the 180-day exclusivity provisions of the Hatch-Waxman Amendments, establishing, among other things, that 180-day exclusivity is determined on a product-by-product basis, eliminating the possibility of multiple 180-day exclusivity periods for ANDAs that reference the same listed drug but contain paragraph IV certifications to different patents.[27] The MMA states:

> if the application contains a [paragraph IV] certification . . . and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days

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[23] Public Law 98-417, 98 Stat. 1589 (1984).

[24] The 180-day exclusivity is distinct from the 180-day exclusivity for competitive generic therapies created by the FDA Reauthorization Act of 2017. See section 505(j)(5)(B)(v) of the FD&C Act.

[25] 21 CFR 314.107(c) (1995); *Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions, Final Rule*, 59 Fed. Reg. 50338, 50350, 50367 (Oct. 3, 1994).

[26] See, e.g., *Apotex Inc. v. FDA*, 414 F. Supp. 2d 61, 74 (D.D.C. 2006).

[27] See 149 Cong. Rec. S 15884 (daily ed., (Nov. 25, 2003)) (Senator Kennedy) ("The Hatch-Waxman provisions in this bill also make the exclusivity available only with respect to the patent or patents challenged on the first day generic applicants challenge brand drug patents, which makes the exclusivity a product-by-product exclusivity rather than a patent-by-patent exclusivity.").

> after the date of the first commercial marketing of the drug . . . by any first applicant.[28]

Thus, under the MMA, 180-day exclusivity is available only to a "first applicant." The MMA defines "first applicant" as an applicant that: "[1] on the first day on which a substantially complete application containing a [paragraph IV] certification . . . is submitted for approval of a drug, [2] submits a substantially complete application that contains [a paragraph IV certification for the drug] and [3] lawfully maintains a [paragraph IV] certification . . . for the drug."[29]

The MMA also sets forth six events that result in a forfeiture of a first applicant's 180-day exclusivity period or eligibility for a period of 180-day exclusivity if it occurs with respect to that first applicant:[30] (1) failure to market; (2) withdrawal of application; (3) amendment of certification; (4) failure to obtain tentative approval; (5) agreement with another applicant, the listed drug holder, or a patent owner; and (6) expiration of all patents.[31] In addition, the MMA added a provision to the FD&C Act specifying that "if all first applicants forfeit the 180-day exclusivity period . . . no applicant shall be eligible for a 180-day exclusivity period."[32] Thus, 180-day exclusivity cannot "roll" to other applicants if all first applicants forfeit.

C. The Suboxone Letter

On July 13, 2018, FDA sent a letter to buprenorphine and naloxone sublingual film ANDA applicants (the Suboxone Letter), describing certain determinations FDA made with respect to 180-day exclusivity for certain strengths of buprenorphine and naloxone sublingual film.[33] FDA determined that one or more applicants that submitted on May 14, 2013 a substantially complete ANDA (or an amendment to a substantially complete ANDA) for buprenorphine and naloxone sublingual film 4 mg/1 mg and 12 mg/3 mg with a paragraph IV certification qualified as a "first applicant," because the applicant(s) submitted their substantially complete ANDA(s) with a paragraph IV certification on the first day such an application was submitted, notwithstanding that the first applicant(s) did not provide notice to the NDA holder and patent owner of the paragraph IV certification before withdrawing their ANDA(s). Moreover, FDA determined that the first applicant(s) forfeited their eligibility for 180-day exclusivity when the applicant(s) withdrew their ANDA(s).

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[28] Section 505(j)(5)(B)(iv)(I) of the FD&C Act.

[29] Section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act. The MMA defines "substantially complete application" as one that "on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A)" of section 505(j) of the FD&C Act. Section 505(j)(5)(B)(iv)(II)(cc) of the FD&C Act. See also 21 CFR 314.3(b) ("*Substantially complete application* is an ANDA that on its face is sufficiently complete to permit a substantive review. Sufficiently complete means that the ANDA contains all of the information required under section 505(j)(2)(A) of the Federal Food, Drug, and Cosmetic Act and does not contain a deficiency described in §314.101(d) and (e).").

[30] Section 505(j)(5)(D)(ii) of the FD&C Act.

[31] Section 505(j)(5)(D)(i)(I)-(VI) of the FD&C Act; see also FDA's draft guidance for industry *180-Day Exclusivity: Questions and Answers* (Jan. 2017) (addressing in section III.F of the draft guidance questions about the six forfeiture events).

[32] Section 505(j)(5)(D)(iii) of the FD&C Act.

[33] FDA published the letter, which is available at: https://www.fda.gov/media/114499/download.

In clarifying its determination, FDA explained in the Suboxone Letter that "prior to enactment of MMA and prior to FDA's exclusivity determination in this case," FDA had taken a "first effective" approach to determining eligibility for 180-day exclusivity when the first paragraph IV certification was submitted in an amendment or supplement to an ANDA.[34] In other words, a paragraph IV certification submitted with an amendment or supplement to a substantially complete ANDA would not be considered "effective" until the applicant provided notice.[35] Under the "first effective" approach, therefore, the day on which the first paragraph IV certification in a substantially complete ANDA was submitted could change if the earlier submitting applicant did not timely comply with the notice requirements. Thus, an applicant that submitted a paragraph IV certification in a substantially complete ANDA *after* another applicant that did so might nevertheless become a first applicant eligible for 180-day exclusivity in certain circumstances.[36]

The Suboxone Letter noted the absence of prior statements by FDA addressing what impact failing to provide timely notice would have on the "first applicant" determination post-MMA, for applications that contain a paragraph IV certification in the original ANDA submission, rather than in an amendment or supplement.[37] FDA then concluded that the "first effective" approach is inconsistent with the text and structure of the MMA because it effectively writes out the "first day" from the statutory definition of "first applicant."[38] The Suboxone Letter instead applied the "first submitted" interpretation, whereby "there can only ever be one 'first day on which a substantially complete application containing a paragraph IV certification [or an amendment to a substantially complete application with a paragraph IV certification] is submitted,' regardless of whether the applicant that submits its application (or an amendment or supplement to its application) on that 'first day' gives or fails to give timely notice of and/or otherwise lawfully maintains its paragraph IV certification."[39] Thus, under the "first submitted" interpretation, the "first day" is a specific date that is "fixed and does not change because of subsequent events."[40]

II. Factual Background

FDA originally approved NDA 050790 for cyclosporine ophthalmic emulsion, 0.05%, which is marketed by Allergan under the trade name Restasis®, on December 23, 2002.[41] By 2009, two

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[34] The Suboxone Letter at 7.
[35] Id.
[36] Id. at 7-8; see also *Purepac Pharm. Co. v. TorPharm, Inc.*, 354 F.3d 877, 888-889 (D.C. Cir. 2004) (upholding FDA's interpretation of the pre-MMA statutory provisions, which delayed the effective date of, but did not invalidate, a paragraph IV certification submitted in an amendment or supplement until notice was provided).
[37] The Suboxone Letter at 8. As noted in the Suboxone Letter, some prior statements suggested that FDA would continue to apply the "first effective" approach to post-MMA paragraph IV certifications submitted in amendments or supplements, an approach ultimately rejected in the Suboxone Letter. Id. at 8-9.
[38] Id. at 9.
[39] Id.
[40] Id. at 10.
[41] See Approval Letter for Restasis (Dec. 23, 2002), available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2002/050790ltr.pdf. Restasis was originally approved in NDA 021023 (see id.); after its approval, the NDA number was changed to 050790. See, e.g., Approval Letter for Supplement 001(Sept. 16, 2003), available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2003/50790slr001ltr.pdf. Separately, FDA approved supplement 024 to NDA 050790 on October 27, 2016, for Restasis Multidose™. See Approval Package for Restasis Multidose, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/50790Orig1s024.pdf.

patents were listed in the Orange Book for Restasis: U.S. Patent Nos. 4,839,342 (the '342 patent) and the '979 patent.[42] The '342 patent expired on August 2, 2009, and the '979 patent expired on May 17, 2014.[43] On January 14, 2014, an additional patent was listed in the Orange Book for Restasis, U.S. Patent No. 8,629,111 (the '111 patent).[44]

After the '342 patent expired but before the '111 patent was listed on January 14, 2014: (1) at least one ANDA was submitted containing a paragraph III certification to the '979 patent;[45] and (2) at least one substantially complete ANDA containing a paragraph IV certification to the '979 patent was submitted.[46] The paragraph IV certification to the '979 patent was the first paragraph IV certification submitted with or to any ANDA referencing Restasis. The Applicant did not provide notice of the paragraph IV certification to the '979 patent because the '979 patent expired before FDA issued a paragraph IV acknowledgement letter to the Applicant.[47] On January 14, 2014, at least one applicant that previously submitted a paragraph III certification to the '979 patent submitted an amendment to its ANDA with a paragraph IV certification to the '111 patent.[48]

In 2015, FDA opened docket number FDA-2015-N-2713 to solicit comments from applicants with ANDAs referencing Restasis and any interested party on two questions:

(1) whether the one or more applicants that submitted a paragraph IV certification to the '979 patent after the '342 patent but before January 14, 2014 and that did not receive an acknowledgement letter until after the '979 patent expired are "first applicants" under FD&C Act section 505(j)(5)(B)(iv)(II)(bb); and

(2) whether the 180-day exclusivity period for this product was forfeited on May 17, 2014, when the '979 patent expired, such that no ANDA applicant for cyclosporine ophthalmic

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[42] E.g., *Approved Drug Products with Therapeutic Equivalence Evaluations* (29th ed.).
[43] Id.
[44] Five patents in addition to the '111 patent were subsequently listed for Restasis, all having expiration dates of August 27, 2024: U.S. Patent Nos. 8,633,162; 8,642,556; 8,648,048; 8,685,930; and 9,248,191. Allergan initiated patent infringement actions in response to paragraph IV certification notices, asserting claims of each of these six listed patents, various claims of which were invalidated in a final court decision. *Allergan, Inc. v. Teva Pharms. USA, Inc.*, 742 Fed. Appx. 511 (Fed. Cir. Nov. 13, 2018), *rehearing en banc denied* (Mar. 4, 2019).
[45] E.g., *Teva Pharm. USA, Inc. v. Azar*, 369 F. Supp. 3d 183, 189-190 (D.D.C. 2019).
[46] See, e.g., Comment from InnoPharma, FDA-2015-N-2713-0002 (Aug. 28, 2015) at 1, 3 ("InnoPharma Licensing LLC submitted an ANDA for Cyclosporine Ophthalmic Emulsion 0.05% on January 13, 2014, which included a paragraph IV certification to patent number 5,474,979 . . . , which was the only PIV patent listed in the Orange Book at that time" and that it received an acknowledgement letter from the Agency stating that "the date the application was deemed to have been received and acceptable for review . . . was January 13, 2014.").
[47] FDA-2015-N-2713-001 at 3-4.
[48] See, e.g., Teva Pharms. USA, Inc.'s Memorandum of Points and Authorities in Support of Its Motion for a Preliminary Injunction, *Teva Pharms. USA, Inc. v. Azar*, No. 1:18-cv-02394 (D.D.C. 2019) (Doc. 2-1) (Teva's Memo), at 26–27 (stating that Teva originally submitted a paragraph III certification to the '979 patent and amended its not-yet-received ANDA on January 14, 2014 to submit a paragraph IV certification to the '111 patent); Comment submitted on behalf of Akorn Pharmaceuticals, FDA-2015-N-2713-0026 (Sept. 28, 2015) at 1-2 (stating that "Akorn amended then not-yet-received ANDA 204561 on January 14, 2014 to include a Paragraph IV certification to U.S. Patent No. 8,629,111" and that Akorn's ANDA initially contained a paragraph III certification to the '979 patent, which it amended to a paragraph II certification when the '979 patent expired).

emulsion, 0.05%, that references Restasis as its RLD is eligible for a 180-day exclusivity period.[49]

Shortly after FDA issued the Suboxone Letter, on October 17, 2018, Teva Pharmaceuticals USA, Inc. (Teva) sued the Agency for "'immediate injunctive and declaratory relief,' barring the [FDA] from 'depriving [Teva] of its statutory rights to 180 days of marketing exclusivity'" for its ANDA referencing Restasis, citing the FDA's first applicant decision in the Suboxone Letter as a substantive and procedural violation of the Administrative Procedure Act.[50] Teva argued that the Suboxone Letter "divested Teva of its statutory right to exclusivity," because even if no ANDA applicant were ever approved, the Suboxone Letter decision strips Teva of the 180-day exclusivity right's "embedded value."[51] In response to the lawsuit, FDA asserted, among other things, that Teva lacked standing and that its claims were not ripe; FDA also stated that it had not answered the questions posed in docket number FDA-2015-N-2713, because FDA generally does not make complex exclusivity decisions before an applicant is ready for approval or tentative approval.[52] The district court concluded that Teva lacked standing and dismissed the case without addressing the merits of Teva's argument.[53]

FDA now believes that the questions are ripe for determination.

III. Discussion

The statutory definition of "first applicant" comprises three distinct prongs; a "first applicant" is:

(1) an applicant that on the first day on which a substantially complete application containing a paragraph IV certification is submitted (the "when" prong)
(2) submits a substantially complete application that contains (the "submit" prong) and
(3) lawfully maintains a paragraph IV certification (the "lawfully maintains" prong).[54]

An applicant must satisfy all three prongs to qualify as a first applicant and potentially be eligible for 180-day exclusivity.[55] Thus, once an applicant submits a substantially complete application containing a paragraph IV certification on the first day such an application is submitted, it must lawfully maintain the paragraph IV certification to remain a first applicant who is eligible for 180-day exclusivity.[56]

There can only be one "first day on which a substantially complete application containing a paragraph IV certification [or an amendment to a substantially complete application with a paragraph IV certification] is submitted, regardless of whether the applicant that submits its application (or an amendment or supplement to its application) on that 'first day' gives or fails to

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[49] See FDA-2015-N-2713-001. A number of general comments was submitted to the docket concerning a bioequivalence demonstration for ANDAs referencing NDA 050790, which was not the subject of the solicitation for comments; those general comments are not addressed herein.
[50] *Teva Pharm. USA*, 369 F. Supp. 3d at 186, 195.
[51] Id. at 196, 197.
[52] Id. at 192, 194.
[53] Id. at 196, 200, 205.
[54] See the Suboxone Letter at 5, 9 (citing section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act).
[55] Id.
[56] Id.

give timely notice of and/or otherwise lawfully maintains its paragraph IV certification."[57] Thus, the inability to provide notice of the paragraph IV certification to the '979 patent before the patent expired because FDA had not yet sent a paragraph IV acknowledgement letter does not alter the date of "the first day" on which a substantially complete application containing a paragraph IV certification was submitted. Nor does it change the fact that the Applicant submitted a substantially complete ANDA containing a paragraph IV certification on "the first day."

Moreover, the expiration of all the qualifying paragraph-IV certified patents results in a forfeiture event under section 505(j)(5)(D)(i)(VI). Thus, eligibility for 180-day exclusivity was forfeited upon the expiration of the '979 patent.[58] Accordingly, there are no 180-day exclusivity barriers to approval of a subsequent applicant's ANDA that references Restasis as the RLD.[59]

A. "The First Day" Is Fixed Once a Substantially Complete Application with a Paragraph IV Certification Is First Submitted

FDA interprets "the first day" as that term is used in the "when" prong to be a permanently fixed date once a substantially complete application containing a paragraph IV certification is submitted; it "does not change based on subsequent events," including whether the applicant satisfies the notice requirements.[60]

Some commenters urge that the Applicant's inability to satisfy the notice requirements means the paragraph IV certification was "legally inoperative," and "the first day" was not fixed, leaving open the possibility that a later-submitting applicant can be a "first applicant."[61] To reach this outcome, FDA would need to take the position that an applicant who does not provide notice violates the "lawfully maintains" prong[62] and changes the date of "the first day" in the "when" prong.[63] This interpretation, like the "first effective" approach, conflates these two prongs, and for similar reasons described in the Suboxone Letter,[64] it contravenes both the plain meaning and structure of the statute.

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[57] The Suboxone Letter at 9.
[58] Section 505(j)(5)(D)(i)(VI) of the FD&C Act.
[59] Section 505(j)(5)(D)(ii), (iii) of the FD&C Act.
[60] The Suboxone Letter at 9-10.
[61] See, e.g., FDA-2015-N-0087-0031 at 7 (arguing that "unless and until" notice is provided, the paragraph IV certification is "legally inoperative"); see also FDA-2015-N-0087-0026 at 5 (arguing that "lawful maintenance" requires "perfect[ing]" the paragraph IV certification by sending notice not later than 20 day after receipt of an acknowledgment letter or simultaneously with an amendment or supplement).
[62] None of the commenters argues that failure to satisfy the notice requirements affects the "submit" prong; nor does FDA believe that such an outcome would be supportable given the statutory definition of "substantially complete application," which is an application that "on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A) [of the FD&C Act]," with no reference to the notice provisions in section 505(j)(2)(B) of the FD&C Act. Section 505(j)(5)(B)(iv)(II)(cc) of the FD&C Act.
[63] One commenter acknowledges that the "first applicant" definition comprises "separate requirements" that are "distinct conditions" but nonetheless argues that the "when" prong and the "lawfully maintains" prong are "linked" such that failing to lawfully maintain a paragraph IV certification renders it a "legal nullity." FDA-2015-N-0087-0031 at 6-7, 10.
[64] The Suboxone Letter at 9-11.

i. The "conflated" interpretation disregards the plain text of the "first applicant" definition

As an initial matter, we note that the statutory and regulatory definitions of "first applicant" do not expressly reference the notice requirements, nor do they expressly condition "first applicant" status on receiving a paragraph IV acknowledgement letter from FDA or satisfying the notice requirements.[65]

The "conflated" interpretation seeks to read the notice requirements into the "lawfully maintains" prong and requires linking the "when" prong to the "lawfully maintains" prong such that the former cannot stand without satisfaction of the latter. For example, under the "conflated interpretation," if a first applicant fails to provide notice, despite being legally unable to do so (in other words, failing to lawfully maintain the paragraph IV certification), the date of "the first day" in the "when" prong would change. As explained in the Suboxone Letter, the conflation of these two prongs is inconsistent with the plain meaning of the statutory text.[66]

The "first applicant" definition uses the indefinite article "a" to modify "substantially complete application," suggesting that the "when" prong date (i.e., "the first day") is set permanently once a substantially complete application (or an amendment or supplement to a substantially complete application) containing a paragraph IV certification is first submitted.[67] There also is no reference in that prong to "lawfully maintains." The plain language of the statutory text suggests there can be only one "first day on which a substantially complete application containing a paragraph IV certification is submitted," and it is not subject to change based on subsequent events.[68]

If the date of "the first day" were determined by the outcome of the "lawfully maintains" prong, as the "conflated" interpretation requires, then the "when" prong would be redundant, because "the first day" could only ever be the date of submission of the first lawfully maintained paragraph IV certification. The "conflated" interpretation, like the "first effective" approach,[69] reads the "when" prong out of the "first applicant" definition, essentially rewriting it to replace the entire "when" prong with "first":

> the term ''first applicant'' means an applicant that~~, on the first day on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug,~~ [first] submits a substantially

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[65] Compare section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act (defining "first applicant), with id. at section 505(j)(2)(B) (describing the provisions pertaining to the notice of a paragraph IV certification); see also *Purepac*, 354 F.3d at 889 (noting the pre-MMA statute does not link the exclusivity award to the requirement to provide notice simultaneously with an amendment or supplement). Although *Purepac* was decided under the pre-MMA statute, the MMA did not change the fact that the 180-day exclusivity provisions and the notice requirements appear in different provisions of the FD&C Act.

[66] Id. at 10.

[67] See section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act; see also the Suboxone Letter at 10.

[68] Ibid.

[69] See the Suboxone Letter at 10.

> complete application that contains and lawfully maintains a certification described in paragraph (2)(A)(vii)(IV) for the drug.[70]

FDA's interpretation of "first applicant," on the other hand, gives full effect to each prong of the "first applicant" definition.[71]

ii. The "conflated" interpretation conflicts with the structure of the statute

Additionally, the "conflated" interpretation, like the "first effective" approach, inverts the structure of the "first applicant" definition, working backwards from an ANDA "that contains and lawfully maintains" a paragraph IV certification to determine the date of "the first day" (i.e., the submission date of the first substantially complete application containing a lawfully maintained paragraph IV certification becomes "the first day"). Had Congress intended to link the "when" prong with the "lawfully maintains" prong in the way the "conflated" interpretation requires, it could have done so by specifying that "the first day" is the day on which a substantially complete application is submitted containing a lawfully maintained paragraph IV certification. As noted in the Suboxone Letter, however, Congress chose not only to create separate, distinct prongs in the "first applicant" definition but also to place the "lawfully maintains" prong only in the second half of the definition, not up front with, or as part of, the "when" prong.[72] The effect, therefore, is that an applicant must "lawfully maintain[]" a paragraph IV certification to *remain* a first applicant eligible for 180-day exclusivity, but the applicant's failure to do so will not change the already-set "first day."

The "conflated" interpretation also causes conflict between the "first applicant" definition in section 505(j)(5)(B) and the forfeiture provisions at section 505(j)(5)(D) of the FD&C Act.[73] Consider multiple applicants that submit substantially complete applications containing paragraph IV certifications on the first day such an application was submitted. Assume each of these applicants subsequently amends or withdraws their qualifying paragraph IV certifications or withdraws their applications, and that these events are grounds to find that an applicant did not lawfully maintain a paragraph IV certification. Under the "conflated" interpretation, these applicants would fail the "lawfully maintains" prong and simultaneously negate the "when" prong, allowing for the next-in-time applicant(s) to become a "first applicant." In other words, it makes possible "rolling" the potential for exclusivity from an earlier-submitting applicant(s) to a later-submitting applicant(s). The forfeiture provisions, conversely, precludes "rolling" exclusivity, stating that if all first applicants forfeit the 180-day exclusivity period no applicant shall be eligible for a 180-day exclusivity period.[74]

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Finally, some commenters argue that notice is required, has always been required, and that submission of a paragraph IV certification alone is insufficient to qualify for eligibility for the

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[70] See section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act.
[71] See, e.g., the Suboxone Letter at 9-10.
[72] See section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act; see also the Suboxone Letter at 10.
[73] See the Suboxone Letter at 10-11.
[74] See section 505(j)(5)(D)(iii)(II); see also the Suboxone Letter at 10-11.

180-day exclusivity reward.[75] The question here is not whether notice is required. Providing notice is a statutory and regulatory requirement separate and apart from the statutory provisions defining "180-day exclusivity period," "first applicant," and "substantially complete application."[76] Moreover, failure to provide notice has consequences, including delaying ANDA approval.[77] Nor is FDA suggesting that submission of a paragraph IV certification "alone" is sufficient to obtain 180-day exclusivity. To obtain 180-day exclusivity, the statute requires that an applicant meet all three prongs in the "first applicant" definition and not trigger any of the forfeiture provisions.[78] Rather, the question here is whether the Applicant's inability to provide notice because the patent expired before FDA sent the paragraph IV acknowledgment letter nullifies the existence of the Applicant's paragraph IV certification submitted in a substantially complete application on "the first day" such an application was submitted, paving the way for an applicant that submits a paragraph IV certification *after* "the first day" to nonetheless qualify as a "first applicant." In other words, does the lack of notice impact the date of "the first day"? For at least the reasons discussed above, the answer must be no.

B. The Applicant Was a "First Applicant" and 180-Day Exclusivity Was Forfeited When the '979 Patent Expired

In this case, the Applicant submitted a substantially complete ANDA containing a paragraph IV certification on "the first day" such an application was submitted. The Applicant could not satisfy the notice requirements because the sole qualifying paragraph-IV certified patent expired before FDA sent a paragraph IV acknowledgment letter.[79] Like the first applicant(s) in the Suboxone Letter that did not comply with the notice requirements before the requirement was rendered moot, the Applicant's inability to provide notice in this case does not change the date of "the first day" on which a substantially complete ANDA containing a paragraph IV certification was submitted and does not alter the fact that the Applicant submitted its substantially complete ANDA containing a paragraph IV certification on "the first day." Thus, the facts in this case compel the same conclusion reached in the Suboxone Letter, such that the Applicant was a "first applicant."

Under FDA's interpretation of "first applicant" described herein, the sole qualifying paragraph-IV certified patent expired on May 17, 2014, triggering a forfeiture event under section 505(j)(5)(D)(i)(VI).

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[75] See, e.g., FDA-2015-N-0087-0031 at 6-7. The commenter argues that "deeming the ANDA applicant to have qualified for 180-day exclusivity upon its lodging of a paragraph IV certification with the Agency *in an ANDA that has not yet been accepted for review* would impermissibly render the 'lawfully maintains' requirement superfluous." Id. at 7 (emphasis added). This incorrectly assumes that no ANDA was deemed substantially complete as of the date when a paragraph IV certification for the '979 patent was submitted on January 13, 2014. See, e.g., FDA-2015-N-0087-002 at 3 (stating that InnoPharma submitted a paragraph IV certification to the '979 patent on January 13, 2014 and that its ANDA "was deemed to have been received and acceptable for review" as of January 13, 2014).

[76] Compare section 505(j)(2)(B) of the FD&C Act, with id. at section 505(j)(5)(B)(iv)(II); 21 CFR 314.95.

[77] See section 505(j)(5)(B)(iii) of the FD&C Act. The 45-day window during which a patent infringement action may be brought against an ANDA applicant, which can result in a 30-month stay of ANDA approval, does not begin to run until the date on which notice is received. Id.

[78] Section 505(j)(5)(B)(iv), (D) of the FD&C Act.

[79] 21 CFR 314.95(b)(2).

C. Even If the Applicant Were Not a "First Applicant," Teva and Akorn Also Would Have Forfeited 180-Day Exclusivity

Even if—as some commenters like Teva and Akorn urge—FDA were to conclude that the Applicant is not a "first applicant", and, instead, Teva and Akorn each is a "first applicant" the ultimate outcome is the same, as both Teva and Akorn also would have forfeited eligibility for 180-day exclusivity.[80]

Teva represents in a public court filing that:

- it submitted ANDA 203880 on January 23, 2012;
- it submitted a paragraph IV certification to the '111 patent "on the first possible day," January 14, 2014;
- FDA sent an acknowledgment letter dated July 9, 2015; and
- Teva "timely notified Allergan."[81]

Akorn represents in a public submission that:

- it also submitted a paragraph IV certification to the '111 patent on January 14, 2014;
- FDA sent an acknowledgment letter to Akorn on June 30, 2015; and
- Akorn "promptly sent notice to Allergan."[82]

Both Teva and Akorn maintain that they qualify as a "first applicant."[83] For the reasons noted above FDA disagrees.

Regardless, even assuming Teva and Akorn were each a "first applicant," both would have forfeited eligibility for 180-day exclusivity under the failure-to-market provision at section 505(j)(5)(D)(i)(I) of the FD&C Act based on the facts presented by each in public documents and the status and rulings of the U.S. Court of Appeals for the Federal Circuit.

i. Statutory Background on the Failure-to-Market Forfeiture Provision

The failure-to-market forfeiture provision provides as follows:

> (I) FAILURE TO MARKET. – The first applicant fails to market the drug by the later of –
>
> (aa) the earlier of the date that is –
>
> (AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or
>
> (BB) 30 months after the date of submission of the application of the first applicant; or

[80] As noted in the discussion below, this conclusion and analysis are based on public representations by Teva and Akorn, as well as publicly filed court documents.
[81] Teva's Memo, at 24, 26–28.
[82] FDA-2015-N-2713-0026 at 1-2.
[83] Teva's Memo at 1; FDA-2015-N-2713-0026 at 2.

(bb) with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a certification qualifying the first applicant for the 180-day exclusivity period under subparagraph (B)(iv), at least 1 of the following has occurred:

(AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the patent is invalid or not infringed.

(BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.

(CC) The patent information submitted under subsection (b) or (c) is withdrawn by the holder of the application approved under subsection (b).[84]

Application of the failure to market forfeiture provision requires a series of analyses based on the timing of specific events. A forfeiture event will occur when the first applicant fails to market the drug by the later of two dates. One of these dates is calculated under item (aa) by determining the earlier of a date that is either 75 days after the first applicant's ANDA is approved (subitem (AA)) or 30 months after the date of submission[85] of the first applicant's ANDA (subitem (BB)).

The other of these dates is calculated under item (bb) by identifying the date that is 75 days after the date as of which at least one of the enumerated events occurred, with respect to each of the patents as to which the first applicant submitted and lawfully maintained a certification that qualified it as a first applicant. These events listed in (bb) include, very generally, a court entering a final decision that the patent is invalid or not infringed, a court signing a settlement order or consent decree entering final judgment that includes a finding that the patent is invalid or not infringed, or the patent information for the listed drug being withdrawn by the NDA holder.

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[84] Section 505(j)(5)(D)(i)(I) of the FD&C Act.

[85] Section 505(j)(5)(D)(i)(I)(aa)(BB) of the FD&C Act states that the 30-month period should be calculated from the date of "submission of the application of the first applicant." In applying the MMA 180-day exclusivity provisions, the FDA considers the date an ANDA containing a paragraph IV certification is submitted to be the date the agency considers the ANDA to have been "received" pursuant to 21 CFR 314.101(b). Both this regulation and the definition of "first applicant" at section 505(j)(5)(B)(iv)(II)(bb) of the FD&C Act require that the ANDA containing the paragraph IV certification be substantially complete, meaning it is sufficiently complete to permit a substantive review. When an ANDA containing a paragraph IV certification is determined, upon review, to have been substantially complete as of the day it was submitted to FDA, it will be considered to be received as of the date it was submitted (i.e., date-stamped by the appropriate FDA mail-room). When the Office of Generic Drugs (OGD) sends the applicant a refusal to receive letter describing the additional information that must be submitted to render an ANDA substantially complete, the ANDA is deemed received on the day the information necessary to find the application substantially complete was submitted.

To meet the requirements of item (bb), an event enumerated under item (bb) (enumerated event) must occur "with respect to the first applicant or any other applicant (which other applicant has received tentative approval)." FDA interprets this clause as identifying the spectrum of potential applicants with respect to which one of the enumerated events must occur in order to be relevant to the question of forfeiture. The parenthetical clarifies that, in order for this provision to apply, FDA must determine at the time forfeiture is analyzed,[86] that an applicant other than the first applicant described earlier in the sentence has had an enumerated event and has received tentative approval. If at the time of the forfeiture determination no other applicant who has had an enumerated event has received a tentative approval, FDA would not find that the requirements for forfeiture under this provision are satisfied, even if there is the possibility of tentative approval in the future.

The second clause of item (bb) describes the time period used to calculate the forfeiture date under item (bb), that is "the date that is 75 days after the date" on which an enumerated event occurs. The occurrence of an enumerated event begins the 75-day period described in item (bb). Forfeiture occurs if this 75-day period is triggered and runs, and the relevant "other applicant" has received tentative approval at the time FDA makes the forfeiture determination.[87] In other words, FDA interprets this clause to mean that an "other applicant" need not be tentatively approved at the time the enumerated event occurs, or within the 75-day period after the event, in order for this provision to apply, so long as the other applicant has secured tentative approval at the time FDA makes the forfeiture determination. This interpretation is consistent with the structure of item (bb), which separately describes, in independent clauses, the spectrum of applicants to which it applies, and the rule for determining timing.

In sum, FDA will consider the item (bb) date to occur if, at the time FDA makes the forfeiture determination, all of the following requirements are met: (1) there is a first applicant or an "other applicant (which other applicant has received tentative approval)"; (2) an enumerated event has occurred with respect to that first applicant or that "other applicant"; and (3) at least 75 days have passed after the event occurred. The relevant date under item (bb) for conducting the calculation in section 505(j)(5)(D)(i)(I) of the FD&C Act is 75 days after the enumerated

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[86] FDA's practice is to make decisions on eligibility for 180-day exclusivity in the context of specific ANDAs that are otherwise ready for approval (i.e., when a first applicant's ANDA or a subsequent applicant's ANDA is ready for approval). See also FDA, Draft Guidance for Industry, *180-Day Exclusivity: Questions and Answers*, at 27 (Jan. 2017).

[87] The holding of the Court of Appeals for the Federal Circuit in *Apotex, Inc. v. Daiichi Sankyo Co., Ltd.*, 781 F.3d 1356 (Fed. Cir. 2015), that a subsequent applicant's action for a judgment declaring invalid or not infringed a disclaimed patent (the subject of a paragraph IV certification), presented a justiciable case or controversy is not inconsistent with the Agency's interpretation. The "case-or-controversy" issue in that case turned, in part, on whether the subsequent applicant's declaratory judgment action, if successful, could potentially cause the first applicant to forfeit under section 505(j)(5)(D)(i)(I) by triggering an event enumerated under (bb). The court reasoned, in part, that the declaratory judgment action potentially could trigger forfeiture, despite the fact that the subsequent applicant had not yet received tentative approval because section 505(j)(5)(D)(i)(I) of the FD&C Act did not require the subsequent applicant's application to have received tentative approval before initiating the action that ultimately would result in an enumerated event. Id. at 1367-71. Although the court also suggested that the 75-day period in (bb) began once the subitem (bb) event occurred and the other applicant had tentative approval, see id. at 1370, those statements were dicta, and we do not find them persuasive. The issue of when the 75-day clock began did not affect the court's holding that there was a justiciable case or controversy, which instead turned on the necessity of having tentative approval prior to initiating an action that could lead to an enumerated event.

event.[88] As explained above, tentative approval could occur at any time prior to or after the enumerated event occurs, as long as the requirement for tentative approval of another applicant has been satisfied at the time FDA makes the forfeiture determination.

FDA believes that this interpretation—that forfeiture requirements under item (bb) are met regardless of whether tentative approval of the application of an "other applicant" occurs before or after an enumerated event—effectuates Congress's purpose in enacting the failure to market provision.[89] The 180-day exclusivity provisions provide an incentive for generic drug applicants who are first to expose themselves to the risk of patent litigation, but provide that such applicants can forfeit that incentive when their failure to begin commercial marketing has the potential to hold up other generic drugs that may otherwise be able to enter the market. Requiring an "other applicant's" application to have received tentative approval in order for an enumerated event that occurred with respect to that applicant to trigger forfeiture effectuates this intent, because in general eligibility for exclusivity will only be forfeited if there is the possibility that forfeiture can result in increased competition (because another applicant is ready to be fully approved but for the exclusivity). However, given that tentative approval can occur at any point before, during, or after patent litigation, we see no discernable policy reason why Congress would intend to require that tentative approval must have occurred before one of the events enumerated under (bb) or during the 75 days thereafter in order to trigger forfeiture. Rather, such an interpretation could lead to arbitrary and unpredictable results and could needlessly keep competing products off the market.

ii. Analysis of the Facts Publicly Presented by Teva and Akorn Under the Failure to Market Provision

As described above, the item (aa) date is the earlier of two dates: (1) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii) and (2) 30 months after the date of submission of the application of the first applicant. Teva publicly represents that it submitted its application on January 23, 2012.[90] Thirty months after January 23, 2012 is July 23, 2014. Akorn has not publicly disclosed the date it submitted its application; assuming, for the sake of argument that its ANDA was submitted on January 14, 2014 (the date that it states that it submitted its paragraph IV certification to the '111 patent), the (aa) date would be July 14, 2016, as thirty months from January 14, 2014 is July 14, 2016. FDA has not approved an ANDA referencing Restasis. Thus, July 23, 2014 would be the earlier item (aa) date for Teva, and July 14, 2016 would be the earlier item (aa) date for Akorn.

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[88] For example, suppose that a subsequent applicant were to receive a judgment described in subitem (BB) on April 1 and to receive tentative approval on August 1. The 75-day period would begin once the (BB) event occurred on April 1, and it would end on June 15. On August 1, all of the requirements of (bb) would be met: (1) there would be an "other applicant" that received tentative approval; (2) an enumerated event would have occurred with respect to that other applicant; and (3) 75 days would have passed since the event occurred. Forfeiture would have occurred because all three requirements are met. The relevant date under (bb) for conducting the calculation in 505(j)(5)(D)(i)(I) of the FD&C Act would be June 15.

[89] Cf. *Apotex*, 781 F.3d at 1370 (rejecting first applicant's argument that, with respect to an "other applicant," an event enumerated under (bb) could trigger forfeiture only if the other applicant's application had received tentative approval before the action was initiated, in part, because that interpretation did not appear to effectuate Congress's purpose).

[90] Teva's Memo at 15.

The item (bb) date is 75 days after at least one of three events has occurred with respect to the first applicant or "any other applicant which other applicant has received tentative approval) as to each patent with respect to which the first applicant submitted and lawfully maintained a paragraph IV certification qualifying the first applicant for the 180-day exclusivity period."[91] At least one of the three item (bb) events has occurred with respect to Teva and Akorn. Specifically, on November 13, 2018, the Federal Circuit affirmed a district court finding of invalidity of the '111 patent, as well as other listed patents in the Orange Book for Restasis at that time, in a lawsuit brought by Allergan against Teva and Akorn, among others, for patent infringement.[92] Allergan filed a petition for panel rehearing and a petition for en banc rehearing, which the Federal Circuit denied in an order entered on March 6, 2019.[93] The mandate issued to the United States District Court for the Eastern District of Texas on March 13, 2019.[94] Thus, the latest item (bb) date for both Teva and Akorn would be 75 days after March 13, 2019, i.e., May 27, 2019.

The later of the item (aa) date (July 23, 2014 and July 14, 2016 for Teva and Akorn, respectively) and the item (bb) date (May 27, 2019) would be May 27, 2019.

Neither Teva nor Akorn has marketed its drug products under ANDA 203880 or ANDA 204561, respectively, by May 27, 2019. Therefore, even if Teva and Akorn were regarded as a "first applicant," both would have forfeited eligibility for 180-day exclusivity under the failure to market provision at section 505(j)(5)(D)(i)(I) of the FD&C Act.

IV. Conclusion

FDA has concluded that the Applicant was a "first applicant" but eligibility for 180-day exclusivity was forfeited when the only qualifying patent, the '979 patent, expired. Moreover, even if FDA were to conclude the Applicant, who submitted a paragraph IV certification to the '979 patent on January 13, 2014, is not a "first applicant," and instead accepted Teva and Akorn's assertions that each is a "first applicant" based on their paragraph IV certifications to the '111 patent on January 14, 2014, it appears from publicly available statements and documents that Teva and Akorn also would have forfeited eligibility for 180-day exclusivity under section 505(j)(5)(D)(i)(I) of the FD&C Act. As such, there are no 180-day exclusivity barriers to approval of a subsequent applicant's ANDA that references Restasis as the RLD.

Sincerely,

Christopher H. Pruitt -S

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Office of Generic Drug Policy

[91] Section 505(j)(5)(D)(i)(I)(bb) of the FD&C Act.
[92] See supra footnote 44 (citing *Allergan*, 742 Fed. Appx. 511).
[93] *Allergan Inc. v. Teva Pharm. USA, Inc.*, Case No. 18-1130 (Fed. Cir.), Dkt. No. 113.
[94] *Allergan*, Case No. 18-1130, Dkt. No. 114.

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