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## The Law of 180-Day Exclusivity

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# The Law of 180-Day Exclusivity\*

ERIKA LIETZAN AND JULIA POST\*\*

When Congress enacted the Hatch–Waxman amendments to the Federal Food, Drug, and Cosmetic Act (FDCA) in 1984, creating a statutory pathway for abbreviated new drug applications (ANDAs), it included an incentive for generic applicants to challenge as invalid, or alternatively design around, patents claiming the innovative drugs on which they based their abbreviated applications.<sup>1</sup> In brief, the first generic applicant to file an ANDA asserting that such a patent was invalid or not infringed would be awarded 180 days of generic market exclusivity. During this exclusivity period, the Food and Drug Administration (FDA) could not approve a subsequent ANDA that challenged a patent claiming the same drug. Congress amended the scheme substantially in 2003 as part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA),<sup>2</sup> and it made minor and temporary changes in 2012 as part of the Food and Drug Administration Safety and Innovation Act (FDASIA).<sup>3</sup>

This is the fourth in a series of articles explaining the law of 180-day exclusivity.<sup>4</sup> Like the others, it takes a descriptive and doctrinal approach to the law that has emerged from the statute, the agency’s implementing materials (which range from regulations to citizen petition responses and decisions to award or deny exclusivity), and court decisions. Its scope is, however, slightly different. For many years, the two schemes—the 1984 scheme and the amended 2003 scheme—operated in parallel. One or the other would apply, depending on the date that the particular ANDA was filed. Today there are few if any pending ANDAs to which the original provisions

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\*This is the fourth in a series that has been published regularly for more than a decade. The authors assumed full responsibility for citations, the format of which conforms to the prior articles in the series and not necessarily to the conventions of the Georgetown University Law Center’s Student Editorial Board.

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<sup>1</sup> Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98–417, 98 Stat. 1585 (1984).

<sup>2</sup> Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108–173, 117 Stat. 2066 (2003).

<sup>3</sup> Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112–144, 126 Stat. 993 (2012).

<sup>4</sup> See David E. Korn, Erika Lietzan & Shaw Scott, *A New History and Discussion of 180-Day Exclusivity*, 64 FOOD & DRUG L. J. 335 (2009) [hereinafter “2009 Exclusivity Article”]; Erika Lietzan & David E. Korn, *Issues in the Interpretation of 180-Day Exclusivity*, 62 FOOD & DRUG L.J. 49 (2007) [hereinafter “2007 Exclusivity Article”]; Erika King Lietzan, *2004 Update: 180-Day Exclusivity Under the Hatch–Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, 59 FOOD & DRUG L.J. 459 (2004); Erika King Lietzan, *A Brief History of 180-Day Exclusivity under the Hatch–Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, 59 FOOD & DRUG L.J. 287 (2004).

apply. Moreover, although the original scheme gave rise to a substantial number of interpretive disputes litigated before FDA and in the courts, those disputes have largely been resolved.

We view the law of the 1984 scheme as worth describing, not only because the scheme may be of historical interest to readers but also because the 2003 amendments made targeted changes and left much of the original statutory language intact. But we have made the decision to truncate discussion of the older scheme. As before, we proceed issue by issue. But as a general rule, for each issue we simply identify the rule of law under the old scheme, generally referring the reader to the pages of the 2009 article (or, if warranted, the 2007 article) that explain its development and noting *briefly* developments subsequent to 2009 that are consistent with earlier conclusions.<sup>5</sup> This article therefore generally does not repeat the detailed discussion of pre-2009 controversies that can be found in earlier articles. Instead it focuses on new developments: new issues that have arisen relating more generally to 180-day exclusivity, such as premature notice of paragraph IV certification, as well as the body of law emerging around the forfeiture provisions enacted in 2003.

Section I of this article provides the necessary background regarding the statutory language as well as a high-level description of the steps FDA has taken to implement the scheme. It defers discussion of the details of FDA's implementing regulations to section II. Section II discusses the discrete interpretive issues, arranged in five categories: which rules apply, earning exclusivity, forfeiture of exclusivity, commencing the exclusivity term, and enjoyment (use) of the exclusivity term. This section presents each issue as a question and then offers a short answer and a more full discussion. In some cases, the issue is sufficiently discrete and the discussion sufficiently brief that the article dispenses with a "short answer" altogether. Because FDA has announced that it will release guidance on 180-day exclusivity sometime in 2016,<sup>6</sup> section II flags open issues as well as apparent agency policies that could be confirmed in guidance. We conclude in section III with a brief discussion of lingering and renewed criticisms of the scheme, in the courts, academic literature, and Congress. We note a variety of proposals, both in Congress and in the secondary literature, to change the scheme yet again.

## I. BACKGROUND

### A. *Original Statutory Language (1984 to 2003)*

As originally enacted, the statute provided that if an ANDA "contains a certification described in subclause (IV) of paragraph (2)(A)(vii) [otherwise known as a "paragraph IV certification"] and is for a drug for which a previous application has been submitted under this subsection continuing [*sic* "containing"] such a certification, the application shall be made effective not earlier than one hundred and eighty days after—(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the

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<sup>5</sup> This article uses the phrase "old ANDAs" to refer to ANDAs governed by the 1984 scheme, including the 1984 scheme as amended (retroactively) in 2003. It also refers to the 1984 scheme as the "old scheme."

<sup>6</sup> FDA, *Guidance Agenda: New & Revised Draft Guidances CDER is Planning to Publish During Calendar Year 2016* (Jan. 22, 2016).

previous application, or (II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier.”<sup>7</sup> Put another way, the first generic applicant to file an ANDA containing a paragraph IV certification was to be awarded 180 days of exclusivity, during which FDA could not approve a subsequent ANDA that challenged a patent for the same drug product. The 180 days were calculated from either the date of the first commercial marketing of the generic drug product by the first applicant or the date of a court decision declaring the patent invalid or not infringed, whichever was sooner.

FDA published a final regulation implementing the 180-day provision in October 1994.<sup>8</sup> Section 314.107(c) stated that if an ANDA contained a paragraph IV certification and was for a generic copy of the same listed drug “for which one or more substantially complete abbreviated new drug applications were previously submitted” containing a paragraph IV certification, and “the applicant submitting the first application has successfully defended against a suit for patent infringement brought within 45 days of the patent owner’s receipt of notice,” then approval of the second ANDA would be made effective no sooner than the earlier of (1) the date the first applicant “first commences commercial marketing of its drug product” or (2) the date “of a decision of the court holding the relevant patent invalid, unenforceable, or not infringed.” The regulations explained that the “applicant submitting the first application” was the applicant that submitted an application that *both* (1) was substantially complete *and* (2) contained a paragraph IV certification, prior to the submission of any other application for the same listed drug that both was substantially complete and contained the same certification. In other words, the first applicant to satisfy both requirements would earn exclusivity. According to the regulation, a “substantially complete” application contained “the results of any required bioequivalence studies, or, if applicable, a request for a waiver of such studies.”<sup>9</sup>

### *B. Amended Statutory Language (2003 to present)*

In 2003, as part of broader amendments to the Hatch–Waxman provisions contained within the Medicare Modernization Act (MMA), Congress revised the language that governs the earning and triggering of exclusivity, added a series of forfeiture provisions, and included definitions for key terms. For the most part, the amended language applies only to ANDAs filed after December 8, 2003, and only if

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<sup>7</sup> 21 U.S.C. § 355(j)(5)(B)(iv) (1984).

<sup>8</sup> 54 Fed. Reg. 28872 (July 10, 1989) (proposed rule); 59 Fed. Reg. 50338 (Oct. 3, 1994) (final rule).

<sup>9</sup> In the preamble to the proposed regulation, FDA had added that a “required bioequivalence study is one that meets any FDA guidance document or is otherwise reasonable in design and purports to show that the drug product for which the applicant seeks exclusivity is bioequivalent to the listed drug.” 54 Fed. Reg. at 28895. Rejecting concerns that generic manufacturers engaged in “file first fix later” practices, however, FDA declined to establish criteria to determine whether changes to an ANDA have been so substantial that it can no longer be considered to have been the first filed. Instead, the agency would rely on its decision in 1992 to no longer accept ANDAs lacking complete bioequivalence study data (if such data are required for approval) and use a “case-by-case approach” to ANDA changes. 59 Fed. Reg. at 50354. FDA added, however, that “[a] decision by the agency after receipt of an application that the bioequivalence information is inadequate for approval does not necessarily mean that the application was not substantially complete at the time of submission.” *Id.*

there was no paragraph IV certification to the listed drug prior to December 8, 2003.<sup>10</sup> Congress made two changes that were explicitly retroactive.<sup>11</sup>

Under the new scheme, if an ANDA “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 after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.”<sup>12</sup> As before, the first generic applicant to file an ANDA containing a paragraph IV certification is eligible for 180 days of exclusivity, during which FDA may not approve a subsequently filed ANDA that challenged a patent for the same drug. Now, however, the exclusivity period is calculated from the date of the first commercial marketing of the drug product (including the listed drug product) by a first applicant. A court decision does not by itself start the 180 days under the new scheme.

Congress also added a scheme for forfeiture of exclusivity.<sup>13</sup> The 180-day exclusivity period is forfeited by a first applicant that fails to market the drug by the later of: (1) 75 days after the date on which approval of its application is effective, or 30 months after its application was submitted, whichever is earlier; or (2) 75 days after the date on which, as to each patent that is the subject of a paragraph IV certification by the first applicant (qualifying it for exclusivity), a court has found the patent invalid or not infringed, a court signs a settlement order or consent decree finding the patent invalid or not infringed, or the patent information is withdrawn by the holder of the approved NDA. The first applicant also forfeits exclusivity if any of the following occurs: (1) the first applicant withdraws its application or FDA considers it withdrawn because it did not meet the requirements for approval; (2) the first applicant amends or withdraws all of the paragraph IV certifications that qualified it for exclusivity; (3) the first applicant fails to obtain tentative approval of its application within 30 months after it was filed (unless the failure is caused by a change in or review of the requirements for approval of the application imposed after it was filed); (4) the first applicant enters into an agreement with another ANDA applicant, the NDA holder, or a patent holder, and the FTC or a court has found that the agreement violates the antitrust laws; or (5) all of the patents as to which the first applicant filed a paragraph IV certification qualifying it for exclusivity have expired. Forfeiture events are determined individually for each first applicant. If all first applicants forfeit their 180-day exclusivity, any subsequent ANDA approval may be made effective immediately; exclusivity does not roll over to a subsequent ANDA applicant.

In 2003 Congress added definitions for terms in the provision, including “180-day exclusivity period,” “first applicant,” “substantially complete application,” and

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<sup>10</sup> Pub. L. No. 108-173, § 1102(a).

<sup>11</sup> *First*, the provision requiring forfeiture of exclusivity if the first applicant enters into a settlement agreement found to violate the antitrust laws, 21 U.S.C. § 355(j)(5)(D)(i)(V), applies retroactively to old ANDAs. *See* Pub. L. No. 108-173 § 1102(b). *Second*, Congress made a retroactive change to the “court decision” trigger for exclusivity. *See id.*; *see also* FDA, Draft Guidance for Industry, *Listed Drugs, 30-Month Stays, and Approval of ANDAs and 505(b)(2) Applications Under Hatch-Waxman, as Amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003* (October 2004), withdrawn in 2013 (78 Fed. Reg. 48175 (Aug. 7, 2013)); *also infra* section 0.

<sup>12</sup> 21 U.S.C. § 355(j)(5)(B)(iv).

<sup>13</sup> 21 U.S.C. § 355(j)(5)(D).

“tentative approval.”<sup>14</sup> The “180-day exclusivity period” is the “180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective” under the 180-day exclusivity provision. A “first applicant” is “an applicant that, on the first day on which a substantially complete application containing a [paragraph IV certification] is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification] for the drug.”<sup>15</sup> A “substantially complete application” is “an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by [section 505(j)(2)(A)].” “Tentative approval” means “notification to an applicant by the Secretary that an application under this subsection meets the requirements of [section 505(j)(2)(A)], but cannot receive effective approval because the application does not meet the requirements of this subparagraph, there is a period of exclusivity for the listed drug under [section 505(j)(2)(F)] or section 505A, or there is a 7-year period of exclusivity for the listed drug under section 527.”

In early 2015, FDA proposed regulations implementing the 2003 amendments to the Hatch–Waxman scheme, including a few regulations addressing 180-day exclusivity.<sup>16</sup> For instance, the agency proposed regulatory definitions that track the new statutory definitions for “180-day exclusivity period,” “first applicant,” and “substantially complete application.”<sup>17</sup> The agency also proposed a new definition for “commercial marketing”<sup>18</sup> and extensive revisions to sections 314.95 and 314.101 of its regulations to address the timing of notice of paragraph IV certifications. The new notice regulations are discussed in section II.B.1 below.

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<sup>14</sup> 21 U.S.C. § 355(j)(5)(B)(iv).

<sup>15</sup> “Lawfully maintains” was not defined in the statute; the phrase was added only when the House-passed and Senate-passed bills were in conference committee. FDA generally takes the view that an applicant cannot “lawfully maintain” a patent challenge if it loses the ensuing litigation. *See, e.g.*, 21 C.F.R. § 314.94(a)(12)(viii)(A) & *Proposed* 21 C.F.R. § 314.94(a)(12)(viii)(A).

<sup>16</sup> 80 Fed. Reg. 6802 (Feb. 6, 2015).

<sup>17</sup> The “180-day exclusivity period” would be defined as the “180-day period beginning on the date of the first commercial marketing of the drug (including commercial marketing of the reference listed drug) by any first applicant. The 180-day period ends on the day before the date on which an ANDA submitted by an applicant other than a first applicant could be approved.” *Proposed* 21 C.F.R. § 314.3(b). A “first applicant” would be “an applicant that, on the first day on which a substantially complete ANDA containing a paragraph IV certification is submitted for approval of a drug, submits a substantially complete ANDA that contains, and for which the applicant lawfully maintains, a paragraph IV certification for the drug.” *Id.* This would replace the definition of the “applicant submitting the first application” in current 21 C.F.R. § 314.107(c)(2). A “substantially complete application” would be “an ANDA that on its face is sufficiently complete to permit a substantive review and contains all the information required under section 505(j)(2)(A) of the Federal Food, Drug, and Cosmetic Act and § 314.94.” *Id.*

<sup>18</sup> “Commercial marketing” would mean “the introduction or delivery for introduction into interstate commerce of a drug product described in an approved ANDA, outside the control of the ANDA holder, except for investigational use under part 312 of this chapter, but does not include transfer of the drug product for reasons other than sale to parties identified in the approved ANDA.” *Proposed* 21 C.F.R. § 314.3(b). This proposed definition is based on the definition of the term in current section 314.107, which in turn would be deleted, although the agency is rewording its treatment of transfers in order to clarify that shipment to a party named in the ANDA for purposes described in the ANDA (e.g., contract packaging) is not “commercial marketing” even though it arguably places the drug products outside of the control of the manufacturer. *See* 80 Fed. Reg. at 6812.

Finally, although the proposed regulations do not address the forfeiture provisions of the 2003 amendments, the agency does propose deleting 21 C.F.R. § 314.107(c)(3), which describes the potential consequences of a first applicant's failure to "actively pursue" approval of its ANDA.<sup>19</sup> In FDA's view, this regulation has been superseded by the statutory forfeiture provisions.<sup>20</sup> The agency otherwise noted that it is implementing 180-day exclusivity "directly from the statute" and that it "will determine if additional rulemaking is necessary in the future."<sup>21</sup> FDA noted that it may open dockets for public comment on factual scenarios that raise novel issues regarding forfeiture of exclusivity, as it has done in the past.<sup>22</sup>

### C. *Food and Drug Administration Safety and Innovation Act (FDASIA)*

In 2012, Congress modified the terms of one forfeiture provision.<sup>23</sup> Under the provision in question, as enacted in 2003, a first applicant forfeits exclusivity if it fails to obtain tentative approval within 30 months of the date on which its application was filed (unless the failure was caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application was filed). Under changes made in 2012, this deadline is extended from 30 months to 40 months (during the period of July 9, 2012 to September 30, 2015) and from 30 months to 36 months (during the period of October 1, 2015 to September 30, 2016) for any ANDA submitted between January 9, 2010 and July 9, 2012 with a paragraph IV certification (and any ANDA amended during that time to include its first paragraph IV certification). Further, for any ANDA submitted prior to July 9, 2012 that is amended between July 10, 2012 and September 30, 2017 to contain its first paragraph IV certification, the amendment date—rather than the original ANDA submission date—starts the 30-month tentative approval forfeiture period.

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<sup>19</sup> This regulation provides that if FDA concludes that the first applicant "is not actively pursuing approval of its abbreviated application, FDA will make the approval of subsequent abbreviated applications immediately effective if they are otherwise eligible for an immediately effective approval." 21 C.F.R. § 314.107(c)(3).

<sup>20</sup> 80 Fed. Reg. at 6866.

<sup>21</sup> 80 Fed. Reg. at 6807.

<sup>22</sup> 80 Fed. Reg. at 6807. As noted *supra*, note 6, the agency plans to release guidance in 2016 on 180-day exclusivity issues. The guidance docket should provide an opportunity for public comment.

<sup>23</sup> Pub. L. No. 112-144 (2012). These changes were part of the Generic Drug User Fee Amendments of 2012, which provided the agency with additional resources in order to reduce its backlog of pending ANDAs and reduce the average time required to review ANDAs.

## II. INTERPRETIVE ISSUES

### A. Which Rules Apply

1. Which scheme applies, if some ANDAs to the reference listed drug were submitted before the MMA and others were submitted after the MMA, and the first paragraph IV certification came after?

*Short answer.* In April 2009, FDA decided that the old scheme applies to every ANDA in this situation.

*Discussion.* The “Effective Date” provision of the 2003 legislation states that the changes to 180-day exclusivity are “effective only with respect to an [ANDA] filed . . . after [December 8, 2003] for a listed drug for which no [paragraph IV certification] was made before [December 8, 2003].”<sup>24</sup> As FDA has noted, this is straightforward to apply when either: (1) all ANDAs for a particular drug were submitted after the MMA, or (2) at least one paragraph IV certification was submitted before the MMA.<sup>25</sup> In 2009, however, it was faced with the first of what it predicted would be “a number” of cases where generic applications straddled the December 8 cutoff (some before, some after), and the first paragraph IV certification occurred *after* the cutoff.

The relevant case involved generic versions of Topamax® (topiramate capsules) Sprinkle Capsules. Barr Laboratories submitted an ANDA in July 2002, containing a paragraph III certification to U.S. Patent No. 4,513,006. After enactment of the MMA, Cobalt submitted an ANDA containing a paragraph IV certification to the same patent. In 2006, the NDA holder listed U.S. Patent No. 7,125,560, and both applicants submitted paragraph IV certifications. The agency concluded, first, that the *same* rules should apply to both ANDAs,<sup>26</sup> and second, that it might lack authority to apply the new rules to old ANDAs.<sup>27</sup> Consequently, both Barr and Cobalt would be subject to the old rules.

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<sup>24</sup> Pub. L. No. 108-173, § 1102(b)(1).

<sup>25</sup> Letter from Gary Buehler, Director, Office of Generic Drugs (OGD), Center for Drug Evaluation and Research (CDER), FDA, to ANDA Applicant (Apr. 15, 2009) (regarding ANDA 76-448 and ANDA 77-868, both for topiramate sprinkle capsules).

<sup>26</sup> FDA reasoned that Congress likely intended the same exclusivity scheme to apply to ANDAs with the same listed drug. The schemes are sufficiently different that conflicts might arise, the agency concluded, and application of different schemes to applicants referencing the same drug could result in disparate treatment of applicants. *Id.*

<sup>27</sup> This is because the effective date provision states that the new scheme applies “only” to an ANDA filed after December 8, 2003. *Id.* at 4. Further, applying the new scheme to pre-MMA ANDAs would mean applying the forfeiture provisions—which include forfeiture for failure to obtain tentative approval within a 30-month deadline. The agency noted that an ANDA applicant might therefore forfeit exclusivity for failure to satisfy a criterion that did not exist at the time the ANDA was submitted or for much of the time the ANDA was pending. This, it added, does not seem consistent with the general principle that statutes are to be applied prospectively unless Congress signals otherwise. *Id.* Other provisions of the MMA were expressly retroactive, the agency added. *Id.* at 4-5.



## B. Earning Exclusivity

1. *Is an ANDA applicant eligible for 180-day exclusivity if it also included a paragraph III certification to a later-expiring patent, suggesting it has no real intent to market before expiry of the patent to which it provided a paragraph IV certification?*

*Short Answer.* Yes. This issue arises only under the new scheme, in which exclusivity is awarded product by product—that is, to the first applicant (or applicants) to submit a paragraph IV certification to a particular reference product. FDA concluded in 2010 that the first applicant to submit a paragraph IV certification to *any* patent listed for the reference listed drug is eligible for 180-day exclusivity, *even if* that applicant also includes a paragraph III certification to a later-expiring patent claiming the same drug.

*Discussion.* The controversy in 2010 involved generic copies of Combivir (lamivudine and zidovudine) tablets. At issue were two listed patents: U.S. Patent No. 5,859,021 (the ‘021 patent) and U.S. Patent No. 5,905,082 (the ‘082 patent), expiring on May 15, 2012 and November 18, 2016, respectively. In June 2007, Teva submitted an ANDA containing a paragraph IV certification to the earlier-expiring ‘021 patent and a paragraph III certification to the later-expiring ‘082 patent. In January 2008, Lupin submitted an ANDA containing paragraph IV certifications to both. Later that year, Teva amended its ANDA to contain a paragraph IV certification to the ‘082 patent. Lupin argued that Teva was not a “first applicant” eligible for exclusivity.<sup>28</sup> It based this argument on Teva’s paragraph III certification to the ‘082 patent. It pointed out that a paragraph III certification to a patent expiring in 2016 *meant* that, in fact, Teva was not *really* seeking permission to market before expiry of the patent expiring in 2012. The paragraph IV certification to the ‘021 patent was “nothing more than a sham filing designed solely to attempt to secure generic exclusivity.”

FDA pointed out that in general the scheme makes it “advantageous for an applicant to submit paragraph IV certifications to as many patents as it appropriately can on that first day.”<sup>29</sup> It added that, with this in mind, it was “not immediately obvious” why Teva had challenged *only* the ‘021 patent in its initial application. Nevertheless, FDA reasoned, under the statute an applicant that submits a paragraph IV certification is a “first applicant . . . if on the first day any applicant submits a substantially complete application containing a paragraph IV certification, the applicant submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification].”<sup>30</sup> FDA denied Lupin’s petition, finding the statute requires “a” paragraph IV certification, not a paragraph IV certification to *each* patent or a paragraph IV certification to the *latest-expiring* patent. Teva had been the first to file a paragraph IV certification to a patent listed for Combivir and otherwise met the statutory requirements, and the agency “need not second guess the

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<sup>28</sup> Lupin Limited, Citizen Petition, Docket No. FDA-2010-P-0549 (Oct. 18, 2010).

<sup>29</sup> Letter from Janet Woodcock, M.D., Director, CDER, to William A. Rakoczy, Esq. and Lara E. FitzSimmons, Esq., Rakoczy Molino Mazzochi Siwik LLP, Docket No. FDA-2010-P-0549 (May 25, 2011).

<sup>30</sup> *Id.* at 6 (citing FDCA § 505(j)(5)(B)(iv)(II)(bb) (emphasis added by FDA) (internal quotations and citations omitted)).

particular strategy Teva has employed in its patent challenge.”<sup>31</sup> Thus Teva was eligible for 180-day exclusivity.

2. *When must an ANDA applicant send notice of its paragraph IV certification to the innovator, in order to be eligible for 180-day exclusivity?*

Short answer. The answer is the same under the old scheme and the new scheme. In the case of an original ANDA containing a paragraph IV certification, the first applicant must send notice of the paragraph IV certification to the patent owner and the NDA holder no later than 20 days after the date of the postmark on the notice from FDA that the ANDA has been filed.<sup>32</sup> In the case of an ANDA amendment (to address a newly issued and listed patent), notice must be provided “when” the generic applicant submits the amendment and certification in question.<sup>33</sup> Further, FDA has taken the position that the controlling dates for determination of first applicant status are the certification date in the case of an original ANDA and the notice date (which should be the same as the certification date) in the case of an ANDA amendment. Moreover, if notice is provided *after* an amendment and certification are filed, i.e., if notice is not timely, agency policy constructively moves the certification’s date (and therefore the controlling date for exclusivity eligibility) to the date on which the applicant mailed the notice. Since the 2009 article, slightly different timing questions have arisen: whether a generic applicant may provide notice before submission or acceptance of the ANDA or ANDA amendment in question, and (separately) whether it may provide notice before a newly issued patent is listed in the Orange Book.<sup>34</sup> As discussed below, FDA and the courts have concluded that an applicant may *not* provide notice before the agency accepts the application or amendment in question, and the agency has separately proposed that notice be deemed invalid if sent before the first working day after the day the patent is listed in the Orange Book.

Discussion. A first applicant must provide timely notice of its paragraph IV certification to the NDA holder and patent owner. As originally enacted, section 505(j)(2)(B) of the statute required an ANDA applicant making a paragraph IV certification to “include in the application” a statement that the applicant “will give” notice to the patent owner and NDA holder. The statute did not explicitly address the timing of that notice, but it added that if the ANDA was amended to include a paragraph IV certification, the notice “shall be given when the amended application is submitted.”<sup>35</sup> Section 505(j)(5) in turn attached exclusivity to the first submitted ANDA with a paragraph IV certification.<sup>36</sup> FDA’s implementing regulations explained that the sponsor of an original ANDA was required to provide notice “when it receives from FDA an acknowledgment letter stating that its [ANDA] is

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<sup>31</sup> *Id.* at 6.

<sup>32</sup> 21 U.S.C. § 355(j)(2)(B)(ii)(II).

<sup>33</sup> 21 U.S.C. § 355(j)(2)(B)(ii)(I).

<sup>34</sup> References to the “Orange Book” in this article are to the relevant edition of FDA’s Approved Drug Products with Therapeutic Equivalence Evaluations, now in its 36th edition.

<sup>35</sup> 21 U.S.C. § 355(j)(2)(B)(i), (iii) (1985).

<sup>36</sup> 21 U.S.C. § 355(j)(5)(B)(iv) (1985).

sufficiently complete to permit a substantive review.”<sup>37</sup> Further, if an ANDA was amended to include a paragraph IV certification, the applicant was to “send the notice . . . at the same time that the amendment to the abbreviated application is submitted to FDA.”<sup>38</sup>

Controversies arising under the initial statutory and regulatory scheme revolved around the timing of notice in connection with paragraph IV certifications in ANDA amendments. For instance, in litigation relating to generic versions of Neurontin® (gabapentin), the D.C. Circuit allowed FDA to penalize Purepac for failure to provide notice simultaneously with its amended ANDA by postponing the paragraph IV certification’s effective date (rather than by nullifying the certification, as a competing generic applicant had urged).<sup>39</sup> In another case involving Purepac and generic versions of Glucophage® (metformin), the agency reasoned that the controlling dates for determination of first applicant status were the certification date in the case of an original ANDA and the notice date in the case of an ANDA amendment. The parties settled before the court could rule on this agency interpretation.<sup>40</sup> These cases are discussed in more detail in the earlier articles, and there have been no relevant developments since 2009 regarding the old scheme.

Congress amended the relevant provisions in 2003. Section 505(j)(2)(B) continues to require a generic applicant to “include” in its application a statement that the applicant “will give notice” as required under that section. But it addressed the timing of the notice more precisely. Specifically, in the case of an original ANDA the paragraph IV notice must be provided no later than 20 days after the date of the postmark on the notice from FDA that the ANDA has been filed.<sup>41</sup> The 2003 amendments did not change the statutory language stating that in the case of an ANDA amendment, notice must be provided “when” the generic applicant submits the amendment in question.<sup>42</sup>

The 2009 article discussed two citizen petitions arising under the new notice language.<sup>43</sup> In the more significant of the two, an ANDA was submitted for a drug with no listed patents; after a patent was later listed, this initial generic applicant filed a certification amendment and provided simultaneous notice, complying therefore with the timing rules. In the interim, however, after the patent issued, a competing generic applicant had filed its own original ANDA with a paragraph IV certification. This subsequent applicant sent its notice *after* the initial applicant’s amendment, complying also with the timing rules. In other words, the initial applicant was subject to the timing rules for amended ANDAs, and the second applicant was subject to the timing rules for original ANDAs. Although each

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<sup>37</sup> 21 C.F.R. § 314.95(b).

<sup>38</sup> 21 C.F.R. § 314.95(d).

<sup>39</sup> *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877 (D.C. Cir. 2004), *aff’g TorPharm, Inc. v. Thompson*, 260 F. Supp. 2d 69 (D.D.C. 2003). See 2009 Exclusivity Article, *supra* note 4, at 341.

<sup>40</sup> See *IVAX, Purepac Settle Metformin 180-Day Generic Drug Exclusivity Suit*, FDA WEEK (Dec. 5, 2003); Sue Sutter, *Glucophage XR Settlement: Purepac, IVAX Split Generic Profits for 180 Days*, 15 HEALTH NEWS DAILY 2 (Nov. 28, 2003). See 2009 Exclusivity Article, *supra* note 4, at 341 n.4.

<sup>41</sup> 21 U.S.C. § 355(j)(2)(B)(ii)(II).

<sup>42</sup> 21 U.S.C. § 355(j)(2)(B)(ii)(I).

<sup>43</sup> *IVAX Pharmaceuticals, Inc., Citizen Petition*, Docket No. 2004P-0520 (Nov. 19, 2004) (withdrawn); *Mylan Pharmaceuticals, Inc., Citizen Petition*, Docket No. 2006P-0245 (June 12, 2006) (withdrawn). See 2009 Exclusivity Article, *supra* note 4, at 342.

complied with the timing rules applicable to its particular situation, the initial applicant argued that the *notice date* in *both* cases (rather than the certification date for original ANDAs) was the key date for determining eligibility for exclusivity. FDA apparently disagreed because it awarded exclusivity to the subsequent applicant, and the controversy was not litigated.<sup>44</sup>

More recently, the question has arisen whether a generic applicant may send notice of its paragraph IV certification prior to FDA acceptance of its application for review. Several courts have found that premature notices are improper, null, void, and without legal effect.

One fairly typical case before the United States District Court for the District of Delaware involved a generic application referencing Samsca® (tolvaptan). FDA approved Samsca on May 19, 2009, for the treatment of hyponatremia. Otsuka Pharmaceutical, the NDA holder, has listed two patents, expiring in 2020 and 2026. On or about October 10, 2013, Par Pharmaceutical sent Otsuka notice of paragraph IV certifications to both patents, despite the fact that (as alleged by Otsuka) Par did not have an ANDA accepted for review by FDA.<sup>45</sup> Otsuka brought suit in November 2013, asking for a declaration that the notice letters were improper, null, void, and without legal effect, and therefore also that the letters did not trigger the patent litigation provisions of section 505(j) of the FDCA.<sup>46</sup> The district court granted the relief requested.<sup>47</sup> Various other district courts have reached the same conclusion.<sup>48</sup>

In another variation, the notice related to a patent listed long after the ANDA had been submitted but before the ANDA had been accepted for review. The case involved an ANDA referencing Allergan's Restasis® (cyclosporine). FDA approved Restasis in 2002 to increase tear production in patients experiencing ocular inflammation associated with keratoconjunctivitis sicca. Actavis submitted its ANDA in November 2011, and FDA responded in August 2013 that it refused to receive the ANDA. Actavis amended the ANDA in October 2013, submitting additional information. A patent issued in January 2014, at which point Actavis sent Allergan a paragraph IV notice.<sup>49</sup> Allergan sought a declaratory judgment that the ANDA in question "cannot trigger infringement" under the Patent Act, meaning

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<sup>44</sup> See 2009 Exclusivity Article, *supra* note 4, at 342.

<sup>45</sup> *Otsuka Pharm. Co. v. Par Pharm., Inc.*, C.A. No. 13-1979-RGA (D. Del. Nov. 26, 2013) (Complaint), ¶¶ 24-26.

<sup>46</sup> *Id.* ¶ 36. Otsuka reasoned that the notice provision uses the past tense when referring to filing of the ANDA. Specifically, the statute stipulates that an ANDA applicant must provide the reference product sponsor notice of a paragraph IV certification "not later than 20 days *after* the date of the postmark on the notice with which the Secretary informs the applicant that the [ANDA] *has been filed*." 21 U.S.C. § 355(j)(2)(B)(ii)(I) (emphasis added).

<sup>47</sup> *Otsuka Pharm. Co. v. Par Pharm., Inc.*, C.A. No. 13-1979-RGA (D. Del. Mar. 10, 2014) (Order).

<sup>48</sup> *E.g.*, *SB Pharmco Puerto Rico, Inc. v. Mutual Pharm. Co.*, 552 F. Supp. 2d 500 (E.D. Pa. 2008) (holding that a paragraph IV certification notice sent prior to FDA's receipt of an ANDA for filing was premature and ineffective); *Merck & Cie. v. Watson Pharm., Inc.*, C.A. No. 12-161-RGA (D. Del. Sept. 25, 2012) (Order) (noting that Watson's paragraph IV notice was sent "absent a received ANDA" and thus "is of no legal effect under 21 U.S.C. § 355(j)(5)(B)(iii) and 21 C.F.R. § 314.95(b)").

<sup>49</sup> See *Allergan v. Actavis*, No. 2:14-CV-638, 2014 WL 7336692, at \*3 (E.D. Tex. Dec. 23, 2014). The court's opinion does not indicate whether Actavis actually amended the ANDA in January to coincide with the notice. Moreover, although the record before the court did not indicate that FDA had responded to the October amendment, the paragraph IV notice apparently stated that FDA had, in fact, "received" the company's ANDA.

section 271(e)(2) of that statute, which creates an artificial act of infringement for purposes of district court jurisdiction where an ANDA contains a paragraph IV certification.<sup>50</sup> The court agreed, ruling that FDA receipt of the ANDA is necessary to trigger section 271(e)(2).<sup>51</sup>

Of relevance here, Actavis had taken the position that its paragraph IV notice was sufficient in itself to trigger jurisdiction. The district court agreed with Allergan and FDA, however, that because FDA had not yet accepted the ANDA, the paragraph IV notice was premature and improper under the FDCA and FDA's implementing regulation.<sup>52</sup> Further, although Actavis was amending its ANDA and the statute requires notice "at the time at which the applicant submits the amendment," the agency took the view that this provision applies *only* if the amendment is to an ANDA that FDA has *already* accepted for filing. The court found this reading of the statute persuasive. According to the court, "[t]o hold otherwise would invite generic manufacturers to submit incomplete or otherwise deficient applications, in order to secure their positions as the first-filed generic."<sup>53</sup> These companies could then "attempt to remedy any deficiencies through an amendment to their premature application, while claiming priority to the original application for purposes of securing exclusive access to the market and other benefits."<sup>54</sup> This is somewhat analogous to the "file first fix later" practices that were raised, but dismissed by FDA, in the original Hatch–Waxman rulemaking.<sup>55</sup>

Another case involved an ANDA referencing Suboxone® (buprenorphine and naloxone), which FDA approved in 2010 for maintenance treatment of opioid dependence. In July 2013, the generic applicant (Par) sent the NDA holder (Reckitt Benckiser) notice that it had submitted an ANDA with paragraph IV certifications to two listed patents. Reckitt Benckiser brought timely patent litigation with respect to this notice,<sup>56</sup> i.e., within 45 days, which ordinarily triggers a 30-month stay.<sup>57</sup> In February 2014, Par submitted a new paragraph IV notice (to a third patent), and Reckitt Benckiser amended its complaint within 45 days to assert infringement of this third patent.<sup>58</sup> Par, however, had sent both letters before receiving notice from FDA that its ANDA had been accepted; thus, an ANDA was not in fact pending. In March 2014, Par provided a third notice, which contained a paragraph IV certification to each of the three patents and *added* that FDA had accepted the ANDA for substantive review. Reckitt Benckiser consequently filed a second,

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<sup>50</sup> See 35 U.S.C. § 271(e)(2).

<sup>51</sup> *Allergan v. Actavis*, 2014 WL 7336692 at \*9–12 (noting that 35 U.S.C. § 271(e)(2), which makes it an act of infringement to "submit" an ANDA with a paragraph IV certification, requires that the ANDA be received, not merely delivered).

<sup>52</sup> *Id.* (citing 21 U.S.C. § 355(j)(2)(B)(ii)(I) and 21 C.F.R. § 314.95(b)).

<sup>53</sup> *Id.* at 11.

<sup>54</sup> *Id.*

<sup>55</sup> See *supra* note 9.

<sup>56</sup> *Reckitt Benckiser Pharm. Inc. v. Par Pharm.*, C.A. No. 13–1461–RGA (D. Del. Aug. 20, 2013) (Complaint, regarding July 2013 notification of ANDA containing a paragraph IV certification to U.S. Patent Nos. 8,475,832 and 8,017,150).

<sup>57</sup> See 21 U.S.C. § 355(j)(5)(B)(iii).

<sup>58</sup> *Reckitt Benckiser Pharms. Inc. v. Par Pharm., Inc.*, C.A. No. 13–1461–RGA (D. Del. Feb. 18, 2014) (Amended complaint, regarding February 2014 notification of a paragraph IV certification to U.S. Patent No. 8,603,514).

separate, lawsuit for patent infringement, and it included a request for declaratory judgment that Par's earlier notices were premature and ineffective to trigger the ANDA patent litigation process, including the 45-day deadline for filing an infringement action that triggers the 30-month stay.<sup>59</sup> It also sought to dismiss the first litigation, without prejudice, arguing that the court had lacked subject matter jurisdiction due to the ineffective notices Par had sent.<sup>60</sup> The motion to dismiss was granted, over Par's objection, without comment.<sup>61</sup> And although most of the pretrial schedule from the dismissed first litigation was adopted by the court in the second litigation, over Reckitt Benckiser's objections, the court made note of Par's "dubious" conduct.<sup>62</sup> Par has conceded that the 45-day deadline for triggering the 30-month stay did not commence until receipt of the March 2014 notice, i.e., that the initial notices had no effect.<sup>63</sup>

Although these disputes focus on whether early paragraph IV notices have legal effect for purposes of triggering a window for patent litigation that will stay ANDA approval, the agency's recent proposed rule *also* addresses whether an early paragraph IV certification qualifies the applicant for first applicant status. FDA's proposal specifies the date before which notice may not be given and the date by which notice must be given.<sup>64</sup>

*First*, with respect to an original ANDA with a paragraph IV certification, the applicant would be required to submit notice *on or after* the day it receives an "acknowledgment letter" or a "paragraph IV acknowledgment letter" from FDA, but no later than 20 days after the date of the postmark on the acknowledgment letter.<sup>65</sup> Put another way, in FDA's view, a window for submitting notice *opens* on the day it receives the acknowledgment letter and *closes* 20 days after the postmark on that letter. Also, to ensure that notices are not sent prematurely, the ANDA applicant would be required to include with the notice a statement that it *has received* the

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<sup>59</sup> *Reckitt Benckiser Pharms. Inc. v. Par Pharm., Inc.*, C.A. No. 14-422-RGA (D. Del. Apr. 4, 2014) (Complaint).

<sup>60</sup> *Reckitt Benckiser Pharms. Inc. v. Par Pharm., Inc.*, C.A. No. 13-1461-RGA (D. Del. Apr. 17, 2014) (Motion to dismiss the amended complaint and opening brief in support of motion to dismiss).

<sup>61</sup> *Reckitt Benckiser Pharms. Inc. v. Par Pharm., Inc.*, C.A. No. 13-1461-RGA (D. Del. May 17, 2014) (Order granting plaintiff's motion to dismiss).

<sup>62</sup> *Reckitt Benckiser Pharms. Inc. v. Par Pharm., Inc.*, C.A. No. 14-422-RGA (D. Del. May 28, 2014) (Order).

<sup>63</sup> E.g., *Reckitt Benckiser Pharms. Inc. v. Par Pharm., Inc.*, C.A. No. 13-1461-RGA (D. Del. May 4, 2014) (plaintiff's reply in support of motion to dismiss) ("Par acknowledges that the 30-month stay of FDA marketing approval of Par's ANDA provided under the Hatch-Waxman Act was not triggered until Par served its March 2014 Paragraph IV Notice.").

<sup>64</sup> See generally 80 Fed. Reg. at 6831-6836; *id.* at 6832 (citing *SB Pharmco Puerto Rico*, 552 F. Supp. 2d at 510, for the proposition that premature notice "could accelerate the timing provisions and litigation process well beyond the framework that Congress intended").

<sup>65</sup> *Proposed 21 C.F.R. §§ 314.95(b)(1), (b)(2)*. An "acknowledgment letter" would be defined as "a written, postmarked communication from FDA to an applicant stating that the Agency has determined that a[n] . . . ANDA is sufficiently complete to permit a substantive review. An acknowledgment letter indicates that the . . . ANDA is regarded as received." A paragraph IV acknowledgment letter would be defined as "a written, postmarked communication from FDA to an applicant stating that the Agency has determined that a[n] . . . ANDA containing a paragraph IV certification is sufficiently complete to permit a substantive review. A paragraph IV acknowledgment letter indicates that . . . the ANDA is regarded as received." *Proposed 21 C.F.R. § 314.3(b)*.

acknowledgment letter in question.<sup>66</sup> This rule would also apply where the ANDA applicant amended a not-yet-received application to contain a new paragraph IV certification. That is, if the original ANDA had not yet been acknowledged (deemed received) by FDA, notice at the time of amendment would be premature.<sup>67</sup> If instead the original ANDA *had* been deemed received, and the applicant amended with a paragraph IV certification, FDA would require the applicant to provide notice *on the day* that it submitted the amendment in question.<sup>68</sup> This would be true only if the patent were already listed in Orange Book; notice would also be premature if sent before the first working day after the day the patent was listed in the Orange Book.<sup>69</sup> This last proposal is intended to “ensure that all ANDA applicants (irrespective of time zone) have a reasonable opportunity to be a first applicant with respect to a newly listed patent” and also to “eliminate the need for . . . burdensome serial notifications,” which result when an ANDA applicant is aware of a newly issued patent but unsure when the patent will appear in the Orange Book.<sup>70</sup> In all cases, premature notice would be invalid. Thus it would not trigger the 45-day period during which the NDA holder and patent owner may file suit and obtain a 30-month stay; moreover, the applicant would need to resend notice at the appropriate time to qualify for 180-day exclusivity.<sup>71</sup>

*Second*, in the case of an original ANDA, the relevant date for determining first applicant status is the submission date. If the applicant sends late notice, i.e., after the window, the ANDA submission date would be adjusted by the number of days beyond the window that the applicant delayed in sending notice.<sup>72</sup> In the case of an amendment to an ANDA, the relevant date for determining first applicant status is the date of submission of the amendment containing the certification in question (assuming timely notice), not the date the original ANDA was submitted.<sup>73</sup> In these cases, the acknowledgment letter may state that the ANDA was received for substantive review on the date on which the original ANDA was submitted, but this will *not* be the controlling date for exclusivity purposes. The *ANDA amendment date* will be the controlling date (assuming timely notice).<sup>74</sup> If the amending applicant sends late notice, the agency will constructively deem the amendment submission date to be the notice date. This memorializes the policy approved by the D.C. Circuit in the 2004 *Purepac* case.<sup>75</sup> Whether an original ANDA or an ANDA amendment,

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<sup>66</sup> Proposed 21 C.F.R. § 314.95(c)(3); see 80 Fed. Reg. at 6832.

<sup>67</sup> See 80 Fed. Reg. at 6832, 6834.

<sup>68</sup> Proposed 21 C.F.R. § 314.95(d)(1); see 80 Fed. Reg. at 6835. The agency also proposed to reiterate the statutory requirement that notice of a paragraph IV certification in an amendment must be provided even if the applicant has already provided notice with respect to another paragraph IV certification contained in the ANDA or an amendment or supplement to the ANDA. Proposed 21 C.F.R. § 314.95(d)(1); see 80 Fed. Reg. at 6834.

<sup>69</sup> 80 Fed. Reg. at 6835. See also proposed 21 C.F.R. §§ 314.95(b)(2), 314.94(a)(12)(viii)(C)(1)(ii).

<sup>70</sup> 80 Fed. Reg. at 6836.

<sup>71</sup> *Id.* at 6832.

<sup>72</sup> Proposed 21 C.F.R. § 314.101(b)(4); see 80 Fed. Reg. at 6840.

<sup>73</sup> See 80 Fed. Reg. at 6832, 6835.

<sup>74</sup> See *id.* at 6832.

<sup>75</sup> See *id.* at 6835 (citing *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877 (D.C. Cir. 2004), discussed *supra* in text accompanying note 39).

late notice results in adjustment of the date used to determine first applicant status. Consequently, if there is a subsequent applicant with a paragraph IV certification, late notice could cause the initial applicant to lose its eligibility for 180-day exclusivity.<sup>76</sup>

*Third*, whether certifying in an original or amended ANDA, the applicant would be required to amend its ANDA with documentation of the notice. Specifically, it would need to provide documentation that its notice was timely sent *and* a dated printout of the Orange Book entry showing the patent that is the subject of the paragraph IV certification.<sup>77</sup> This amendment would be due within 30 days after the last date on which notice was received by a person required to receive notice.<sup>78</sup>

3. *Is an applicant that submits a paragraph IV certification before patent expiry, but whose application is not accepted for review until after patent expiry, a “first applicant”?*

*Short answer.* This is a matter of first impression pending before the agency.

*Discussion.* This issue has arisen in connection with abbreviated applications referencing Restasis, discussed in the preceding subsection. Allergan listed U.S. Patent No. 5,474,979 (the ‘979 patent) in the Orange Book. InnoPharma submitted an ANDA on January 13, 2014, with a paragraph IV certification to the ‘979 patent, which was the only patent listed in the Orange Book at the time.<sup>79</sup> InnoPharma was the first to file a paragraph IV to the ‘979 patent, but the patent expired on May 27, 2014, before FDA issued an acknowledgment letter to the company and therefore before the company sent notice to Allergan. One day *after* InnoPharma submitted its application, Allergan listed another patent—U.S. Patent No. 8,629,111 (the ‘111 patent). It appears from docket filings that Akorn was the first (or one of the first) to file a paragraph IV certification to the ‘111 patent.<sup>80</sup> InnoPharma may not have been. FDA has opened a docket asking, in part, whether InnoPharma (who is not identified in its notice) is a “first applicant” for purposes of exclusivity.<sup>81</sup> InnoPharma has argued that it qualifies, noting that the acknowledgement letter from the agency, received by InnoPharma on July 21, 2015, “expressly stated that the date the application was deemed to have been received and acceptable for review (i.e., ‘substantially complete’)” was, in fact, January 13, 2014.<sup>82</sup> Akorn has argued that InnoPharma does not qualify, because it did not “perfect” its certification with valid

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<sup>76</sup> See *id.* at 6840.

<sup>77</sup> Proposed 21 C.F.R. § 314.95(e); see 80 Fed. Reg. at 6836, 6838.

<sup>78</sup> See 80 Fed. Reg. at 6840.

<sup>79</sup> See Comments of John Minogue, Senior Director, InnoPharma, Docket No. FDA-2015-N-2713 (Aug. 26, 2015) [hereinafter InnoPharma Comments].

<sup>80</sup> FDA noted that “one or more applicants” submitted paragraph IV certifications to the ‘111 patent when it was listed in January. See Letter from Johnny Young, Director (Acting), Division of Filing Review, OGD, CDER, FDA to Cyclosporine Ophthalmic Emulsion ANDA Applicant, Docket No. FDA-2015-N-2713. Akorn self-identified as one. See Comments of Kurt R. Karst, Counsel to Akorn Pharmaceuticals, Hyman, Phelps & McNamara, P.C., Docket No. FDA-2015-N-2713 (Sept. 28, 2015) [hereinafter Akorn Comments].

<sup>81</sup> See Letter from Johnny Young, Director (Acting), Division of Filing Review, OGD, CDER, FDA, to Cyclosporine Ophthalmic Emulsion ANDA Applicant, Docket No. FDA-2015-N-2713.

<sup>82</sup> InnoPharma Comments, *supra* note 79, at 3.



notice before patent expiry.<sup>83</sup> This matter was still pending at the time this Article was written.

4. *Must the ANDA applicant have been sued for patent infringement, and must it have prevailed in that litigation, in order to enjoy the benefit of 180-day exclusivity?*

*Short answer.* This issue arose with respect to old ANDAs, and the answer is that there is no suit or "successful defense" requirement. By way of contrast, if the first applicant is sued and *loses* the patent litigation, it is no longer eligible for exclusivity. There have been no meaningful developments with respect to this issue since the earlier articles.<sup>84</sup>

*Discussion.* As a reminder, under the original statutory scheme, approval of a subsequent ANDA could not take effect until the earlier of 180 days after: (1) the date FDA receives notice of the first commercial marketing of the first applicant's drug, or (2) the date of a court decision of invalidity or non-infringement with respect to the patent that was the subject of the paragraph IV certification. In the early years, FDA took the position that a first applicant was entitled to exclusivity only if it had been sued for patent infringement and it had prevailed.<sup>85</sup> In 1998, however, the D.C. Circuit ruled in *Mova Pharmaceutical v. Shalala* that the "successful defense" requirement was "gravely inconsistent with the text and structure of the statute."<sup>86</sup> FDA responded by issuing guidance confirming that the first applicant to submit a substantially complete abbreviated application with a paragraph IV certification was eligible for 180 days of exclusivity even though it had not been sued for patent infringement,<sup>87</sup> and it removed the successful defense requirement from its regulations.<sup>88</sup> That said, although the first applicant need not be sued, let alone prevail, to enjoy its 180-day exclusivity, if it is sued and *loses* (or for any other reason changes its certification from a paragraph IV to a paragraph III), it will no longer be eligible for exclusivity.<sup>89</sup> This is true today for new ANDAs as well.

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<sup>83</sup> See Akorn Comments, *supra* note 80.

<sup>84</sup> See 2009 Exclusivity Article, *supra* note 4, at 349-52.

<sup>85</sup> E.g., 54 Fed. Reg. at 28894 (proposed regulations); 59 Fed. Reg. at 50353 (final regulations).

<sup>86</sup> *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1069 (D.C.Cir. 1998); see also *Inwood Labs., Inc. v. Young*, 723 F. Supp. 1523, 1526 (D.D.C. 1989), *vacated as moot*, No. 89-5209 (D.C. Cir., Nov. 13, 1989) (finding that the statute does not permit FDA "to read into it a requirement of a lawsuit which is simply not there"); *Granutec, Inc. v. Shalala*, 139 F.3d 889 (4th Cir. 1998) (unpublished) (finding that the statute did not require successful defense against a patent infringement suit).

<sup>87</sup> See FDA, Guidance for Industry, *180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act* (June 1998).

<sup>88</sup> 63 Fed. Reg. 59710 (Nov. 5, 1998). See *Purepac Pharm. Co. v. Friedman*, 162 F.3d 1201 (D.C. Cir. 1998) (finding that FDA's "revised system for granting exclusivity" was consistent with the statute and *Mova* decision).

<sup>89</sup> FDA's regulations implementing the scheme have always provided that following a "final" judgment of infringement, a generic applicant must amend its paragraph IV certification to be a paragraph III certification, and that the application in question would no longer be considered one containing a paragraph IV certification. See 21 C.F.R. §314.94(a)(12)(viii)(A) (1995). Accordingly, it would no longer be eligible for 180-day exclusivity. The courts have agreed. In a dispute involving an ANDA referencing Novaldex® (tamoxifen), marketed by Zeneca for treatment of breast cancer, the innovator and first applicant settled their patent litigation, and the first applicant amended its ANDA to change the

5. *Does 180-day exclusivity “roll over” to a second ANDA applicant in the event that the first does not perfect its rights?*

*Answer.* No. FDA’s 1994 regulations implied as much, when they indicated that if the first applicant was “not actively pursuing approval” of its ANDA, FDA would make approval of subsequent ANDAs immediately effective.<sup>90</sup> In August 1999 draft regulations, the agency confirmed that exclusivity would not roll over to a second applicant, even if the first applicant withdrew its ANDA.<sup>91</sup> Although these regulations were not finalized, this has been FDA’s policy since the proposal issued. The new statutory language requires this result as well,<sup>92</sup> and there have been no meaningful developments since the prior articles. In some situations, however, the first applicant may waive its exclusivity in favor of a second applicant, as discussed in subsection II.B.7. To the outside observer, this may appear as a rollover.

6. *Can more than one ANDA applicant hold exclusivity at the same time for copies of the same innovator product?*

*Short answer.* Yes. For old ANDAs, FDA follows a policy of awarding exclusivity on a “patent-by-patent” basis, which can create multiple exclusivity periods for different first applicants for a single reference product. The agency has recently decided that although reissued patents may give rise to new paragraph IV certifications, those paragraph IV certifications do not give rise to new periods of exclusivity under the old scheme. Instead, if the original patent was the basis for the certification that gave rise to eligibility for exclusivity, a *new* paragraph IV certification is necessary to *remain* eligible for exclusivity. For new ANDAs, the statute provides that exclusivity will be “product by product,” rather than “patent by patent.” In other words, it provides for a single 180-day exclusivity period per reference product. But, if multiple applicants file substantially complete ANDAs with paragraph IV certifications on the same day as the first to do so, those applicants can share exclusivity. Under both the new scheme and the old scheme, FDA treats different dosage forms and strengths of the reference product as distinct products for which different (or the same) applicants may be first applicants.

a) *Multiple Patents for a Single Reference Product*

As discussed in the earlier articles, FDA developed the patent-by-patent approach to 180-day exclusivity for old ANDAs after judicial invalidation of the successful defense requirement. That policy had held that a generic applicant must prevail in patent litigation in order to receive exclusivity, and it effectively precluded more than one applicant from earning exclusivity. With the elimination of this rule

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certification from a paragraph IV to a paragraph III. The district court held that the ANDA in question was no longer considered to have “contained” a paragraph IV certification and that the generic applicant had thereby waived its eligibility for 180-day exclusivity. *Mylan Pharm. v. Henney*, 94 F. Supp. 2d 36 (D.D.C. 2000), *vacated and dismissed as moot*, 276 F.3d 627 (D.C. Cir. 2002). *See also supra* note 15 (one cannot “lawfully maintain” a paragraph IV certification under the post-MMA statutory language if one loses the resulting patent litigation).

<sup>90</sup> *See* 21 C.F.R. § 314.107(c)(4); 59 Fed. Reg. at 50367–50368.

<sup>91</sup> 64 Fed. Reg. 42873, 42875 (Aug. 6, 1999).

<sup>92</sup> *See* 21 U.S.C. § 355(j)(5)(D)(iii) (if all first applicants forfeit exclusivity, “no applicant shall be eligible”).

following *Mova Pharmaceutical v. Shalala*,<sup>93</sup> multiple eligible first applicants became a possibility. In a 1999 response to citizen petitions filed by American Pharmaceutical Partners (APP) and Pharmachemie, which involved paragraph IV certifications to different patents on different days, the agency concluded that “eligibility for exclusivity is to be determined on a patent-by-patent basis.”<sup>94</sup> In that case and the others cited in footnote 94, the subsequent ANDA applicants sharing in exclusivity were the first to file with respect to *different* patents and, in particular, the first to submit a paragraph IV certification to later listed patents.

In 2003, the agency issued guidance reaching the same conclusion—shared exclusivity—with respect to certifications (whether to one or multiple patents) submitted *on the same day*. This was in large part an effort to address—as FDA put it—the “number of cases in which multiple ANDA applicants or their representatives have sought to be the first to submit a patent challenge by lining up outside, and literally camping out adjacent to, an FDA building for periods ranging from 1 day to more than 3 weeks.”<sup>95</sup> Thus, when, on the same day, more than one applicant submits an ANDA for the same drug containing a paragraph IV certification to a listed patent, and no such certification was submitted previously, all the applicants share exclusivity.<sup>96</sup> In a case involving ANDAs referencing AstraZeneca’s Prilosec® (omeprazole), a federal district court found the statute ambiguous with respect to how many exclusivity periods may arise in connection with a single drug product, found FDA’s approach “not entirely irrational,” and granted the agency’s motion for summary judgment.<sup>97</sup> The D.C. Circuit affirmed.<sup>98</sup>

More recent cases have involved situations where a second company was the first to file a paragraph IV certification to a patent that had been listed all along. The first dispute involved generic applications referencing Aricept® (donepezil hydrochloride tablets). Ranbaxy filed an ANDA in the summer of 2003 and was the first to submit paragraph IV certifications to four listed patents. It included a paragraph III certification to a fifth patent, U.S. Patent No. 4,895,841 (the ‘841 patent), which was slated to expire first, in November 2010. Subsequent ANDA filers, including Teva, Apotex, and Eisai, did the same thing. In October 2005, however, Teva converted its paragraph III certification to a paragraph IV certification, meaning that it was the first applicant to submit a paragraph IV certification to the ‘841 patent. Although Ranbaxy’s ANDA remained unapproved, on account of the paragraph III

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<sup>93</sup> *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998); see *supra* section 0.

<sup>94</sup> Letter from Janet Woodcock, M.D., Director, CDER, to Robert F. Green, Esq. and Steven H. Sklar, Esq. Leydig, Voit & Mayer, Ltd. and Kate C. Beardsley, Esq. Buc & Beardsley, Docket No. 99P-1271 (Aug. 2, 1999). The earlier articles discussed two other controversies involving paragraph IV certifications to different patents on different days, one relating to ANDAs referencing Paxil® (paroxetine) and the other relating to ANDAs referencing Neurontin® (gabapentin). In both cases, the sharing applicant had been the first to file a paragraph IV certification to a later listed patent. See 2007 Exclusivity Article, *supra* note 4, at 57–58.

<sup>95</sup> FDA, Guidance for Industry, *180-Day Exclusivity When Multiple ANDAs Are Submitted on the Same Day* (July 2003), at 4.

<sup>96</sup> Exclusivity would be triggered for all first applicants for a specific listed patent when one of them began to market its product (or on the date of any court decision finding that patent invalid, unenforceable, or not infringing, if earlier). The commercial marketing trigger would begin the 180-day period as to all listed patents; a relevant court decision would trigger it only as to patents addressed in the decision. *Id.*

<sup>97</sup> *Apotex Inc. v. FDA*, 414 F. Supp. 2d 61, 74, 76 (D.D.C. 2006).

<sup>98</sup> *Apotex Inc. v. FDA*, 226 F. App’x 4 (D.C. Cir. 2007) (unpublished).

certification, FDA granted final approval to Teva in April 2008. (The agency was not aware that a court had preliminarily enjoined Teva from launching its product.<sup>99</sup>)

Apotex filed an emergency petition arguing that approval was erroneous because Teva was not entitled to share in the exclusivity, and Eisai submitted a citizen petition in 2010 asking (among other things) that the final approval be revoked.<sup>100</sup> In September 2010, FDA converted Teva's final approval to tentative approval, concluding that Teva's application was in fact blocked by Ranbaxy's 180-day exclusivity.<sup>101</sup> Further, it explained that its "shared exclusivity" policy did not apply. The agency explained that it invokes shared exclusivity when two applicants would otherwise *block each other*, as happens if both file paragraph IV certifications to every patent but each is first with respect to a different patent (for instance, because one patent was later listed). Shared exclusivity does not apply, however, in situations where one applicant (in this case, Ranbaxy) was first to file a paragraph IV certification to one patent and filed a paragraph III certification to another patent, to which another applicant (in this case, Teva) filed a paragraph IV certification.<sup>102</sup> FDA approved the Ranbaxy ANDA in November 2010, awarding it alone 180-day exclusivity.<sup>103</sup>

The second case involved ANDA amendments converting section viii statements to paragraph IV certifications.<sup>104</sup> In 2003, Watson filed an ANDA referencing Actos (pioglitazone) on the first day that ANDAs could be filed, and it included paragraph IV certifications to all ten patents listed in the Orange Book. Eight patents had only method-of-use claims, and the remaining two had both drug composition and method-of-use claims. All of the method-of-use claims related to combination therapy, however, and Watson was not seeking approval for combination therapy. Following discussions with the agency, Watson amended the paragraph IV certifications relating to those patents and claims to section viii statements. In 2012, after reaching an agreement with the innovator pursuant to which it would receive a license to the use patents and claims, Watson amended the section viii statements *back* to paragraph IV certifications. Mylan had submitted an ANDA on the same day as Watson, with paragraph IV certifications to the composition claims, but from the

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<sup>99</sup> Letter from Keith O. Webber, Deputy Director, Office of Pharmaceutical Science (OPS), CDER, FDA, to William B. Shultz, Esq., Zuckerman Spaeder LLP and Robert A. Dormer, Esq. and Kurt R. Karst, Esq., Hyman Phelps & McNamara P.C. (Sept. 17, 2010), at 1.

<sup>100</sup> Apotex Inc., Emergency Petition for Stay of Action, Docket No. FDA-2009-P-0326 (July 14, 2009); Eisai Inc., Citizen Petition, Docket No. FDA-2010-P-0430 (Aug. 12, 2010).

<sup>101</sup> Letter from Webber, *supra* note 99.

<sup>102</sup> *Id.*

<sup>103</sup> FDA also responded to the Apotex and Eisai petitions. The agency denied, as moot, the request to convert Teva's final approval to tentative approval. It also confirmed that Ranbaxy was the sole applicant eligible for 180-day exclusivity. Letter from Janet Woodcock, M.D., Director, CDER, to Shashank Upadhye, Esq., Apotex, Inc. and David M. Fox, Esq., Hogan Lovells US LLP, Docket Nos. FDA-2009-P-0326 and FDA-2010-P-0430 (Nov. 26, 2010). In the intervening years, two federal courts had stated, without ruling on the issue, that Ranbaxy and Teva shared exclusivity, because Teva had been the first to submit a paragraph IV certification to the '841 patent. *Teva Pharm. USA, Inc. v. Eisai Co., Ltd.*, C.A. No. 08-2344-GEB (D.N.J. Sept. 9, 2009) (Memorandum Opinion) (noting that the companies held "shared 180-day exclusivity"); *Apotex Inc. v. Eisai Inc.*, C.A. No. 1:09-cv-00477-JAB-LPA (M.D.N.C. Aug. 27, 2010) (stating that "Teva thus became eligible to share in Ranbaxy's 180-day marketing exclusivity period").

<sup>104</sup> See 21 U.S.C. § 355(j)(2)(A)(viii) (permitting an ANDA applicant to file a statement that a method of use patent does not claim a use for which the applicant is seeking approval).

outset it had included section viii statements to the method-of-use patents and claims. It amended its ANDA converting those to paragraph IV certifications, however, in 2010—two years before Watson amended its own section viii statements back to paragraph IV certifications.

In short, both companies were first filers with respect to the composition claims, but Mylan amended with paragraph IV certifications to the use patents and claims *before* Watson did. FDA took the view that Watson's original ANDA was defective because it included paragraph IV certifications to patents claiming uses that it sought to carve out.<sup>105</sup> Under the patent-by-patent approach applicable to old ANDAs, FDA determined that Mylan was the first to file with respect to the use patents and claims—through its earlier-filed ANDA amendment—and that its resulting exclusivity would block approval of Watson's ANDA.<sup>106</sup> The district court disagreed, holding that when Watson eventually amended its ANDA to include a paragraph IV certification to the use patents, the relevant date for first applicant status (as to those patents) was the date its original ANDA had been submitted. This, according to the court, made it a first applicant entitled to share exclusivity with Mylan.<sup>107</sup> As noted above (subsection II.B.2), FDA has proposed regulations consistent with its position in this litigation: the relevant date for determining first applicant status is the date of submission of the amendment containing the certification in question (as long as notice is timely), not the date the original ANDA was submitted.

*b) Reissue Patents for a Single Reference Product*

In the last few years, the question has arisen how FDA will handle paragraph IV certifications to reissued patents under the old ANDA patent-by-patent scheme. The Patent and Trademark Office will reissue a patent that was “through error, deemed wholly or partly inoperative or invalid, by reason of a defective specification or drawing, or by reason of the patentee claiming more or less than he had the right to claim.”<sup>108</sup> When a patent reissues, the patentee surrenders the original patent; a new patent issues, with a new patent number, and it lasts for the unexpired part of the term of the original patent.

FDA's recent proposal indicates that although the original patent is technically surrendered upon patent reissuance, the agency will treat the original and reissued patent as a “single bundle” of patent rights for purposes of patent certification requirements and 180-day exclusivity.<sup>109</sup> Accordingly, in order to lawfully maintain its paragraph IV certification for purposes of eligibility for 180-day exclusivity (unless that original patent was untimely filed), a first applicant would need to amend its pending ANDA to certify to a reissued patent within 30 days of the date of

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<sup>105</sup> *Watson Labs., Inc. v. Sebelius*, C.A. No. 12-1344 (ABJ) (D.D.C. Oct. 22, 2012) (Memorandum Opinion) at 9.

<sup>106</sup> *Id.* at 13 (emphasis added).

<sup>107</sup> FDA appealed that decision to the DC Circuit. The case was mooted in June 2013 due to the expiration of the 180-day exclusivity period, and the district court was ordered to vacate its opinion. *Watson Labs., Inc. v. Sebelius*, C.A. Nos. 12-5332 & 12-5342 (D.C. Cir. June 10, 2013) (Per Curiam Order).

<sup>108</sup> 35 U.S.C. § 251.

<sup>109</sup> 80 Fed. Reg. at 6821.

listing of the reissued patent in the Orange Book.<sup>110</sup> The original patent qualifying the first applicant for exclusivity will remain listed in the Orange Book until FDA determines that any 180-day exclusivity was extinguished.<sup>111</sup> If no applicant had submitted a paragraph IV certification to the original patent, the first ANDA applicant to submit a paragraph IV certification to the reissued patent could be eligible for 180-day exclusivity, “*if no other applicant already has qualified as a first applicant based on an earlier paragraph IV certification to another listed patent.*”<sup>112</sup> By implication, an applicant could not receive 180-day exclusivity for its paragraph IV certification to a reissued patent if the original patent already was the subject of a paragraph IV certification submitted by a different applicant.

This appears to be the approach that FDA took in 2008 and 2012 with respect to reissued patents covering Ultracet® (tramadol hydrochloride and acetaminophen) and Adderall XR® (dextroamphetamine mixed salts), respectively, although there do not appear to be any formal agency statements tied to those decisions. With respect to Ultracet, the agency approved an ANDA from Kali Laboratories in 2005, granting the company 180-day exclusivity stemming from its paragraph IV certification to U.S. Patent No. 5,336,691 (the ‘691 patent).<sup>113</sup> Three years later, when FDA approved an ANDA from Mylan with the first paragraph IV certification to U.S. Patent No. RE39,221 patent (the ‘221 patent), it did *not* grant exclusivity—even though the ANDAs in question were old ANDAs subject to the patent-by-patent scheme.<sup>114</sup> This would be consistent with having deemed the reissue patent (the ‘221 patent) the same as the parent patent (the ‘691 patent) for purposes of exclusivity. It appears that FDA took the same approach with an Actavis ANDA for a generic version of Adderall XR®, after Actavis was the first to submit a paragraph IV certification to a patent that was a reissue of another patent that previously had been the subject of another company’s paragraph IV certification. The approval letter does not indicate that Actavis was eligible for 180-day exclusivity.<sup>115</sup>

There is, however, a contrary December 2014 ruling from the Fourth Circuit in a controversy involving generic applications referencing Celebrex® (celecoxib). Teva was the first to file an ANDA with paragraph IV certifications, including to U.S. Patent No. 5,760,068. After the Federal Circuit found that many of the claims in the patent were invalid, Pfizer obtained a reissue of the patent, U.S. Patent No. RE44048. Several companies—Teva, Mylan, and Watson (Actavis)—filed paragraph IV certifications to the reissued patent on the same day. In a letter to the ANDA applicants, the agency addressed “whether a paragraph IV certification to a reissued patent gives rise to a new opportunity for 180-day exclusivity when one or more paragraph IV certifications to the original patent gave rise to the opportunity

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<sup>110</sup> Proposed 21 C.F.R. § 314.94(A)(12)(viii)(B).

<sup>111</sup> *Id.*

<sup>112</sup> 80 Fed. Reg. at 6846 (emphasis added).

<sup>113</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to W. Scott Groner, Kali Laboratories, Inc., approving ANDA 76-475 (Apr. 21, 2005).

<sup>114</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA to Ronald T. Groman, Director, Regulatory Affairs, Mylan Pharmaceuticals Inc., U.S. Agent for Alphapharm Pty Ltd approving ANDA 77-858 (Sept. 26, 2008).

<sup>115</sup> See Letter from Keith Webber, Ph.D. Deputy Director, OPS, CDER, FDA, to Janak Jadeja, Director, Regulatory Affairs, Actavis Elizabeth LLC, approving ANDA 077302 (June 22, 2012); see also Actavis Elizabeth LLC, Citizen Petition, Docket No. FDA-2010-P-0188 (Apr. 6, 2010) (withdrawn).

for 180-day exclusivity, a final court decision has issued determining that the original patent is invalid or not infringed, but subsequent to that decision, and prior to (a) any commercial marketing by a first applicant to the original patent, and (b) the agency needing to make a decision regarding 180-day exclusivity, the Patent and Trademark Office issues a reissued patent that references the original patent.”<sup>116</sup>

FDA concluded that the original and reissued patent represent a “single bundle of patent rights.” Thus, paragraph IV certifications to the reissued patent by subsequent ANDA filers cannot be the basis for separate periods of 180-day exclusivity.<sup>117</sup> Further, “eligibility for 180-day exclusivity is only available to the applicant that first filed a paragraph IV certification to the original patent, and that applicant must make a timely submission of a paragraph IV certification to the reissued patent to remain eligible for 180-day exclusivity.”<sup>118</sup> Although not relevant to the issue at hand, the agency also stated that the court decision invalidating the original patent—which did not address the reissued patent—did not trigger the first applicant’s exclusivity. Thus, Teva, who had been the first to file a paragraph IV certification to the original patent and who had also filed a paragraph IV certification to the reissued patent, was the sole first applicant eligible for 180-day exclusivity.

Mylan, Lupin, and Watson brought suit arguing, among other things, that they were entitled to share 180-day exclusivity, as a result of their paragraph IV certifications to the reissued patent.<sup>119</sup> Although the district court granted Mylan’s motion for judgment in favor of the FDA and dismissed the case,<sup>120</sup> the Fourth Circuit reversed and remanded. In a non-binding and unpublished but unanimous opinion, the court of appeals wrote that “the plain language of the statute indicates that each patent that is the subject of a certification may trigger exclusivity.” FDA’s interpretation of an original patent and reissued patent as a single bundle of rights, resulting in only a single 180-day exclusivity period, “violated plain statutory language.”<sup>121</sup> FDA’s recent proposed rule, which post-dates this decision, takes a contrary position, and there may therefore be more litigation ahead.

In the 2003 amendments, Congress effectively took a product-by-product approach to 180-day exclusivity for new ANDAs, by making exclusivity available only with respect to paragraph IV certifications made on the first day that any paragraph IV certification is made. Specifically, the statute now precludes approval for 180 days after first commercial marketing by “any” first applicant and precludes

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<sup>116</sup> Letter from Kathleen Uhl, Acting Director, OGD, CDER, FDA, to Celecoxib ANDA Applicants (April 24, 2014), at 1.

<sup>117</sup> FDA noted that it had taken this approach with respect to 180-day exclusivity for ANDAs referencing Mircette® (desogestrel/ethinyl estradiol and ethinyl estradiol), Ultracet® (tramadol hydrochloride/acetaminophen), and Adderall XR® (amphetamine/dextroamphetamine). *Id.* at 7–8.

<sup>118</sup> *Id.* at 11.

<sup>119</sup> See, e.g., *Mylan Pharms., Inc. v. FDA*, C.A. No. 1:14-CV-00075-IMK (N.D. W.Va. Apr. 25, 2014) (Complaint); *Mylan Pharms., Inc. v. FDA*, C.A. No. 1:14-CV-00075-IMK (N.D. W.Va. May 2, 2014) (Motion to Intervene and Complaint-in-Intervention by Lupin Pharmaceuticals, Inc.).

<sup>120</sup> *Mylan Pharms., Inc. v. FDA*, C.A. No. 1:14-CV-00075-IMK (N.D. W.Va. June 16, 2014) (Order).

<sup>121</sup> *Id.* at 15–17.

rollover if “all first applicants” forfeit their exclusivity.<sup>122</sup> Accordingly, there is one 180-day exclusivity period per reference product.<sup>123</sup>

c) *Different Reference Listed Drugs*

Since at least 1990, FDA has taken the position that different *strengths* of the reference product constitute different *products* for purposes of 180-day exclusivity—permitting a separate 180-day exclusivity period.<sup>124</sup> (This will be true under either scheme; it has nothing to do with the old scheme being patent by patent.) A federal district court found this permissible in a 1999 court decision involving generic applications referencing Zantac® (ranitidine), even where the differing strengths were covered by the same patent.<sup>125</sup> The court’s holding was later cited for the proposition that the same rule would pertain in the case of differing dosage forms.<sup>126</sup> FDA’s recently proposed regulations take the same approach by providing that an applicant that amends or supplements its ANDA, in order to seek approval for a different strength, must provide notice of any paragraph IV certification.<sup>127</sup> “Unlike other amendments and supplements,” the agency explains, “an amendment or supplement seeking approval of a different strength may refer to a different listed drug.”<sup>128</sup> Elsewhere FDA explains the connection to 180-day exclusivity, citing the Zantac litigation: “different strengths of a drug product constitute different drug products” and thus, “different ANDA applicants seeking

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<sup>122</sup> 21 U.S.C. § 355(j)(5)(B)(iv)(II)(bb) (defining “first applicant” to mean “an applicant that, on the first day on which a substantially complete application containing a [paragraph IV certification] is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification] for the drug.”); *see also* 149 Cong. Rec. 31783 (Nov. 25, 2003) (Senator Kennedy) (“and the exclusivity is available to more than one generic applicant, if they all challenge patents on the same day”); 21 U.S.C. § 355(j)(5)(D)(iii) (if all first applicants forfeit exclusivity, “no applicant shall be eligible”).

<sup>123</sup> *See also* 149 Cong. Rec. 31783 (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.”)

<sup>124</sup> *See Apotex, Inc. v. Shalala*, 53 F. Supp. 2d 454, 456 n.3 (D.D.C. 1999) (quoting FDA response to TorPharm citizen petition, in which the agency wrote: “In 1990, FDA determined that Purepac Pharmaceutical was not barred from final approval of its 20 mg nifedipine product by the 180-day market exclusivity the Agency had already awarded to Chase Laboratories for its 10 mg nifedipine product. Because each strength of the drug was a different drug product, exclusivity for the 10 mg product did not block approval of the 20 mg product. As a result, each strength was separately eligible for exclusivity.”).

<sup>125</sup> *See id.* at 463 (permitting Novopharm exclusivity for ANDA for 75-mg tablet, after Genpharm had enjoyed exclusivity for 150 and 300 mg tablets). In other words, exclusivity for old ANDAs was effectively *both* product-by-product *and* patent-by-patent; the first applicant (with a paragraph IV certification) to either a new product or a new patent would be eligible.

<sup>126</sup> *See, e.g., Mylan Pharm., Inc. v. Shalala*, 81 F. Supp. 2d 30, 35 n.8 (D.D.C. 2000) (“The tablet and capsule forms of the drug, however, are distinct products for FDA purposes and are thus each eligible for their own exclusivity.”); *see also* Susan Levine, Regulatory Counsel, OGD, CDER, FDA and Christopher Sorenson, Merchant & Gould P.C., *Forfeiture of 180-Day Exclusivity*, Presentation at GPhA Fall 2010 Technical Conference (2010), at slide 2, <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM237479.pdf> (“There can be more than one ‘first applicant’ IF ANDAs are submitted on the same day, OR on different days for different dosage forms and different strengths.”).

<sup>127</sup> *Proposed* 21 C.F.R. § 314.52(d)(3).

<sup>128</sup> 80 Fed. Reg. at 6835.



approval for different strengths of a drug product approved in a single NDA may each be first applicants with respect to a different strength of the drug product, if other applicable statutory and regulatory requirements are met.”<sup>129</sup>

7. *Are 180-day exclusivity rights waivable and/or transferable?*

*Short answer.* Yes. The first generic may relinquish its exclusivity altogether at any time and may waive its 180-day exclusivity rights in favor of another specific generic applicant after the exclusivity is triggered. This policy was developed under the old scheme, but it appears to remain true under the new scheme.

*Discussion.* Although the statute is silent on the issue, FDA has consistently permitted both waiver of exclusivity (meaning the decision to abandon exclusivity and permit FDA to approve any and all eligible subsequent applicants) and transfers of exclusivity (meaning the decision to sell the exclusivity term to a specific subsequent applicant). The terminology in FDA approval letters, decision letters, and policy statements, and the court decisions, can be a bit confusing; waiver is also called relinquishment, transfer is also called selective waiver, and the agency sometimes uses relinquishment when referring to an agreement between two companies.<sup>130</sup> However they are labeled, the distinction between the two types of decision is important, as the agency has developed differing policies. Specifically, in the late 1990s, the agency developed a policy that although the first generic could relinquish exclusivity at any time, it could transfer the exclusivity to another company only *after* the exclusivity had been triggered.<sup>131</sup> (Under the scheme at the time, exclusivity would be triggered by commercial marketing or a court decision of invalidity or non-infringement.) In 2004, the agency explained its reasoning for the distinction: if the first applicant could transfer its exclusivity at any time, a “market” for 180-day exclusivity might develop, leading to the submission of ANDAs “solely to claim exclusivity.”<sup>132</sup>

The courts have declined to intervene where FDA has permitted transfers of exclusivity. For instance, in 1997, a federal district court declined to “undo” a transfer of 180-day exclusivity for consideration, finding the agency’s interpretation of the statute neither impermissible nor arbitrary and capricious.<sup>133</sup> In that case, the agency also pointed out that it approves waivers and transfers of five-year and three-

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<sup>129</sup> *Id.* at 6813(citing *Apotex, Inc. v. Shalala*, 53 F. Supp. 2d 454 (D.D.C. 1999), *aff’d*, 1999 U.S. App. LEXIS 29571 (D.C. Cir. Oct. 8, 1999)). As a result, an amendment seeking approval for a different strength may have a later “submission date” (than the ANDA it amended) for purposes of determining eligibility for 180-day exclusivity relating to the (separate) reference product and for purposes of calculating forfeiture for failure to obtain timely tentative approval. *See id.*

<sup>130</sup> *E.g.*, Letter from Gary Buehler, Director, OGD, CDER, FDA, to Mark C. Shaw, Vice President, Regulatory Affairs and Compliance, Impax Laboratories, Inc. regarding ANDA 77-415 (Dec. 15, 2006) (“[W]e note that IMPAX and its marketing partner, TEVA Pharmaceuticals, have entered into an agreement with Anchem regarding the relinquishment or selective waiver of exclusivity for the 300 mg strength.”).

<sup>131</sup> *E.g.*, 64 Fed. Reg. 42873, 42881 (Aug. 6, 1999) (proposed regulation).

<sup>132</sup> Letter from William K. Hubbard, Associate Commissioner for Policy and Planning, FDA, to Bert W. Rein and William A. McGrath, Wiley Rein & Fielding LLP, Docket No. 2004P-0227 (July 2, 2004).

<sup>133</sup> *Boehringer Ingelheim Corp. v. Shalala*, 993 F. Supp. 1 (D.D.C. 1997); *see also Mylan Pharm., Inc. v. Shalala*, 81 F. Supp. 2d 30 (D.D.C. 2000) (confirming that “[c]xclusivity periods are a transferable commodity which can be waived in favor of another generic manufacturer for a substantial price”).

year exclusivity under the Hatch–Waxman amendments.<sup>134</sup> Further, it appears that FDA continues to permit transfers of exclusivity under the new scheme. Anchen Pharmaceuticals was the first ANDA applicant to submit a substantially complete ANDA with paragraph IV certifications to two patents listed by GlaxoSmithKline with respect to Wellbutrin® XL (bupropion hydrochloride, extended release, 150 mg and 300 mg tablets). FDA approved the ANDA on December 14, 2006, after a federal court ruled that one patent was not infringed and dismissed the infringement case with respect to the second patent. The approval letter indicated that Anchen would enjoy 180–day exclusivity.<sup>135</sup> One day later, the agency issued final approval to another generic applicant, IMPAX Laboratories, with respect to the 300 mg tablets, noting that Anchen had been the first applicant entitled to exclusivity *and* that the companies had entered into an agreement regarding “relinquishment or selective waiver of exclusivity for the 300 mg strength.”<sup>136</sup>

It also appears that, for old ANDAs where exclusivity is earned on a patent-by-patent basis, relinquishment is also patent by patent. This is manifest in FDA’s March 2014 decision to approve Teva’s ANDA referencing Evista® (raloxifene hydrochloride), as follows.<sup>137</sup> FDA approved Evista® in 1997, and Lilly has listed a variety of patents in connection with the drug. The only patents relevant here are those that expired in March 2014 and the four expiring in March 2017. An unidentified applicant filed an ANDA prior to December 8, 2003, and was the first to challenge three patents then listed by Lilly and slated to expire in March 2017. Teva filed its ANDA in 2006. In 2011 Lilly listed a fourth patent that would expire in March 2017. The unidentified applicant and Teva amended their pending ANDAs on the same day and were therefore *both* first applicants with respect to the fourth patent. The unidentified applicant proceeded to relinquish its entitlement to exclusivity with respect to the first three patents, leaving only the fourth—as to which it shared first applicant status with Teva. On March 4, 2014, two days after the last of the other patents listed by Lilly in the Orange Book expired, FDA approved Teva’s application.

FDA has also permitted applicants to transfer their exclusivity without the permission of other ANDA applicants with whom they share exclusivity. So far it appears to have done so only with respect to ANDAs under the old scheme. To give an example, as already noted, there were ten patents listed for Actos (pioglitazone hydrochloride), and ANDAs were subject to the old patent-by-patent exclusivity scheme.<sup>138</sup> And, as already noted, exclusivity was shared by Watson and Mylan. A

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<sup>134</sup> *Boehringer Ingelheim Corp. v. Shalala*, 993 F. Supp. 1 (D.D.C. 1997).

<sup>135</sup> See Letter from Gary Buehler, Director, OGD, CDER, FDA, to Margaret L. Choy, Vice President, Regulatory Affairs, Anchen Pharmaceuticals Inc. approving ANDA 77–284 (Dec. 14, 2006).

<sup>136</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to Mark C. Shaw, Vice President, Regulatory Affairs & Compliance, Impax Laboratories, Inc. approving ANDA 77–415 (Dec. 16, 2006). The same letter issued a tentative approval with respect to the 150 mg strength, because litigation had been brought with respect to that patent within the statutory 45–day window, triggering a 30–month stay of approval. Litigation on the patent tied to the 300 mg strength was brought outside the 45–day window. *Id.*

<sup>137</sup> The facts that follow derive from the Teva approval letter and a review of historical Orange Books. See Letter from Kathleen Uhl, M.D., Acting Director, OGD, CDER, FDA, to Scott D. Tomsky, Vice President, N.A. Generics Regulatory Affairs, Teva Pharmaceuticals USA, approving ANDA 078193 (Mar. 4, 2014).

<sup>138</sup> See *supra* 0.

third generic applicant, Ranbaxy, also shared in that exclusivity.<sup>139</sup> This exclusivity was triggered on August 17, 2012, when Ranbaxy launched an authorized generic of all three strengths of the drug. On February 6, 2013, roughly one week *before* the exclusivity expired, FDA approved another ANDA. The approval letter indicates that exclusivity had been selectively waived (transferred)—presumably by Ranbaxy. (At the time, FDA was appealing a district court decision that Watson was entitled to share exclusivity with the other first applicants. See discussion in subsection II.B.6.)

### C. Forfeiting Exclusivity

This subsection explores four of the six grounds for forfeiture of exclusivity added by Congress in 2003 and codified in section 505(j)(5)(D)(i) of the FDCA: failure to market within certain deadlines, amendment of the underlying paragraph IV certification(s), failure to obtain tentative approval within 30 months, and patent expiry. This subsection also considers analogous ways that a first applicant might have *lost* its exclusivity under the old scheme. For instance, when considering whether and how patent delisting may lead to forfeiture under the 2003 provisions, it notes the impact of delisting the qualifying patent under the old scheme. This subsection concludes with additional questions about losing exclusivity that are not tied to specific statutory forfeiture provisions.

This section of our article does not take up the forfeiture provisions relating to withdrawal of the generic application in question, or patent settlements found to violate the antitrust laws. It appears that these forfeiture provisions have not given rise to significant interpretive issues or disputes. Section III of our article, however, does take up recent developments relating to the application of antitrust law to patent settlements.

#### ***Failure to Market***

With respect to old ANDAs, generally speaking, there is no effect if the first applicant fails to market its product within 30 months of submitting its ANDA application. For new ANDAs, the first ground for forfeiture in the statute is failure to market within 30 months of submission. Although this provision—section 505(j)(5)(D)(i)(I)—refers to *submission* of the ANDA, and another forfeiture provision (failure to obtain timely tentative approval) refers to *filing* of the ANDA, the agency interprets the words interchangeably in this context; the date in question is the date on which the agency determines the ANDA to be substantially complete to permit substantive review.<sup>140</sup> The failure to market provision requires two triggers for forfeiture: the (aa) trigger relating to submission or approval of the first applicant's ANDA, and the (bb) trigger relating to the patents as to which the first applicant's paragraph IV certifications resulted in its eligibility for exclusivity. In short, if the (bb) trigger is satisfied—specifically if 75 days have elapsed since an appellate court entered a final decision in an infringement or declaratory judgment

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<sup>139</sup> See Letter from Gregory P. Geba, M.D., M.P.H., to Andrej Gasperlin, President, AB Pharmaceuticals LLC U.S. Agent for Macleods Pharmaceuticals Limited approving ANDA 202467 (Feb. 6, 2013) (“Ranbaxy Laboratories Limited (Ranbaxy) was a first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the listed patents. Therefore, Ranbaxy is eligible for 180-day exclusivity for Pioglitazone Tablets USP, 15 mg, 30 mg, and 45 mg.”).

<sup>140</sup> See Letter from Gary Buehler, Director, OGD, CDER, FDA, to William A. Rakoczy, Esq., Rakoczy, Molino, Mazzochi & Siwik, LLP, Docket No. FDA-2007-N-0445 (May 7, 2008), at 10 n. 15.

action that the last patent qualifying the first applicant for exclusivity is invalid or not infringed, a court signed a settlement order or consent decree finding this patent invalid or not infringed, or this patent was delisted—then the first applicant will forfeit exclusivity if it *fails to market* by the date that is 30 months after submission of its application.<sup>141</sup>

Both triggers, however, must be satisfied. For instance, as discussed in the 2009 article, FDA declined to find forfeiture *simply* because 30 months had passed since Teva submitted its ANDA referencing Kytril® (granisetron hydrochloride).<sup>142</sup> No claim of infringement on the patent at issue had been brought against Teva or any subsequent applicant, nor had any ANDA applicant brought a declaratory judgment action regarding the patent. Consequently, no court had entered a final judgment of invalidity or non-infringement, and no court had signed a settlement order or consent decree entering final judgment of invalidity or non-infringement. Further, Roche, the holder of the NDA for Kytril, had not requested the patent be withdrawn from the Orange Book. As none of these three events had occurred—a court decision, a court order, or delisting—the agency reasoned there had been no forfeiture and granted Teva's generic granisetron hydrochloride product 180-day exclusivity.<sup>143</sup> The fact that none of these events ever *could* occur was irrelevant.<sup>144</sup>

The agency has found forfeiture under this provision at least twice.<sup>145</sup> Several interpretive issues have arisen, as follows.

*I. Will delisting the underlying patent cause the first applicant to lose 180-day exclusivity under the old scheme or the new scheme's failure-to-market provision?*

*Short answer.* With respect to old ANDAs, as a general rule FDA will not remove a patent from the Orange Book if it is the subject of a paragraph IV certification giving rise to 180-day exclusivity. With respect to new ANDAs, delisting of the patent(s) giving rise to exclusivity satisfies the (bb) trigger for forfeiture, and the applicant will therefore forfeit exclusivity if the (aa) trigger is also met. A court has, however, ruled that a delisting will not give rise to forfeiture unless it results from

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<sup>141</sup> 21 U.S.C. § 355(j)(5)(D)(i)(I).

<sup>142</sup> Letter from Gary J. Buehler, Director, OGD, CDER, FDA, to Marc A. Goshko, Executive Director, Teva North America, Teva Parenteral Medicines regarding Granisetron Hydrochloride Injection and 180-Day Generic Drug Exclusivity, Docket No. 2007N-0389 (Docket No. FDA-2007-N-0269) (Jan. 17, 2008) [hereinafter Buehler Letter to Teva Parenteral Medicines].

<sup>143</sup> *Id.*

<sup>144</sup> Critics of this decision alleged that it “removes teeth” from the forfeiture provision. *See, e.g.,* Chad Landmon, *FDA Removes Teeth From Exclusivity Forfeiture*, IP LAW 360 (Jan. 24, 2008); *In re Nexium (Esomeprazole) Antitrust Litig.*, 309 F.R.D. 107, 139 (D. Mass. 2015) (“Critics have pointed out that loopholes in the MMA allow first-filers to “park” their 180-day exclusivity by entering into delayed entry settlement agreements. This also reveals the shortcomings of the FDA in enforcing their own regulations on generic drugs”) (citing Landmon piece and granisetron decision for proposition that “Teva did not have to forfeit exclusivity even though it failed to come to market within thirty months of filing its ANDA”).

<sup>145</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to William A. Rakoczy, Esq., Rakoczy, Molino, Mazzochi & Siwik, LLP regarding Acarbose Tablets and 180-Day Exclusivity, Docket No. 2007N-0417 (Docket No. FDA-2007-N-0445) (May 8, 2008) (finding forfeiture for failure to market within 30 months plus delisting of the patent); Letter from Gary Buehler, Director, OGD, CDER, FDA, to ANDA applicant regarding, Dorzolamide Hydrochloride/Timolol Maleate Tablets and 180-Day Exclusivity, Docket No. FDA-2008-N-0483 (Oct. 28, 2008) (same).

the innovator's loss (or unfavorable settlement) in court. Further, FDA will not actually delist the patent unless it has determined that the applicant has forfeited (or used) its exclusivity.

*Discussion.* With respect to old ANDAs, generally speaking, if a patent is removed from the Orange Book, ANDA applicants must delete their paragraph IV certifications. FDA's policy creating an exception if a first ANDA applicant was sued by the patent owner was found inconsistent with the statute. The case in question, involving generic simvastatin and usually referred to as the "*Ranbaxy case*," was discussed in the 2009 article.<sup>146</sup> The court indicated that FDA could adopt a delisting rule, but not one that favored sued ANDA applicants over not-sued ANDA applicants.<sup>147</sup> FDA subsequently adopted the practice of noting delist requests in the Orange Book but *retaining* the listings where the patents gave rise to 180-day exclusivity. There have been no significant developments since the 2009 article, apart from cases assessing whether federal courts have jurisdiction to hear requests for declaratory relief with respect to disclaimed patents that are the subject of delisting requests.<sup>148</sup>

With respect to new ANDAs, delisting can lead to forfeiture of exclusivity. Specifically, the first applicant will forfeit exclusivity if: (1) 75 days have elapsed since approval of its ANDA or 30 months have elapsed since the ANDA was submitted, and (2) 75 days have elapsed since all (and the last) of the patents qualifying it for exclusivity have been found invalid or not infringed *or have been delisted*.<sup>149</sup>

The D.C. Circuit ruled in 2010 that the delisting in question must result from an adverse ruling or settlement and cannot be prompted simply by unilateral request of the NDA holder. The case involved generic applications referencing Merck's Cozaar® (losartan potassium) and Hyzaar® (losartan potassium-hydrochlorothiazide). Merck listed three patents in the Orange Book covering both products. As to each product, Teva was the first applicant to submit a substantially complete ANDA including a paragraph IV certification—to U.S. Patent No. 5,608,075 (the '075 patent). It was therefore eligible for 180-day exclusivity with respect to both ANDAs.<sup>150</sup> These applications also included paragraph III certifications, which meant that approval of the ANDAs could take effect no earlier

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<sup>146</sup> See *Ranbaxy Labs., Ltd. v. Leavitt*, 459 F. Supp. 2d 1 (D.D.C. 2006), *aff'd*, 469 F.3d 120 (D.C. Cir. 2006); see 2009 Exclusivity Article, *supra* note 4, at 365–66.

<sup>147</sup> *Id.*, *Glenmark Generics Ltd. v. Ferring B.V.*, No. 3:14CV422–HEH, 2014 WL 5162097, at \*4 (E.D. Va. Oct. 14, 2014) (regarding a patent that remained in the Orange Book with a "Patent Delist Request Flag").

<sup>148</sup> See, e.g., *Glenmark Generics Ltd. v. Ferring B.V.*, No. 3:14CV422–HEH, 2014 WL 5162097, at \*4 (E.D. Va. Oct. 14, 2014) (finding jurisdiction to hear a declaratory judgment action brought by a subsequent applicant because continued listing of disclaimed patent caused injury by obstructing FDA approval of subsequent applicant's ANDA); *Apotex, Inc. v. Daiichi Sankyo*, 781 F.3d 1356 (Fed. Cir. 2015), *cert. denied*, 136 S.Ct. 481 (2015) (finding jurisdiction in challenge of disclaimed patent because the parties had adverse concrete interests in the truncation—or preservation—of Mylan's exclusivity eligibility).

<sup>149</sup> 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC).

<sup>150</sup> *Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1307 (D.C. Cir. 2010).

than April 2010.<sup>151</sup> Merck did not bring a patent infringement action against Teva with respect to the single challenged patent and instead, in March 2005, asked FDA to delist the patent from the Orange Book.<sup>152</sup>

Decision letters that had been issued by FDA in 2008—relating to generic applications referencing Precose® (acarbose) and Cosopt® (dorzolamide hydrochloride/timolol maleate)—suggested that Merck’s delisting of the ‘075 patent would cause Teva to forfeit its exclusivity. FDA had concluded in these letters that an NDA holder’s unilateral request to withdraw patent information from the Orange Book satisfies the delisting trigger. FDA noted that forfeiture results if the delisted patent in question is the last of the patents qualifying the product for exclusivity and the first applicant fails to market within 75 days (assuming 75 days have elapsed since approval of the first applicant’s ANDA was made effective or 30 months have elapsed since the first applicant’s ANDA was submitted).<sup>153</sup> Under these decision letters, Teva would forfeit exclusivity because the patent in question was the only one qualifying it for 180-day exclusivity and more than 30 months had passed since it submitted its ANDAs.<sup>154</sup>

FDA delisted the ‘075 patent at Merck’s request and, expecting that the agency would deem its exclusivity forfeit, Teva brought suit seeking an order that FDA instead grant it exclusivity. On appeal from a ruling in the agency’s favor, the D.C. Circuit held that no forfeiture can occur *unless*: (1) the NDA holder sues and (2) delisting results because the NDA holder either loses on the merits or enters an “unfavorable settlement.”<sup>155</sup> The reasoning in the earlier *Ranbaxy* ruling controlled.<sup>156</sup> In that case, the court had rejected FDA’s policy with respect to delisting requests under the old scheme. The *Ranbaxy* court found that removing patent listings at the NDA holder’s request—the agency’s policy under the old scheme, unless the generic applicant had been sued—would deprive the generic applicant of exclusivity that it had earned, undermining the statutory incentive to challenge patents.<sup>157</sup> Here, the new failure-to-market forfeiture provision explicitly requires, with respect to every challenged patent, suit by the NDA holder and either a loss on the merits or an unfavorable settlement, or delisting (at issue here).<sup>158</sup> In other words, the subsections *other than the delisting subsection* do not “permit a brand

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<sup>151</sup> *Teva Pharm. USA, Inc. v. Sebelius*, C.A. No. 09–01111 (RMC) (D.D.C. July 1, 2009) (Consolidated Memorandum in Support of Defendants’ Motion to Dismiss and in Opposition to Plaintiff’s Motion for a Preliminary Injunction).

<sup>152</sup> *Id.*

<sup>153</sup> See 2009 Exclusivity Article, *supra* note 4, at 368–71.

<sup>154</sup> As of June 19, 2006, 30 months had passed from the date Teva submitted its ANDA referencing Cozaar, and as of November 25, 2006, 30 months had passed from the date Teva submitted its ANDA referencing Hyzaar. These dates thus triggered the first prong of the failure to market provision. The second prong was triggered 75 days after Merck withdrew the patent, i.e., March 2005. *Teva Pharms. USA, Inc. v. Sebelius*, Nos. 09-5281, 09-5308, 2009 WL 6155282 (D.C. Cir. Sept. 16, 2009) (Brief of Appellant Teva Pharmaceuticals USA, Inc.).

<sup>155</sup> *Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1317 (D.C. Cir. 2010).

<sup>156</sup> See *Ranbaxy Labs., Ltd. v. Leavitt*, 459 F. Supp. 2d 1 (D.D.C. 2006), *aff’d*, 469 F.3d 120 (D.C. Cir. 2006).

<sup>157</sup> *Teva Pharm. USA, Inc.*, 595 F.3d at 1316. It also functionally eliminated the commercial marketing trigger, by allowing NDA holders to restrict exclusivity to first filers who had been sued. *Id.*

<sup>158</sup> *Id.* at 1317.

manufacturer to vitiate a generic's exclusivity without the generic manufacturer's having had some say in the matter."<sup>159</sup> The same basic principle, it concluded, should apply to the delisting provision. To hold otherwise would allow NDA holders to "deprive[] generic companies of the period of marketing exclusivity they otherwise deserve."<sup>160</sup>

Following this ruling, FDA adopted the policy of not removing a patent from the Orange Book if the patent is the basis of a paragraph IV certification giving rise to eligibility for 180-day exclusivity. The issue that has since arisen is whether a subsequent applicant can persuade a federal court to take jurisdiction over a declaratory judgment action challenging a disclaimed—but still listed—patent. The Federal Circuit has reasoned that the subsequent applicant has a justiciable case or controversy in these situations.

The dispute among Daiichi Sankyo, Apotex, and Mylan regarding their applications referencing Benicar® (omesartan medoxomil) is illustrative. Daiichi listed two patents covering Benicar: U.S. Patent No. 5,616,599 (the '599 patent) and U.S. Patent No. 6,878,703 (the '703 patent). Mylan was the first to file paragraph IV certifications to both patents. Daiichi sued Mylan for infringing the '599 patent and disclaimed all claims of the '703 patent. The district court upheld (and the Federal Circuit subsequently affirmed) the validity of the '599 patent and entered judgment of infringement against Mylan. Apotex later filed an ANDA with a paragraph IV certification as to the '703 patent. Consistent with *Teva Pharm. v. Sebelius* (just discussed), FDA did not remove the '703 patent from the Orange Book, despite Daiichi's request that it do so, because the patent was the subject of a paragraph IV certification by first applicant Mylan. Apotex then sued Daiichi for a declaratory judgment on this patent, which had been disclaimed but remained listed. Although the district court found no case or controversy, the Federal Circuit reversed.<sup>161</sup> The court reasoned that the continued listing of the patent supported Mylan's exclusivity, with the consequence of preventing FDA approval of Apotex's application. A ruling on the patent would redress Apotex's injury by activating the court decision trigger. Therefore, the parties had adverse concrete interests in the truncation—or preservation—of Mylan's exclusivity eligibility.<sup>162</sup>

In its recent proposed rule, FDA has proposed to require an NDA holder to submit a copy of the court order requiring withdrawal of patent information; it will then remove the patent from the Orange Book *if* there is no first applicant for 180-day

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<sup>159</sup> *Id.*

<sup>160</sup> *Id.* at 1318. On remand, the district court found that Teva had not forfeited its exclusivity period. Mary Anne Pazanowski, *D.C. Circuit Rejects Generic Firms' Challenge to Denial of Injunction Against Competitor*, PHARM. LAW & INDUS. REP. (July 9, 2010). Following this decision, it was discovered that the delisted patent had expired due to Merck's failure to pay maintenance fees. This, however, did not result in a forfeiture. See *infra* subsection 0. The agency set Teva's exclusivity to begin in April 2010. Apotex, a subsequent ANDA applicant, filed suit challenging the award of exclusivity to Teva, but this was rejected by the courts. *Apotex v. Sebelius*, 700 F. Supp. 2d 138 (D.D.C. 2010), *aff'd*, 384 F. App'x 4 (D.C. Cir. 2010).

<sup>161</sup> See generally *Apotex Inc. v. Daiichi Sankyo*, 781 F.3d 1356 (Fed. Cir. 2015), *cert. denied*, 136 S.Ct. 481 (2015).

<sup>162</sup> On January 8, 2016, a federal district court granted Apotex a declaratory judgment of non-infringement with respect to the '703 patent. *Apotex Inc. v. Daiichi Sankyo Inc.*, Nos. 12-cv-9295, 15-cv-3695, 2016 U.S. Dist. LEXIS 2126 (N.D. Ill. Jan. 8, 2016). A final judgment that is affirmed on appeal, or not appealed, should activate the 75-day window for Mylan to launch or forfeit exclusivity.

exclusivity or upon expiration of the 180-day exclusivity period.<sup>163</sup> The agency would indicate a delisting request in the Orange Book and note that the patent remains listed to preserve a first applicant's eligibility for exclusivity.<sup>164</sup>

2. *Can a subsequent applicant that obtains a final court decision in its favor trigger the (bb) forfeiture clock if it does not yet have tentative approval?*

*Short answer.* Although it appears that FDA has not yet weighed in on this question, the Federal Circuit has found that a favorable court decision involving a subsequent applicant was sufficient for purposes of the forfeiture clock, even though the subsequent applicant lacked tentative approval. The 75-day clock would not begin to run, however, until this applicant obtained tentative approval.

*Discussion.* As noted, the failure-to-market forfeiture provision requires two triggering events. The second triggering event involves each of the patents as to which the first applicant submitted and lawfully maintained a paragraph IV certification qualifying it for exclusivity. As to each, one of three events must occur, "with respect to the first applicant or any other applicant (which other applicant has received tentative approval)": a court decision that the patent is invalid or not infringed, a settlement order or consent decree finding the patent invalid or not infringed, or withdrawal of the patent from the Orange Book by the NDA holder.<sup>165</sup> The emphasized words make it clear that a subsequent applicant can trigger forfeiture with a court decision or settlement, but the question is whether the parenthetical requires it to obtain tentative approval of its ANDA *first*—or if instead forfeiture simply happens once both are true (i.e., there is a court decision *and* the applicant has tentative approval).

The Federal Circuit addressed this question in the case involving generic applications referencing Benicar®, discussed in the immediately preceding subsection (II.C.1). As already discussed, Mylan was eligible for exclusivity as the first applicant with respect to the '703 patent, which the innovator subsequently disclaimed. Apotex sought a declaratory judgment with respect to the disclaimed patent. To support jurisdiction, it argued that a declaratory judgment of non-infringement would cause Mylan to forfeit its 180-day exclusivity eligibility, assuming Mylan did not market its drug within 75 days after appeal rights were exhausted (certiorari aside) and Apotex had obtained tentative approval.<sup>166</sup> Mylan responded that a subsequent applicant needs tentative approval *before* it initiates the declaratory judgment action, which Apotex did not have.

When the Federal Circuit ruled that the district court had jurisdiction to entertain the declaratory judgment action, it rejected Mylan's argument about tentative approval. The first applicant forfeits its exclusivity if it has not entered the market 75 days after two things have happened: a court has entered a final decision of non-

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<sup>163</sup> Proposed 21 C.F.R. § 314.53(f)(2); see 80 Fed. Reg. at 6829, 6844–45.

<sup>164</sup> *Id.* The agency also proposed to amend 21 C.F.R. §§ 314.50(i)(6)(ii) and 314.94(a)(12)(viii)(B) regarding amended patent certifications after an NDA holder has requested delisting.

<sup>165</sup> 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb) (emphasis added).

<sup>166</sup> Mylan had submitted its ANDA in early 2006, so the first prong of the failure to market provision had been satisfied; more than 30 months had elapsed since submission of the ANDA. See *Apotex, Inc. v. Daiichi Sankyo*, 781 F.3d at 1359 (noting date of ANDA submission).



infringement that is no longer appealable, and the second (or later) filer has tentative approval.<sup>167</sup> The 75-day clock does not begin until both have happened, but the order does not matter. From a policy perspective, the court wrote, tentative approval is needed “because exclusivity should not be lost unless the second filer is on the verge of having an approved product to deliver the benefits of competition.”<sup>168</sup> In other words, “the purpose of requiring tentative approval has nothing to do with Apotex’s approval status at the time it brought the declaratory judgment action, and it has everything to do with its approval status when forfeiture is triggered.”<sup>169</sup> The lower court, on remand, has now issued a declaratory judgment of non-infringement.<sup>170</sup>

### ***Amendment of Certification***

The third ground for forfeiture in the statute is amendment of the paragraph IV certification. Specifically, exclusivity is forfeited under section 505(j)(5)(D)(i)(III) if the first applicant “amends or withdraws the certification for all of the patents with respect to which that applicant submitted” a paragraph IV certification qualifying it for exclusivity.<sup>171</sup>

3. *If FDA requires a first applicant to re-certify to the patent that gave rise to exclusivity eligibility, in connection with a formulation change, is this an “amendment” or “withdrawal” of the original certification giving rise to forfeiture under subparagraph (D)(i)(III)?*

*Short answer.* No. FDA takes the position that a new paragraph IV certification required by the agency in order to accept an ANDA amendment (for example, for a reformulated product) relates back to the original paragraph IV certification that formed the basis for a claim to 180-day exclusivity. Re-certification is not amendment of the original certification, nor does it withdraw the original certification.

*Discussion.* This issue arose in connection with generic applications referencing Genzyme’s Hectorol® (doxercalciferol injection, 2 mcg/mL). FDA approved Genzyme’s NDA for Hectorol® in an ampule presentation. In October 2007, Cobrek was the first to submit an ANDA containing a paragraph IV certification to three patents claiming Hectorol, including U.S. Patent No. 5,602,116 (the ‘116 patent). Genzyme brought a patent infringement suit on the ‘116 patent.<sup>172</sup> In December 2008, FDA approved Genzyme’s supplemental NDA for a new injectable formulation (and packaging configuration) of Hectorol in a vial presentation. Genzyme indicated that the original ampule formulation was no longer being

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<sup>167</sup> *Id.*

<sup>168</sup> *Id.* at 1370.

<sup>169</sup> *Id.*

<sup>170</sup> See *supra* note 162.

<sup>171</sup> 21 U.S.C. § 355(j)(5)(D)(i)(III).

<sup>172</sup> The other patents were U.S. Patent Nos. 5,707,980 (expiring in 2010) and 6,903,083 (expiring in 2021). ORANGE BOOK (27th ed. 2007), at ADA 37. Cobrek included paragraph IV certifications to both, but Genzyme later requested that FDA delist both from the Orange Book. Letter from Janet Woodcock, M.D., Director, CDER, FDA, to Gerald F. Masoudi, Covington & Burling LLP, Docket No. FDA-2010-P-0223 (Oct. 19, 2010), at 3 n.7.

manufactured and that it planned to discontinue the product once inventory was exhausted.<sup>173</sup> Genzyme submitted information again for the '116 patent *and* listed a new formulation patent, U.S. Patent No. 7,148,211 (the '211 patent). Cobrek amended its pending application to include a paragraph IV certification to the '211 patent.<sup>174</sup> Genzyme did not bring suit, apparently concluding that Cobrek's ampule formulation would not infringe the vial formulation.<sup>175</sup> Shortly afterwards, FDA informed Cobrek that it could not approve the ANDA because the proposed ampule formulation was not quantitatively and qualitatively the same as the new vial formulation, and it recommended Cobrek reformulate its generic.<sup>176</sup> Cobrek reformulated its product, switched from an ampule presentation to a vial presentation, and amended its ANDA. FDA then refused to accept the ANDA amendment without *new* certifications to *both* patents, so in November 2009 Cobrek certified to the two patents in its ANDA amendment.<sup>177</sup>

Again, section 505(j)(5)(D)(i)(III) requires forfeiture of exclusivity if the first applicant "amends or withdraws" the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for 180-day exclusivity. Sandoz, which had pending ANDAs for both presentations, filed a citizen petition asserting that Cobrek had forfeited its exclusivity.<sup>178</sup> It cited two reasons, one of which was that Cobrek's certification in November 2009 to the '116 patent constituted either an "amendment" or a "withdrawal" of the original October 2007 certification to the same patent. FDA regulations, it pointed out, require applicants to "amend" certifications that are no "longer accurate," and they also provide that once an amendment is submitted, "the application will no longer be considered to contain the prior certification."<sup>179</sup> If FDA required Cobrek to submit a new certification to the '116 patent, it must have concluded the original certification was "no longer accurate" (because it related to Cobrek's original ampule formulation, for which the company was no longer seeking approval). Thus, Cobrek had "amended" its certification, triggering forfeiture.

FDA denied Sandoz's citizen petition, explaining that "resubmission of patent certifications" after reformulation—to respond to a change in formulation of the listed drug—does not constitute an amendment or withdrawal that would lead to loss of exclusivity.<sup>180</sup> Indeed, the agency noted, this had arisen in the late 1990s under the

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<sup>173</sup> Letter from Janet Woodcock, M.D., Director, CDER, FDA, to Gerald F. Masoudi, Covington & Burling LLP, Docket No. FDA-2010-P-0223 (Oct. 19, 2010), at 2.

<sup>174</sup> *Id.* at 2-3.

<sup>175</sup> *Id.* at 3 ("Genzyme did not initiate patent litigation against Cobrek based on this paragraph iv certification as it believed that Cobrek's ampule formulation for which it was seeking approval at the time would not infringe the '211 patent claims.").

<sup>176</sup> *Id.*

<sup>177</sup> *Id.* at 3-4, 6.

<sup>178</sup> Sandoz Inc., Citizen Petition, Docket No. FDA-2010-P-0632 (Dec. 8, 2010).

<sup>179</sup> *Id.*, at 7-8 (citing 21 C.F.R. § 314.94(a)(12)(viii)).

<sup>180</sup> Letter from Janet Woodcock, M.D., Director, CDER, FDA, to Stephen Auten, Vice President, Legal-Intellectual Property, Sandoz Inc., Docket No. 2010-P-0632 (Sept. 20, 2011). FDA explained that when a change in formulation for a reference listed drug requires an ANDA applicant to respond—*either* by seeking approval for a change in formulation *or* by seeking a determination that the old formulation was not withdrawn for safety reasons and a waiver—the agency will consider this a "change in or review of the requirements for approval" within the meaning of section 505(j)(5)(D)(i)(IV). *Id.* at 9. For further discussion, see *infra* subsection 0.

old scheme. Genpharm had reformulated its generic ranitidine product after making paragraph IV certifications and had resubmitted those patent certifications; the agency had not found that the company “amended” its certification resulting in loss of exclusivity, and the Fourth Circuit had agreed.<sup>181</sup> The recertification requirement in these cases is “based on the premise that the patent holder should have notice relating to the formulation that is before FDA for approval,” but it would be “unfair” to ANDA applicants if this were interpreted to constitute amendment or withdrawal leading to forfeiture.<sup>182</sup>

In the preamble to its February 2015 proposed rule, the agency addressed forfeiture under subparagraph (D)(i)(III), but did not explicitly address recertification in connection with reformulation. Specifically, as already mentioned, FDA noted that if an ANDA applicant is eligible for exclusivity based on a paragraph IV certification and the patent is *reissued*, the applicant would be required to submit a paragraph IV certification to the reissued patent within 30 days to be considered to have lawfully maintained the certification for purposes of the new definition of “first applicant” and the forfeiture provision in subparagraph (D)(i)(III).<sup>183</sup> If the ANDA applicant were to submit a paragraph III certification or section viii statement, however, it would be considered to have amended or withdrawn the original certification.<sup>184</sup> The agency also wrote that a first applicant would be considered to have “lawfully maintained” its certification to a patent, for purposes of 180-day exclusivity, if the amendment or supplement is accompanied by *another* paragraph IV certification to *that* patent (and notice is sent as required).<sup>185</sup> Further, “an amendment to a substantially complete ANDA does not mean that the ANDA is no longer substantially complete or that a first applicant has not lawfully maintained its paragraph IV certification (unless the amendment requires a new patent certification and the amended patent certification is not a paragraph IV certification).”<sup>186</sup>

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<sup>181</sup> Although this case predated the forfeiture provisions, FDA’s regulations then (as now) indicated that once an amendment is submitted, the application will no longer be considered to contain the prior certification. Consequently, FDA explained to Sandoz, had Genpharm’s recertification constituted amendment, the company could have lost exclusivity. *See id.* at 7 n.10 (citing *Granutec, Inc. v. Shalala*, 139 F.3d 889 (Table) n.1 (4th Cir. 1998) (“We reject Geneva’s argument that Genpharm lost its place in line as the first ANDA applicant, and thus the only ANDA applicant, eligible for exclusivity. FDA maintains that, although Genpharm did not make the Paragraph IV certification relevant to these proceedings until 1996, Genpharm qualifies as the first ANDA applicant for purposes of the exclusivity because the certification relates back to the date of its ANDA application. This interpretation does not clearly conflict with either the regulations or the statute, and thus we find no reason to substitute a contrary judgment on this matter for that of FDA.”)).

<sup>182</sup> *Id.* at 8.

<sup>183</sup> 80 Fed. Reg. at 6846. The forfeiture provision in section 505(j)(5)(D)(i)(III) does not explicitly mention lawfully maintaining the paragraph IV certification. The definition of “first applicant” does. An applicant that does not “lawfully maintain” its certification is not a “first applicant” under the statute. 21 U.S.C. § 355(j)(5)(B)(iv)(II)(bb).

<sup>184</sup> 80 Fed. Reg. at 6846.

<sup>185</sup> *Id.* at 6850.

<sup>186</sup> *Id.* at 6814.

4. *Does a settlement agreement result in “amendment” of the certification and thus give rise to forfeiture under subparagraph (D)(i)(III)?*

*Short Answer:* Only if it includes a finding of *infringement*. This will require the first applicant to amend its paragraph IV certification to a paragraph III certification, giving rise to forfeiture under section 505(j)(5)(D)(i)(III).

*Discussion.* Prior to the passage of the MMA in 2003, FDA had concluded that a settlement agreement ending patent infringement litigation effectively turned a paragraph IV certification into a paragraph III certification. A federal court in West Virginia found the agency’s decision on this issue unreasonable.<sup>187</sup> In 2003, Congress added a provision relating to settlements finding the patent invalid or not infringed,<sup>188</sup> and it added a provision relating to settlements found to violate the antitrust laws.<sup>189</sup> It did not address any other type of settlement, and as a result, in cases under the new rules, the agency has declined to find forfeiture—or to require certification amendment—where settlement agreements are silent.<sup>190</sup> In its recent proposed rule, the agency stood by its long-standing view that an ANDA applicant must amend its certification in the event of a court decision, settlement order, or consent decree that includes a finding that the patent is infringed.<sup>191</sup> FDA noted that changing the paragraph IV certification that qualified an applicant for 180-day exclusivity to a paragraph III certification or a statement under section viii “has implications for continuing eligibility for 180-day exclusivity,” and it cited section 505(j)(5)(D)(i)(III).<sup>192</sup> The agency added that if a settlement is reached without a finding of patent infringement or invalidity, a paragraph IV certification may continue to be appropriate.<sup>193</sup>

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<sup>187</sup> *Mylan Pharm., Inc. v. Thompson*, 207 F. Supp. 2d 476, 487 (N.D. W.Va. 2001); see 2009 Exclusivity Article, *supra* note 4, at 374.

<sup>188</sup> As noted above in subsections 0 and 0, the (bb) trigger for failure-to-market forfeiture requires each patent giving rise to exclusivity to be the subject of an adverse court ruling, withdrawal from the Orange Book, or settlement that includes a finding of invalidity or non-infringement. 21 U.S.C. § 355(j)(5)(D)(i)(I).

<sup>189</sup> The first applicant forfeits exclusivity if there is a final decision of the FTC or a court (from which no appeal other than a petition for certiorari has been or can be taken) that the settlement agreement violated antitrust law. 21 U.S.C. § 355(j)(5)(D)(i)(V).

<sup>190</sup> *E.g.*, Letter from Gary Buehler, Director, OGD, CDER, FDA, to Carmen M. Shepard, Esq., & Kate C. Beardsley, Esq., Buc & Beardsley, Docket No. 2007N-0382 (Jan. 29, 2008) (rejecting argument that Cobalt’s paragraph IV certification was inaccurate because the settlement meant Cobalt was no longer asserting the patent was invalid).

<sup>191</sup> 80 Fed. Reg. at 6843–44; proposed 21 C.F.R. § 314.94(a)(12)(viii)(A). If the decision, order, or decree also includes a finding that the patent is invalid (in addition to infringed), an amended certification is not required. *Id.*

<sup>192</sup> 80 Fed. Reg. at 6844.

<sup>193</sup> *Id.* (“For example, if the . . . ANDA applicant is granted a patent license such that the applicant would be permitted to obtain approval and commence marketing prior to patent expiration, the . . . ANDA applicant would maintain its paragraph IV certification with respect to the patent at issue and should submit an amendment pursuant to proposed § . . . 314.94(a)(12)(v) to advise the Agency of the patent licensing agreement.”).

### ***Failure to Obtain Tentative Approval***

The fourth ground for forfeiture in the statute—section 505(j)(5)(D)(i)(IV)—is failure to obtain tentative approval. Specifically, the first applicant will forfeit exclusivity if it “fails 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.” Separately, under section 505(q) of the statute, if approval was delayed because of a citizen petition, the 30-month period is “deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates).”<sup>194</sup> Uncodified provisions of FDASIA temporarily modify the length of the forfeiture clock.<sup>195</sup> For first applicants whose original applications (with qualifying paragraph IV certifications) or amendments (with qualifying paragraph IV certifications) were filed in the 30 months preceding its enactment (July 9, 2012), the 30-month period is amended to 40 months until September 30, 2015, and thereafter to 36 months, until September 30, 2016.

5. *When is the relevant “date of submission” if the paragraph IV certification appears in an ANDA amendment, rather than the original ANDA?*

***Short Answer.*** The relevant date is the date of submission of the *amendment*.

***Discussion.*** Although subparagraph (D)(i)(IV) refers to *filing* of the ANDA, whereas subparagraph (D)(i)(I) (failure to market) refers to *submission* of the ANDA, FDA interprets the words interchangeably for purposes of 180-day exclusivity; the date in question is the date on which the agency determined an ANDA to be substantially complete to permit substantive review.<sup>196</sup> Ordinarily, a first applicant’s original ANDA contains paragraph IV certifications giving rise to exclusivity eligibility, and the 30 months for purposes of forfeiture under subparagraph (D)(i)(IV) are calculated from the date that FDA determines the original application substantially complete.

The question has arisen what start date would apply if the ANDA applicant *amended* its application to include a paragraph IV certification. In 2011, the agency resolved this in a matter involving generic applications referencing Doryx® (doxycycline hyclate delayed-release tablets), calculating the forfeiture clock from submission of the *original* ANDA. Understanding this dispute requires a brief digression into the rules governing old antibiotics. Doxycycline has been marketed in the United States for decades.<sup>197</sup> Prior to 1997, FDA approved antibiotics under section 507 of the FDCA, and many aspects of the Hatch–Waxman Amendments did not apply to them—including patent listing and 180-day exclusivity for first applicants. In 1997, Congress moved antibiotics to section 505 and the full Hatch–Waxman scheme, but it partially exempted “old” antibiotics—meaning new

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<sup>194</sup> 21 U.S.C. § 355(q)(1)(G).

<sup>195</sup> Pub. L. No. 112–144, 126 Stat. 993 § 1133 (2012).

<sup>196</sup> See Letter from Gary Buehler, Director, OGD, CDER, FDA, to William A. Rakoczy, Esq., Rakoczy, Molino, Mazzochi & Siwik, LLP, Docket No. FDA–2007–N–0445 (May 7, 2008), at 10 n. 15.

<sup>197</sup> E.g., ORANGE BOOK (1st ed. 1980), at 47.

applications that contained old antibiotic ingredients.<sup>198</sup> FDA approved Mayne Pharma's NDA for Doryx in 2005, and as a result of this history, there were no listed patents when Impax submitted its ANDA on March 18, 2008.

In October 2008, Congress amended the FDCA to further address the application of the Hatch–Waxman Amendments to old antibiotics.<sup>199</sup> Transitional rules that were *not* codified effectively required Mayne to list its patents within 60 days of enactment.<sup>200</sup> Further, as to any patent so listed, any generic applicant that amended—within 120 days of enactment—its “substantially complete application” to contain a paragraph IV certification would be “deemed” a first applicant for purposes of 180–day exclusivity.<sup>201</sup> Impax amended its ANDA to contain a paragraph IV certification to the patent listed by Mayne. FDA issued final approval to Impax's ANDA on December 28, 2010, roughly 33 months after the ANDA was submitted, and noted that Impax had not obtained tentative approval within 30 months of submission, which would ordinarily lead to forfeiture.<sup>202</sup> In this case, there was no forfeiture because one of the exceptions applied.<sup>203</sup> One curious result of the agency's decision to begin the clock with submission of the original ANDA even if the qualifying paragraph IV certification appears in an ANDA amendment, as Kurt Karst has noted, is that a company could become eligible for—and forfeit—exclusivity on the same day.<sup>204</sup>

Congress addressed the issue in FDASIA, enacted in July 2012.<sup>205</sup> For applications filed on or before this statute's enactment date that are amended until and including September 30, 2017 to contain a first paragraph IV certification, the

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<sup>198</sup> More precisely, the exemption applied if the application contained an antibiotic drug that was the subject of an application received by FDA under section 507 prior to enactment of the Food and Drug Administration Modernization Act of 1997 (FDAMA) (i.e., November 21, 1997). FDAMA, Pub. L. No. 105-115, § 125(d)(2), 111 Stat. 2296, 2327 (1997).

<sup>199</sup> QI Program Supplemental Funding Act of 2008, Pub. L. No. 110-379, 122 Stat. 4080 (adding 21 U.S.C. § 355(v)).

<sup>200</sup> Pub. L. No. 110-379, § 4(b)(1).

<sup>201</sup> Pub. L. No. 110-379, § 4(b)(3).

<sup>202</sup> Impax never obtained “tentative” approval; its application was simply approved. Although Mayne brought suit following the paragraph IV certification, FDA takes the position that no 30-month stay of approval applies to an ANDA referencing an old antibiotic when the ANDA contains a paragraph IV certification to a newly listed patent and the NDA holder or patent owner has sued the ANDA applicant for patent infringement as a result of notice of the paragraph IV certification. *See* Letter from Keith Webber, Ph.D., Deputy Director, OPS, CDER, FDA, to Michelle P. Wong, Senior Director, Regulatory Affairs, Impax Laboratories, Inc. approving ANDA 090505 (Dec. 28, 2010) [hereinafter Impax Approval Letter], at 4 n.1; *see also* Letter from Janet Woodcock to Michael S. Labson, Covington & Burling, et al., Docket Nos. FDA-2009-P-0038, FDA-2009-P-0081, FDA-2009-P-0103, FDA-2009-P-0120 (Mar. 17, 2009) (explaining the agency's reasoning, the previous year, with respect to ANDAs pending when the patent was submitted).

<sup>203</sup> *See* Impax Approval Letter, *supra* note 202, at 3 (footnote omitted) (“Nevertheless, the agency has determined that the failure to obtain tentative within the 30-month period was caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application was filed. We therefore conclude that the 180-day exclusivity period described in section 505(j)(5)(B)(iv) of the Act was not forfeited by Impax, and that with this approval Impax is eligible for 180 days of generic drug exclusivity . . .”).

<sup>204</sup> *See* Kurt R. Karst, *Simultaneously Qualifying for and Forfeiting 180-Day Exclusivity Eligibility for Failure to Obtain Timely Tentative Approval* (Apr. 12, 2011).

<sup>205</sup> Pub. L. No. 112-144, 126 Stat. 993 § 1133 (2012).

date of the filing of the *amendment* (“rather than the date of the original ANDA submission”) is the start of the 30-month forfeiture period. Moreover, FDA’s recently proposed rule follows this approach for *all* ANDA amendments. Under the proposed rule, the date of submission for purposes of starting the 30-month clock is the same as the date of submission for purposes of determining first applicant status. In both cases, the relevant date is the date on which the amendment containing the certification was submitted.<sup>206</sup> If the applicant delays in sending its paragraph IV notice, however, the 30-month clock will begin when it actually sent notice.<sup>207</sup>

#### 6. *On which days do the 30 months begin and end?*

*Short Answer.* Under FDA policy, the 30 months begin the day *after* the date on which the ANDA was submitted, and the deadline has been met (and no forfeiture results) if the applicant obtains approval before *or on* the date that is 30 months later.

*Discussion.* FDA announced its policy in 2015 in a matter concerning generic applications referencing Nexium® Delayed Release Capsules (esomeprazole magnesium). Ranbaxy was the first to file an ANDA with a paragraph IV certification. It submitted its ANDA on August 5, 2005, and obtained tentative approval on February 5, 2008. Sandoz, a subsequent filer, submitted a citizen petition in June 2012 arguing that Ranbaxy had obtained tentative approval “a day too late” and had therefore forfeited exclusivity.<sup>208</sup> The company argued that the plain meaning of “within 30 months” is “inside” the 30-month period. Further, the company argued, a calendar month for purposes of counting passage of time is the period terminating with the numerically corresponding day of the following month—that is, August 4, September 4, and so forth. Thus, the company argued, February 4, 2008, was the last day on which Ranbaxy could obtain tentative approval without forfeiture of its exclusivity. In a footnote, Sandoz added that its argument “applies with equal force to the same factual scenario as found for generic versions of Prandin® (repaglinide) Tablets,” suggesting that Sandoz had there too found itself blocked by a company whose tentative approval issued “a day too late” by its reckoning.<sup>209</sup>

FDA denied the petition on January 26, 2015.<sup>210</sup> Although the petition had been mooted by subsequent events, the agency responded to Sandoz’s arguments about computation of the 30-month period.<sup>211</sup> The 30-month period “begins the day *after*

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<sup>206</sup> 80 Fed. Reg. at 6835 (“For purposes of determining an ANDA applicant’s eligibility for 180-day exclusivity and the date from which a first ANDA applicant’s compliance with section 505(j)(5)(D)(i)(IV) [failure to obtain tentative approval within 30 months forfeiture event] of the [FDCA] is assessed, the date of the submission of the paragraph IV certification is the date on which the amendment [containing the certification] was submitted.”).

<sup>207</sup> As already noted, in this situation the notice date is also the relevant date for determining first filer status in the first instance. *See supra* subsection 0. *See* 80 Fed. Reg. at 6840–41 (“We note that this proposed administrative consequence would not reduce the 30-month timeframe set forth in sections 505(j)(5)(D)(i)(I)(aa)(BB) and (j)(5)(D)(i)(IV) of the FD&C Act in the forfeiture calculus for a first applicant; rather, the 30-month period would begin on the revised date of submission.”).

<sup>208</sup> Sandoz Inc., Citizen Petition, Docket No. FDA–2012–P–0661 (Jun. 19, 2012).

<sup>209</sup> *Id.* at 20 n.17.

<sup>210</sup> Letter from Janet Woodcock, Director, M.D., CDER, to Stephen R. Auten, Vice-President, Head of Intellectual Property, North America, Sandoz, Inc., Docket No. FDA–2012–P–0661 (Jan. 26, 2015).

<sup>211</sup> FDA rescinded the tentative approval in 2014 after determining it had been granted in error; this is discussed further in subsection 0.

the date on which the ANDA is filed, not on the date of filing.” In other words, the 30 months do not include the date the ANDA was filed. Thus, “the last day of the 30-month period lands on the 30-month anniversary date.” Ranbaxy’s 30 month period therefore began on August 6, 2005, and the last day of the period was February 5, 2008. The agency cited instances in which it had found forfeiture, calculating the 30-month period in this fashion.<sup>212</sup> FDA also noted that the federal district court considering Ranbaxy’s forfeiture of exclusivity with respect to generic valsartan (see subsection II.C.8) had in dictum noted the 30-month forfeiture date using the same calculation method.<sup>213</sup>

7. *Does the first applicant forfeit exclusivity, if the agency rescinds tentative approval that was granted within the deadline?*

*Short answer.* Yes, at least if the rescission is attributed to agency error. A federal district court recently affirmed FDA’s decision to deem Ranbaxy’s exclusivity forfeited after the agency rescinded two tentative approvals that had met the deadline, citing error.

*Discussion.* This issue arose in connection with the ANDA discussed in the preceding subsection—Ranbaxy’s ANDA referencing Nexium—as well as another ANDA submitted by Ranbaxy. As noted, FDA granted Ranbaxy tentative approval of its ANDA referencing Nexium on February 5, 2008, within 30 months of its filing date.<sup>214</sup> Ranbaxy was also the first to file a paragraph IV certification to a patent claiming Valcyte® (valganciclovir hydrochloride). FDA tentatively approved Ranbaxy’s generic valganciclovir within 30 months of the ANDA’s filing date, on June 20, 2008. Thus, both received tentative approval within the statutory 30-month deadline.

In 2006 and 2008, FDA issued three warning letters asserting that Ranbaxy had failed to follow current good manufacturing practices at two of its manufacturing facilities.<sup>215</sup> Each warning letter indicated that the Office of Compliance would

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<sup>212</sup> Watson forfeited exclusivity for generic irinotecan hydrochloride injection, and Caraco forfeited exclusivity for cetirizine hydrochloride chewable tablets, under these computational rules. *Id.* at 5–6. Indeed, the agency had applied this interpretation in July 2013 when it approved Caraco’s generic repaglinide tablets and awarded Caraco 180-day exclusivity, implicitly rejecting the Sandoz petition, which had mentioned the product in a footnote. *See Sandoz Inc., Citizen Petition, Docket No. FDA-2012-P-0661* (June 19, 2012), at 20 n. 17 (“Although this petition is specific to 180-day exclusivity in connection with generic versions of NEXIUM® Delayed Release Capsules, the relief sought is based on the plain language of the FDC Act and applies with equal force to the same factual scenario as found for generic versions of PRANDIN® (repaglinide) Tablets.”). Sandoz had noted many instances in which the agency had calculated in this fashion but argued that these did not represent “full vetting” of the topic and that there had been no public comment on the issue. *Id.* at 10-11 and n.11.

<sup>213</sup> Letter from Janet Woodcock, Director, CDER, to Stephen R. Auten, Vice-President, Head of Intellectual Property, North America, Sandoz, Inc., Docket No. FDA-2012-P-0661 (Jan. 26, 2015), at 6, *citing Mylan Labs. Ltd. v. FDA*, 910 F. Supp. 2d 299, 302–03 (D.D.C. 2012) (noting that for ANDA received on December 28, 2004, 30-month forfeiture date was June 28, 2007).

<sup>214</sup> *See generally Ranbaxy Labs., Ltd., v. Burwell*, Civ. A. No. 1:14-cv-01923 (BAH) (D.D.C. Nov. 11, 2014) (Complaint).

<sup>215</sup> Letter from Nicholas Buhay, Acting Director, Division of Manufacturing and Product Quality, CDER, FDA, to Ramesh Parekh, Vice President, Manufacturing, Ranbaxy Laboratories Limited, Warning Letter 320-06-03 (June 15, 2006); Letter from Richard L. Freidman, Director, Division of Manufacturing and Product Quality, CDER, FDA, to Malvinder Singh, CEO and Managing Director, Ranbaxy Laboratories Limited, Warning Letter 320-08-02 (Sept. 16, 2008); Letter from Richard L. Freidman,



recommend withholding approval of any new applications listing the facilities in question as the manufacturing location for finished drug products. In January 2012, Ranbaxy entered into a Consent Decree and Permanent Injunction that resolved certain claims—relating to the two facilities in question—brought by DOJ against the company.<sup>216</sup> The consent decree handled Ranbaxy's various pending ANDAs differently. For instance, Ranbaxy agreed to relinquish any claim to 180-day exclusivity for certain ANDAs; as to other ANDAs, the provision was slightly more complicated, specifying relinquishment if certain deadlines were not met. The ANDAs for generic esomeprazole magnesium and generic valganciclovir were categorized as "Excepted Applications."<sup>217</sup> They would be ineligible for exclusivity if FDA determined that they were not substantially complete at the time of filing.<sup>218</sup> They would also be ineligible if a data integrity audit revealed that they contained "any untrue statements of material fact" or "a pattern or practice of data irregularities affecting approval."<sup>219</sup> The agency later found that these ANDAs were substantially complete at the time of submission and that neither contained an untrue statement of material fact or a pattern or practice of data irregularities.<sup>220</sup>

In November 2014, FDA rescinded the tentative approval of both ANDAs and announced that Ranbaxy had forfeited exclusivity for generic valganciclovir for failure to obtain tentative approval within 30 months of submission.<sup>221</sup> It later reached the same conclusion with respect to the generic esomeprazole.<sup>222</sup> The agency explained that its prior decisions granting tentative approval were erroneous, because the compliance status of the facilities referenced in the applications was unacceptable to support tentative approval.<sup>223</sup> The prior decisions had been a "mistake."<sup>224</sup> The company had therefore "failed to obtain tentative approval" within 30 months of the ANDA submission dates, leading to forfeiture.

Ranbaxy brought suit against FDA ten days later, arguing among other things that the earlier decisions were not "mistakes" as to which new facts had been brought to

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Director, Division of Manufacturing and Product Quality, CDER, FDA, to Malvinder Singh, CEO and Managing Director, Ranbaxy Laboratories Limited, Warning Letter 320-08-03 (Sept. 16, 2008).

<sup>216</sup> *United States v. Ranbaxy Labs. Ltd.*, C.A. No. 1:12-cv-00250-JFM (D. Md. Jan. 25, 2012) (Consent Decree of Permanent Injunction).

<sup>217</sup> See *Ranbaxy Labs., Inc. v. Burwell*, C.A. No. 1:14-cv-01923-BAH (D.D.C. Nov. 14, 2014) (Memorandum of Points and Authorities in Support of Motion for a Temporary Restraining Order and Expedited Preliminary Injunction) at 11 (explaining which paragraphs applied to these ANDAs).

<sup>218</sup> *United States v. Ranbaxy Labs., Inc.*, Consent Decree, *supra* note 216, ¶ XIV.

<sup>219</sup> *Id.* ¶ XV.

<sup>220</sup> *United States v. Ranbaxy Labs., Inc.*, Memorandum of Points and Authorities, *supra* note 217, at 18-20.

<sup>221</sup> Letter from Kathleen Uhl, M.D., Acting Director, OGD, CDER, FDA, to Sameer Manan, U.S. Agent for Ranbaxy Laboratories Limited regarding ANDA 077830 & ANDA 078078 (Nov. 4, 2014) [hereinafter Uhl Letter to Ranbaxy].

<sup>222</sup> See *Ranbaxy forfeits 180 days exclusivity for generic Nexium*, BUSINESS STANDARD (Jan. 27, 2015).

<sup>223</sup> "Tentative approval," the agency explained, is appropriate when the application cannot receive final effective approval for specific statutory reasons, such as patent-based exclusivity or a 30-month stay. It is not appropriate when the application is unapprovable for other reasons. Tentative approval thus requires the applicant be able to demonstrate compliance with current good manufacturing practices. See Uhl Letter to Ranbaxy, *supra* note 221, at 3-4.

<sup>224</sup> *Id.* at 12.

light requiring their correction; instead, the agency had been aware of the compliance situation at the facilities when it issued those decisions.<sup>225</sup> The company also argued that forfeiture would be inconsistent with the plain language of the forfeiture provision; the company had, in fact, received tentative approval within the deadline.<sup>226</sup> The district court denied the company's motion for a temporary restraining order and later granted FDA's motion for summary judgment.<sup>227</sup> Among other things, the court concluded that the approval process had been "slipshod" and that the agency had clearly erred when it tentatively approved the ANDAs.<sup>228</sup> Further, after concluding that FDA was reasonable in interpreting the statute to permit rescission of erroneously issued tentative approvals, the court found FDA's interpretation of the forfeiture trigger reasonable.<sup>229</sup>

The forfeiture trigger, the court wrote, is "ambiguous." Specifically, an applicant forfeits exclusivity if it fails to "obtain tentative approval" within 30 months. Tentative approval, in turn, is defined as "notification to an applicant by the Secretary that an application under this subsection meets the requirements" of section 505(j)(2)(A) but "cannot receive effective approval because of blocking patents or exclusivity."<sup>230</sup> The statute "does not say anything about whether a 'notification,' once given, may never be withdrawn" or whether—more importantly—"rescission of tentative approval nullifies a previous notification and causes a retroactive forfeiture of 180-day exclusivity."<sup>231</sup> Statutory silence "weighs strong" in favor of "finding that a statute is ambiguous," and FDA's interpretation—that forfeiture "is avoided only when a tentative approval is valid"—was reasonable.<sup>232</sup> Allowing the retroactive forfeiture of exclusivity if tentative approval is later rescinded is "entirely in keeping with" the "Hatch-Waxman goal of streamlining generic drug approvals" to allow them to reach the market sooner. Ranbaxy's approach—disallowing retroactive forfeiture—"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."<sup>233</sup>

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<sup>225</sup> *United States v. Ranbaxy Labs., Inc.*, Memorandum of Points and Authorities, *supra* note 217, at 23.

<sup>226</sup> *Id.* at 33–34.

<sup>227</sup> See generally *Ranbaxy Labs., Ltd., v. Burwell*, 82 F. Supp. 3d 159 (D.D.C. 2015).

<sup>228</sup> *Id.* at 191–92.

<sup>229</sup> *Id.* at 196–97.

<sup>230</sup> *Id.* at 197 (citing 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd)(AA)).

<sup>231</sup> *Id.*

<sup>232</sup> *Id.*

<sup>233</sup> *Id.* at 198. Sun Pharma acquired Ranbaxy in March 2015 and withdrew the appeal that had been filed. See *Sun Pharm. Indus. Ltd. v. Burwell*, No. 15-5063 (D.C. Cir. Oct. 7, 2015) (Order); see also Eric Palmer, *Sun Kills Lawsuit Ranbaxy Filed Against FDA for Pulling its Nexium Generic*, FIERCEPHARMA (Oct. 9, 2015) ("Ranbaxy is now owned by Sun Pharmaceutical, which sees no upside to fighting with the agency, and so it has dropped the litigation").

8. *Will amendments to an ANDA to conform to changes in the reference listed drug “excuse” failure to obtain tentative approval within 30 months?*

*Short Answer.* If the agency *requires* the first applicant to make changes to its ANDA, failure to obtain tentative approval within 30 months will not lead to forfeiture.

*Discussion.* Subparagraph (D)(i)(IV) excuses the first applicant from failure to obtain tentative approval by the statutory deadline, where the failure to obtain tentative approval “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.”<sup>234</sup> Citing this provision, the agency has excused first applicants whom it *required* to make changes to their pending applications.

One notable dispute arose in connection with Cobrek’s application referencing Genzyme’s Hecitorol, discussed in subsection II.C.3. As noted, FDA had allowed Cobrek to recertify to Genzyme’s patent without deeming the recertification a disqualifying amendment or withdrawal of the original certification. The underlying facts involved a formulation change. Specifically, after Cobrek filed its ANDA for doxercalciferol in an ampule presentation, qualifying for exclusivity, Genzyme developed and introduced a new injectable formulation in a vial presentation. It also decided to stop marketing the ampule presentation. FDA informed Cobrek that the agency could not approve the original ANDA because the ampule formulation was not quantitatively and qualitatively the same as the new vial drug product, and it recommended Cobrek reformulate. Cobrek did so, but as a result it failed to obtain tentative approval by the 30-month deadline. Sandoz’s citizen petition—which had argued that recertification to a Genzyme patent disqualified Cobrek for exclusivity—also argued that the formulation change did not excuse failure to obtain tentative approval.<sup>235</sup> Specifically, Sandoz argued that there was no change in or review of the requirements for approval of a generic *ampule* (for which Cobrek had submitted its original ANDA) or for approval of a generic *vial* (for which Cobrek was now seeking approval). “[I]f anything,” according to Sandoz, “Cobrek’s delay in receiving tentative approval is attributed to its *voluntary* decision to seek approval for a generic vial version of Hecitorol® Injection.”<sup>236</sup>

The agency denied the Sandoz petition, essentially by explaining that Cobrek’s decision was not voluntary. This matter involved an injectable drug and therefore a requirement that a generic formulation be qualitatively and quantitatively the same as the reference listed drug. FDA explained that once Genzyme withdrew the old formulation, any applicant with a pending ANDA was required to either (1) reformulate or (2) obtain a determination that the old formulation was not withdrawn for safety reasons and a corresponding waiver. Either way, the agency concluded, there had been a “change in or review of the requirements for approval” of the ANDA in question.<sup>237</sup> Cobrek therefore had not forfeited exclusivity when it failed to obtain tentative approval within 30 months.

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<sup>234</sup> 21 U.S.C. § 355(j)(5)(D)(i)(IV).

<sup>235</sup> Sandoz Inc., Citizen Petition, Docket No. FDA-2010-P-0632 (Dec. 8, 2010).

<sup>236</sup> *Id.* at 13 (emphasis in original).

<sup>237</sup> Letter from Janet Woodcock, M.D., Director, CDER, FDA, to Stephen Auten, Vice President, Legal-Intellectual Property, Sandoz Inc., Docket No. FDA-2010-P-0632 (Sept. 20, 2011), at 9.

The agency has similarly forgiven the failure to obtain timely tentative approval where the first applicant made labeling amendments to conform to changes made to the labeling of the reference listed drug or to comply with agency requests. This is why Teva did not forfeit exclusivity in 2012 with respect to its application referencing Pfizer's Zyvox® (linezolid). FDA approved three changes to the labeling of Zyvox while Teva's application was pending.<sup>238</sup> The agency reviewed Teva's labeling two weeks before the 30-month forfeiture date and asked the company to revise the labeling to conform to Pfizer's most recent labeling; FDA's subsequent review of the labeling amendment extended one month past the deadline. The agency then asked for additional labeling changes, and approval of the ANDA required another review cycle. Finding that "there were changes to the requirements for approval with respect to labeling" and that "these labeling changes were a cause of Teva's failure to obtain tentative approval by the forfeiture date," the agency found that Teva's exclusivity was not forfeited.<sup>239</sup> Other examples—where labeling changes to the reference listed drug required labeling changes to the generic and excused failure to achieve timely tentative approval—include Impax's exclusivity with respect to generic lamotrigine orally disintegrating tablets,<sup>240</sup> Synthon's exclusivity with respect to generic levocetirizine dihydrochloride tablets,<sup>241</sup> and Anchen's exclusivity with respect to generic flvoxamine maleate in 150 mg strength.<sup>242</sup>

In other situations, FDA has released applicants from the 30-month forfeiture clock when the delay in tentative approval is attributable to an ongoing agency review of a pertinent generic drug approval requirement. This appears to have been the case for two ANDAs approved in 2012, as to which the delay was attributed to a review of requirements with respect to generic drug tablet size.<sup>243</sup> FDA similarly

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<sup>238</sup> These were changes to the Clinical Pharmacology (Pharmacokinetics and Drug-Drug Interactions), Precautions (Drug Interactions), and Adverse Reactions (Postmarketing Experience) sections; changes to the Clinical Pharmacology (Pharmacodynamics) section regarding a QT study; and addition of hypoglycemia to the Warnings section and the Adverse Reactions (Postmarketing Experience) sub-section of the package insert. Memorandum from Martin Shimer, Deputy Director, Division of Legal and Regulatory Support, Office of Generic Drug Policy, CDER, FDA, to ANDA 200222 (May 15, 2015).

<sup>239</sup> *Id.*

<sup>240</sup> Memorandum from Martin Shimer, Deputy Director, Division of Legal and Regulatory Support, Office of Generic Drug Policy, CDER, FDA, to ANDA 200828 (Oct. 29, 2014) (modification of the risk evaluation and mitigation strategy and associated supporting documents, and five labeling changes between June 2010 and August 2012, where ANDA had been submitted in December 2009).

<sup>241</sup> Letter from Keith Webber, Ph.D., Deputy Director, OPS, CDER, FDA, to Shannon F. Holmes, Ph.D., Senior Regulatory Affairs Specialist, Synthon Pharmaceuticals, Inc. approving ANDA 090229 (Nov. 26, 2010) (noting that there had been "a change in the requirements for approval of this ANDA"—specifically a change in the labeling of the reference listed drug—that caused the company's failure to obtain timely tentative approval).

<sup>242</sup> Letter from Gregory P. Geba, M.D., M.P.H., Director, OGD, CDER, FDA, to David Quiggle, Director, Regulatory Affairs, Anchen Pharmaceuticals, Inc. approving ANDA 091476 (Mar. 13, 2013) (noting that Anchen's failure to obtain tentative approval of the 150-mg strength "was caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application was filed"—specifically revisions in the labeling of the reference listed drug "that necessitated changes in Anchen's labeling that were not resolved until" after the forfeiture date).

<sup>243</sup> Letter from Gregory P. Geba, M.D., M.P.H., Director, OGD, CDER, FDA, to John Derstine, Director, Regulatory Affairs, Teva Pharmaceuticals USA approving ANDA 200435 (Sept. 25, 2012) (concluding that Teva's failure to obtain timely tentative approval of a generic amlodipine, hydrochlorothiazide, and valsartan fixed dose combination product was "caused by a change in or a

released Actavis from the forfeiture clock with respect to a generic clobetasol propionate shampoo when it approved the drug in June 2011, because the agency had been reviewing the appropriateness of vasoconstrictor bioassay studies for topical corticosteroid drug products applied to the hirsute scalp and had asked the company to perform comparative vasoconstrictor bioassay studies.<sup>244</sup> Indeed, the agency issued a draft guidance on the issue three months before approving the Actavis product.<sup>245</sup>

Even if the agency ends up *not* requiring a change, it may excuse the applicant for failure to obtain tentative approval within 30 months. For instance, Eon Labs (which became Sandoz) was the first to file a substantially complete ANDA for generic metaxalone tablets, 800 mg, with paragraph IV certifications to two patents listed for the reference listed drug, Skelaxin® (metaxalone). Eon Labs submitted the ANDA in November 2004 but did not obtain tentative approval within 30 months. The agency's eventual March 2010 approval letter concluded that the delay was attributable to review of the labeling requirements for metaxalone, which fit within the four corners of the exception in subparagraph (D)(i)(IV).<sup>246</sup> Further, the review had been prompted by a citizen petition, and section 505(q) of the FDCA now tolls the 30-month clock while a petition is pending.<sup>247</sup> Citing the tolling provision, FDA found Teva had not forfeited exclusivity for generic methylphenidate hydrochloride extended release capsules,<sup>248</sup> nor had Impax forfeited exclusivity for generic doxycycline hyclate delayed-release tablets.<sup>249</sup>

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review of the requirements for approval of the application imposed after the date on which the application was filed, specifically a review of ANDA approval requirements with respect to tablet size"); Letter from Keith Webber, Ph.D., Deputy Director, OPS, CDER, FDA, to Monique Weitz, Actavis South Atlantic LLC approving ANDA 090869 (May 17, 2012) (concluding that Actavis's failure to obtain timely tentative approval of generic ropinirole hydrochloride extended-release tablets was caused by the agency's review of "ANDA approval requirements with respect to the size of certain solid oral dosage form products").

<sup>244</sup> Letter from Keith Webber, Ph.D., Deputy Director, OPS, CDER, FDA, to Elizabeth Trowbridge, R.A.C., Director, Regulatory Affairs, Actavis Mid Atlantic LLC approving ANDA 078854 (June 7, 2011).

<sup>245</sup> FDA, *Draft Guidance on Clobetasol Propionate* (Feb. 2011).

<sup>246</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to Mary McDonald, Director, Regulatory Affairs, Sandoz Inc. approving ANDA 040445 (Mar. 31, 2010) ("We have determined, however, that this was caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application was filed. Namely, Sandoz submitted its amendment for the 800 mg strength on November 4, 2004, and during the entire time the ANDA was under review, the agency had pending before it a citizen petition that created a review of the appropriate labeling for generic metaxalone in light of certain patent-protected language in the labeling of the RLD.").

<sup>247</sup> It provides that if approval of a first applicant's "ANDA is delayed because of a petition," presumably a petition covered by section 505(q), "the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition."

<sup>248</sup> Letters from Gregory P. Geba, M.D., M.P.H., Director, OGD, CDER, FDA, to Jean W. Zwicker, Senior Director, Regulatory Affairs, Teva Pharmaceuticals USA approving ANDAs 077707 & 078873 (July 19, 2012) (approving ANDAs for generic methylphenidate hydrochloride extended release capsules and explaining that Teva remained eligible for 180-day exclusivity because a citizen petition had been submitted that required the agency to review the requirements for approval for generic drug products referencing Metadate CD®).

<sup>249</sup> Impax Approval Letter, *supra* note 202 (approving ANDA for doxycycline hyclate delayed-release tablets and explaining that Impax remained eligible for 180-day exclusivity because a citizen

One issue that has been briefly litigated—and may generate more disputes—is when, exactly, a delay is “caused” by a change in or a review of the requirements for approval of the application. The litigated case involved the ANDA filed by Ranbaxy (through its subsidiary Ohm Laboratories) referencing Diovan® (valsartan). In December 2004, Ranbaxy was the first to file an ANDA for generic valsartan tablets with a paragraph IV certification to the reference product patents. The 30-month deadline was June 28, 2007, but the USP published a final monograph for valsartan tablets on May 1, 2007. Ranbaxy submitted a chemistry amendment on June 26, to revise its drug substance specifications and test methods to comply with the monograph. On July 2, FDA asked Ranbaxy to provide data showing that its in-house testing methods were equivalent to those set forth in the monograph. Ranbaxy submitted the chemistry amendment in question on July 5, and the agency issued tentative approval in October, nearly four months after the forfeiture date. After noting that whether publication of, or a change to, a USP monograph has “caused” a failure to obtain timely tentative approval is a “very fact-specific question” involving numerous factors, the agency ruled that Ranbaxy’s failure *was* attributable to the publication of the monograph.<sup>250</sup> A subsequent applicant, Mylan, challenged the agency’s reasoning. The heart of Mylan’s argument was that Ranbaxy had already been doing what the USP later required, which was evident from the agency request that the company simply demonstrate that its *methods* were equivalent to the methods specified in the monograph.<sup>251</sup> Relying heavily on the agency’s forfeiture memorandum, the district court dismissed the case,<sup>252</sup> and the final approval issued with an award of exclusivity.<sup>253</sup>

The agency’s own delay, however, may not otherwise excuse a first applicant from failure to obtain tentative approval. This is why Teva forfeited exclusivity for its generic risedronate sodium when it missed the forfeiture clock by six months—

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petition had been submitted that required FDA to review the requirements applicable to the product). In this instance, the requirements for approval were *also* changed, because the reference listed drug was approved for a second tablet configuration, and Impax was required to change to a scored tablet and conduct additional dissolution testing. *Id.*

<sup>250</sup> Memorandum from Martin Shimer, Branch Chief, Regulatory Support Branch, OGD, CDER, FDA, to ANDA 077492 (Sept. 28, 2012). According to FDA, the factors include: (1) whether the monograph change is in a proposed or final monograph; (2) the timing of any publication of or change in a monograph in relation to a particular 30-month forfeiture date; (3) whether FDA requires compliance with the new/changed standard; (4) whether the statute itself requires compliance with the new/changed standard; (5) the consistency of the new/changed monograph with pre-existing approval requirements; (6) the nature and timing of the sponsor’s efforts to comply with USP monographs; and (7) the nature and timing of FDA’s review of such efforts. *See id.* at 11; *see also Mylan Labs. Ltd. v. FDA*, 910 F. Supp. 2d 299 (D.D.C. 2012).

<sup>251</sup> *Mylan Labs.*, 910 F. Supp. 2d at 309.

<sup>252</sup> *Id.* (“A new, final USP monograph was published; Ranbaxy made an initial effort to comply with the monograph; FDA then asked for more data; Ranbaxy gave FDA more data; and because FDA had to review Ranbaxy’s amendments and the additional data to ensure that Ranbaxy’s drug substance specifications and test methods met the standards set forth in the new monograph, tentative approval was delayed. This connection between the specific facts and FDA’s conclusion is apparent from the face of the Forfeiture Memo and is both logical and rational.”)

<sup>253</sup> *Id.*; *see* Letter from Kathleen Uhl, M.D., Acting Director, OGD, CDER, FDA, to Sameer Manan, Senior Manager, Regulatory Affairs, Ohm Laboratories approving ANDA 077492 (June 26, 2014) (“The applicant’s effort to comply with this new requirement, and FDA’s review of that effort, was a cause of the applicant’s failure to obtain tentative approval by the 30-month forfeiture date described in section 505(j)(5)(D)(i)(IV).”).

even though all FDA review disciplines had actually completed their reviews of the ANDA *one day prior* to the forfeiture date. The agency explained that it had not completed its final review of the ANDA by the forfeiture date; approval requires not only evaluation by the relevant disciplines, but also review by management of the Office of Generic Drugs. That review was not completed until six months later. Further, and in any case, the agency explained, the statute does not contemplate arguments that the applicant could have received timely approval “had the review been conducted more quickly.” Indeed, the agency pointed out, the FDASIA amendments extending the clock to 40 months for certain ANDAs is predicated on the understanding “both that the length of time that it takes FDA to review an ANDA might contribute to a sponsor’s failure to obtain tentative approval by the 30-month forfeiture date, and that in such instances forfeiture nonetheless may occur.”<sup>254</sup>

### ***Patent Expiry***

A first applicant forfeits the exclusivity period if “[a]ll of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.”<sup>255</sup> Since the 2009 article, two issues pertaining to this forfeiture provision have emerged.

9. *If the only patent listed when the first paragraph IV ANDA is submitted expires before any ANDA has been accepted for review, is “all” 180-day exclusivity for the product forfeit?*

*Short answer.* This is a matter of first impression pending before the agency.

*Discussion.* This issue has arisen in connection with Restasis, discussed in subsection II.B.3. As a reminder, Allergan listed the ‘979 patent, which was slated to expire on May 17, 2014. InnoPharma submitted an ANDA on January 13, 2014, with a paragraph IV certification to the ‘979 patent, which was the only patent listed in the Orange Book at the time. InnoPharma was the first to file a paragraph IV to the ‘979 patent, but the patent expired on May 27, 2014, before FDA issued an acknowledgment letter to *any* company that had submitted an ANDA. On January 14, Allergan listed the ‘111 patent. It appears from docket filings that Akorn was the first (or one of the first) to file a paragraph IV certification to the ‘111 patent. As noted earlier, FDA has asked whether InnoPharma is a “first applicant” for purposes of 180-day exclusivity.

The agency has also asked whether all 180-day exclusivity for this product was forfeited on May 17, 2014, when the ‘979 patent expired, “such that no ANDA applicant for Cyclosporine Ophthalmic Emulsion, 0.05%, is eligible for 180-day generic drug exclusivity.” Axar, which appears to be a subsequent filer, has argued that it is forfeited: InnoPharm was a first applicant, and it forfeited exclusivity when the ‘979 patent expired. “In the post-MMA context,” the company argues, “once that exclusivity is forfeited, it is gone forever.” Moreover, “[n]o other patents can give rise to a separate period of exclusivity.”<sup>256</sup> InnoPharma agrees; “upon the expiration of the 979 patent, all first applicants forfeited their 180-day exclusivity period, and,

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<sup>254</sup> Memorandum from Robert L. West, Deputy Director, OGD, CDER, FDA to ANDA 079215 (June 10, 2014).

<sup>255</sup> 21 U.S.C. § 355(j)(5)(D)(i)(VI).

<sup>256</sup> Comments of Axar Pharmaceuticals, Inc., Docket No. FDA-2015-N-2713 (Aug. 27, 2015).

as expressly provided in the FDCA, no other applicants are eligible for a 180-day exclusivity period."<sup>257</sup> Akorn, which believes itself the first applicant (*because* Innopharm does not qualify) disagrees.

10. *What is the effect of patent expiry once a paragraph IV certification has been submitted?*

Under section 505(j)(5)(D)(i)(IV), expiry of all of the patents qualifying the first applicant for exclusivity leads to forfeiture. Subsection II.C.1, above, discusses a dispute regarding Teva's applications referencing Cozaar and Hyzaar. The discussion earlier related to Merck's delisting of the '075 patent and the D.C. Circuit's ruling that Teva had not forfeited its 180-day exclusivity due to its failure to market in a timely fashion after the delisting in question. The court determined that forfeiture for delisting was appropriate only if the NDA holder had brought a patent infringement suit and then sought delisting as a result of losing on the merits or entering an unfavorable settlement agreement. In other words, unilateral action by the innovator to delist a patent does not result in forfeiture. As the case continued, FDA adopted analogous reasoning and declined to find forfeiture when the patent *expired* due to unilateral action—or, more precisely, inaction—on the part of the NDA holder. Specifically, before the court of appeals issued its mandate, FDA learned that Merck had failed to pay maintenance fees on the patent in question, leading to its expiration as a matter of law.<sup>258</sup> FDA concluded—shortly after the mandate issued—that Teva had not forfeited exclusivity. The reasoning of the court of appeals with respect to delisting—that the statute was not meant to give the innovator “a right to unilaterally vitiate a generic's exclusivity”—leads to the same result with respect to non-payment of maintenance fees.<sup>259</sup> The district court rejected a challenge brought by subsequent applicants seeking to vitiate the exclusivity award, noting that it could not “find that the FDA was arbitrary or capricious when it politely expressed its disagreement with a D.C. Circuit decision that had ruled

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<sup>257</sup> InnoPharma Comments, *supra* note 79.

<sup>258</sup> See 35 U.S.C. § 41(b).

<sup>259</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to ANDA Applicants Docket No. FDA-2010-N-0134 (Mar. 26, 2010) (“This reasoning thus appears to preclude a forfeiture of exclusivity on the basis of a patent expiration where the expiration is in the control of the NDA holder. Because the ‘075 patent expired due to Merck’s failure to pay applicable fees, that expiration, consistent with the Court of Appeals’ reasoning in *Teva*, is not grounds for forfeiture of the first applicant’s exclusivity.”). The agency made it clear that it disagreed with the decision of the court of appeals. See *id.* at 4-5 (“The Agency’s view is that, if it were writing on a clean slate, it would interpret the statute so that patent expiration for any reason is a patent expiration forfeiture event. FDA believes that interpretation is most consistent with the plain meaning of the words of the statute and with a workable and appropriate approach to administration of the statute.”); *id.* at 6 (“Thus, permitting the first applicant to retain exclusivity as to an expired patent requires FDA to take an action that is not sanctioned by the words of the statute.”); *id.* at 7 (“For the reasons described above, FDA concludes that if it were assessing this issue without reference to the *Teva* decision, it would find that, under the plain language of the statute, because the ‘075 patent will have expired by the time any ANDA referencing Cozaar or Hyzaar is ready for approval, any first applicant previously eligible for 180-day exclusivity as to the ‘075 patent forfeits that exclusivity. Moreover, even if the statutory language is considered ambiguous, FDA concludes loss of exclusivity under these circumstances is most consistent with the statute’s text and goals, and provides the most reasonable way of administering the statute.”); *id.* at 8 (“Although FDA believes this result is inconsistent with the plain language of the statute, as discussed above, it believes it is appropriate to apply the Court of Appeals’ reasoning to the present facts.”).



against the agency, but nonetheless applied the reasoning of the Circuit to a different but, on these facts, closely related question.”<sup>260</sup>

FDA’s recent proposed rule briefly notes forfeiture under subparagraph (D)(i)(IV), but it does not address the situation where patent expiry results from unilateral inaction on the part of the innovator. First, in connection with amended patent certifications, and the existing regulation that an applicant may not convert a paragraph IV certification to a paragraph III certification if another applicant is eligible for exclusivity,<sup>261</sup> the agency notes that 180-day exclusivity “does not extend beyond patent expiry.”<sup>262</sup> Citing the forfeiture provision, it then notes that the applicant’s exclusivity would, in any event, “terminate” upon “expiration of all of the patents as to which the applicant submitted a paragraph IV certification qualifying it for 180-day exclusivity.”<sup>263</sup> The new regulations would provide that “[a]ny applicable 180-day exclusivity period cannot extend beyond the expiration of the patent upon which the 180-day exclusivity period was based.”<sup>264</sup> Second, and also in connection with amended certifications, the agency notes that the new forfeiture provision is “consistent with FDA’s longstanding position” that exclusivity is “extinguished” with patent expiry.<sup>265</sup> It has therefore proposed to “codify” its “longstanding” rule that if the patent expires and the first applicant does *not* amend its certification to reflect patent expiry, the agency will *deem* the applicant to have “constructively changed its patent certification to a paragraph II certification.”<sup>266</sup>

The agency’s “longstanding position”—that exclusivity is extinguished with patent expiry—was discussed in the earlier articles.<sup>267</sup> In one subsequent dispute involving an old ANDA, the agency again found that exclusivity ended with patent expiry, and this was upheld by the courts. The dispute related to generic applications referencing Shire’s Carbatrol® (carbamazepine) 300 mg extended release capsules. Two patents were listed in the Orange Book for Carbatrol®—U.S. Patent No. 5,912,013 (the ‘013 patent, slated to expire in 2016) and U.S. Patent No. 5,326,570 (the ‘570 patent, slated to expire on July 23, 2011). Nostrum was the first to file an ANDA containing a paragraph IV certification to each patent, and the resulting patent litigation settled giving it the right to launch in October 2010.<sup>268</sup> FDA

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<sup>260</sup> *Apotex v. Sebelius*, 700 F. Supp. 2d 138 (D.D.C. 2010), *aff’d*, 384 F. App’x. 4 (D.C. Cir. 2010) (unpublished), *cert. denied*, 562 U.S. 1194 (2011).

<sup>261</sup> 21 C.F.R. § 314.94(a)(12)(viii); *see also* 59 Fed. Reg. at 50348 (“[T]he protection offered by 180-day exclusivity should not be undermined by changes from paragraph IV certification . . . [T]he agency has required that a patent remain on the list after being declared invalid or unenforceable until the end of any applicable 180-day exclusivity period . . . [W]here there is a patent that has been challenged by a paragraph IV applicant, a subsequent applicant will not be able to file a certification that there is no relevant patent or seek an immediately effective approval until either the patent or the 180-day exclusivity period expires.”)

<sup>262</sup> 80 Fed. Reg. at 6841.

<sup>263</sup> *Id.*

<sup>264</sup> *Proposed* 21 C.F.R. § 314.107(c)(1).

<sup>265</sup> 80 Fed. Reg. at 6846.

<sup>266</sup> 80 Fed. Reg. at 6847. Although the preamble states that this position would be codified in 21 C.F.R. § 314.94(a)(12)(viii)(C)(1)(i), *id.* at 6843, it appears that the corresponding proposed regulation does not incorporate this change. This might be an oversight.

<sup>267</sup> *See* 2009 Exclusivity Article, *supra* note 4, at 363.

<sup>268</sup> *Nostrum Pharms., LLC v. FDA*, C.A. No. 11-3111, 2011 WL 2652147 (D.N.J. July 6, 2011).

approved the ANDA on May 20, 2011, and the company launched on that day, triggering its exclusivity.<sup>269</sup> The exclusivity on the '013 patent had been triggered by a court decision involving a subsequent filer and had long since expired, and thus FDA determined that Nostrum would enjoy exclusivity based on only the '570 patent. This, in turn, would expire on July 23, 2011, roughly two months after launch.<sup>270</sup> A district court in New Jersey rejected Nostrum's challenge, noting that "[t]he statutory provision entitling Nostrum to exclusivity, by its terms, applies only to paragraph IV certifications, 'which cease to exist upon patent expiration.'"<sup>271</sup>

### ***General Issues Relating to Forfeiture Provisions***

#### *11. When will FDA rule on a particular applicant's forfeiture?*

FDA will not make a forfeiture decision when it approves the first applicant's application unless and until there is a subsequent applicant affected by the exclusivity or forfeiture in question. The agency explained this policy when it awarded Teva exclusivity in connection with the company's ANDA referencing Kytril, discussed in the paragraphs immediately preceding subsection II.C.1. Although 30 months had lapsed since Teva submitted its ANDA, the second failure-to-market trigger had not been met. In a decision letter on 180-day exclusivity, FDA stated that when it makes an approval decision for an ANDA subject to the new rules, the agency will inform the applicant whether it is (1) a first applicant and entitled to exclusivity, (2) a first applicant that has forfeited its exclusivity, or (3) eligible only for a tentative approval because one or more first applicants are eligible for 180-day exclusivity. The agency noted that "[i]t is possible that an ANDA applicant could be informed upon approval that it is a 'first applicant' eligible for 180-day exclusivity . . . but later forfeit that exclusivity. . . . FDA will consider whether there has been a forfeiture of 180-day exclusivity when approval of a subsequent ANDA may be blocked by a first applicant's exclusivity."<sup>272</sup>

The agency made the same comment when faced with possible forfeiture under subparagraph (D)(i)(IV) (failure to obtain tentative approval). Sandoz was the first ANDA applicant to submit a substantially complete ANDA for generic metoprolol succinate extended-release tablets with a paragraph IV certification to the four patents listed by AstraZeneca for the reference listed drug, Toprol-XL®. When FDA approved Sandoz's generic in July 2006, it noted that Sandoz had failed to obtain tentative approval of the ANDA within 30 months after the date on which the ANDA

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<sup>269</sup> Letter from Keith O. Webber, Ph.D., Deputy Director, OPS, CDER, FDA, to Shashank Upadhye, Esq., Vice President, Global Intellectual Property, Apotex, Inc. regarding ANDAs 078986, 076697, and 078159 (May 20, 2011) [hereinafter Webber Letter to Apotex]; Letter from Zoia Ploscaru, Regulatory Agent for NPLLC, Senior Director, Regulatory Affairs, Nostrum Laboratories, Inc., to Keith Webber, Ph.D., Acting Director, OGD, CDER, FDA (May 20, 2011).

<sup>270</sup> FDA's letter approving the Nostrum ANDA indicated the '570 patent would expire on July 5, 2011. See Letter from Keith Webber, Ph.D., Deputy Director, OPS, CDER, FDA, to Zoia Ploscaru, Contact/Agent, Nostrum Pharmaceuticals, LLC approving ANDA 076697 (May 20, 2011). So did the Orange Book at the time. See ORANGE BOOK (31st ed. 2011), at ADA 30. The district court opinion notes: "The parties originally believed and had advised the Court that the patent expired on July 5, 2011. A recent filing with the FDA by the patent holder provided the corrected date." *Nostrum Pharms., LLC v. FDA*, 2011 WL 2652147 at \*3 n.2.

<sup>271</sup> *Id.* at \*9 (citing Mylan Labs., Inc. v. Leavitt, 484 F. Supp. 2d 109, 123 (D.D.C. 2007)).

<sup>272</sup> Buehler Letter to Teva Parenteral Medicines, *supra* note 142.

was submitted. At the same time, it declined to make a formal determination of the company's eligibility for 180-day exclusivity. It would do so only if another applicant became "eligible for approval within 180 days after Sandoz begins commercial marketing" of its product.<sup>273</sup>

*12. What is the effect of a forfeiture of 180-day exclusivity by a first applicant if another other first applicant remains eligible for exclusivity?*

*Short answer.* As a practical matter, if a first applicant forfeits exclusivity but others still hold exclusivity, the effect will be negligible. The first applicant may still obtain approval of its application immediately; it is not blocked by the exclusivity of the remaining first applicants. And its commercial launch will still trigger the exclusivity period.

*Discussion.* This question was addressed in a matter involving generic applications referencing Starlix® (nateglinide) tablets. Several companies submitted ANDAs with paragraph IV certifications on the same first day, each with paragraph IV certifications to four of the patents listed for Starlix in the Orange Book.<sup>274</sup> Dr. Reddy's forfeited its 180-day exclusivity period, when it failed to obtain tentative approval within 30 months of ANDA submission.<sup>275</sup> When FDA granted final approval to the Dr. Reddy's ANDA—without exclusivity—it noted that at least one first applicant *remained* eligible, and it noted that the exclusivity in question would commence on the date of commercial marketing by *any* first applicant. Par's approval letter, issued on the same day, indicates that it retained exclusivity,<sup>276</sup> as does Teva's approval letter.<sup>277</sup> Two days later, in a general letter to ANDA applicants referencing Starlix®, the agency explained the situation. "Certain applicants remain eligible for 180-day exclusivity," it wrote, "while at least one applicant has forfeited 180-day exclusivity . . . because it has failed to obtain tentative approval for its ANDA within 30 months of submission and there has been no change in or review of the approval requirements for these applications."<sup>278</sup> FDA noted that while the statute contemplates forfeiture by a first applicant—and provides that if all first applicants forfeit exclusivity, approval of any ANDA may be made effective immediately and no applicant will be eligible for 180-day exclusivity—"[t]he statute does not . . . specifically address the effect of forfeiture of exclusivity

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<sup>273</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to Dietrich Bartel, B.S., Director, Regulatory Affairs, Sandoz Inc. approving ANDA 76-969 (July 31, 2006).

<sup>274</sup> FDA subsequently listed another patent at the request of the NDA holder, Novartis, and all ANDA applicants submitted paragraph IV certifications to this patent.

<sup>275</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to Kumara Sekar, Ph.D., Director, Global Regulatory Affairs, Dr. Reddy's Laboratories, Inc. approving ANDA 77-461 (Sept. 9, 2009) ("The Agency has determined, however, that DRL has forfeited its 180 day exclusivity period because it failed to obtain tentative approval of this ANDA within 30 months after the date on which the ANDA was filed.").

<sup>276</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to Michelle Bonomi-Huvala, Vice President, Regulatory Affairs, Par Pharmaceuticals, Inc. approving ANDA 77-463 (Sept. 9, 2009).

<sup>277</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to Philip Erickson, R.Ph., Senior Director, Regulatory Affairs, Teva Pharmaceuticals USA approving ANDA 77-467 (Sept. 9, 2009).

<sup>278</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to Applicant (Sept. 11, 2009) [hereinafter Starlix Letter].

by fewer than all of the first applicants.”<sup>279</sup> In particular, the statute does not address two questions: when the forfeiting applicant’s ANDA may be approved, and whether its commercial marketing affects the exclusivity held by others.

As to the first question, the agency noted that the statute differentiates between a “first applicant,” as defined in section 505(j)(5)(B)(iv)(II)(bb), and “an applicant other than a first applicant” (i.e., a subsequent applicant) as referred to in sections 505(j)(5)(B)(iv)(II)(aa) and 505(j)(5)(D)(iii). The timing of approval of an ANDA turns on whether the applicant is a first applicant or a subsequent applicant. Moreover, the statute does not state that a first applicant who forfeits exclusivity becomes a subsequent applicant; it states only that “the 180-day exclusivity period . . . shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.”<sup>280</sup> The agency reasoned that a first applicant forfeiting exclusivity *does not* become a subsequent applicant and consequently *does not* have to wait until expiry of the exclusivity enjoyed by first applicants. Instead, its ANDA, like those of first applicants who remain eligible for exclusivity, may be approved immediately (assuming any applicable 30-month stay has expired and the application is otherwise ready for approval). As to the second question, the agency noted that “[s]ection 505(j)(5)(B)(iv), which governs the running of exclusivity, does not distinguish among first applicants, providing instead that a subsequent applicant’s ANDA may be approved 180 days after the date of first commercial marketing by *any* first applicant.” Thus commercial marketing by any first applicant—including a first applicant who has forfeited exclusivity—will trigger the 180-day exclusivity period. As a result, “when fewer than all first applicants forfeit exclusivity, the practical effects of that forfeiture on the timing of approval of ANDAs will be negligible.”<sup>281</sup>

### ***Other Ways To Lose Exclusivity***

#### *13. Is it possible to lose a “portion” of the exclusivity period?*

Yes, it is possible to effectively forfeit a portion of the 180-day exclusivity period through failure to comply with FDA’s regulations governing notice of commercial marketing. Specifically, under agency regulations, if an applicant does not promptly notify FDA of its date of first commercial marketing, the agency will deem commercial marketing to have begun on the date of approval.<sup>282</sup> If, in fact, the applicant delayed launch, this rule will shorten the exclusivity period in practice. FDA’s recent proposed rule retains this approach: in the case of a first applicant that fails to notify FDA within 30 days of first commercial marketing, the date of product approval will be deemed the date of first commercial marketing.<sup>283</sup>

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<sup>279</sup> *Id.*

<sup>280</sup> 21 U.S.C. § 355(j)(5)(D)(ii).

<sup>281</sup> Starlix Letter, *supra* note 278.

<sup>282</sup> 21 C.F.R. § 314.107(c)(4).

<sup>283</sup> *Proposed* 21 C.F.R. § 314.107(c)(2).

14. *Is an ANDA holder with a paragraph IV certification still eligible for 180-day exclusivity if its parent company acquires the NDA and patent holder?*

*Short Answer.* This is an area of uncertainty. In the one dispute litigated to date, the agency permitted the first applicant to market with exclusivity. But it is not clear what will happen in the future.

*Discussion.* This litigated dispute related to generic applications, subject to old rules, referencing Provigil® (modafinil). Cephalon holds the NDA for Provigil, which FDA approved in 1998. U.S. Patent No. RE37,516 (the '516 patent) was slated to expire in 2014. Four manufacturers—Mylan, Teva USA, Ranbaxy, and Barr—were the first to file (on the same day) ANDAs with paragraph IV certifications to the '516 patent. Cephalon reached a patent settlement with all four, permitting them to launch on April 6, 2012. In December 2007, however, Cephalon submitted another patent for listing in the Orange Book: U.S. Patent No. 7,297,346 (the '346 patent), which expires in 2024. Two companies—Teva USA and Watson—amended their pending ANDAs on the first day with paragraph IV certifications. Teva USA had been one of the original first applicants; it was now the *only* company that was first to file as to both patents. Cephalon did not sue.

In 2011, Teva USA's parent company, Israel-based Teva Pharmaceuticals Industries Ltd. (Teva Ltd.) acquired Cephalon.<sup>284</sup> Thus, both the NDA holder and the first applicant were subsidiaries of the same parent company. On March 30, 2012, Teva USA—which did not have approval of its ANDA—began commercial marketing of an authorized generic under Cephalon's NDA. Teva also sought assurances from FDA that it alone held the 180-exclusivity rights. FDA responded on April 4, 2012, confirming that Teva USA was the sole holder of 180-day exclusivity and indicating that this exclusivity had been triggered by its launch of an authorized generic on March 30, 2012.<sup>285</sup> It also noted that Teva had not been pursuing its own ANDA and mentioned that a first applicant might not maintain its eligibility for exclusivity if it is not actively seeking approval of its ANDA.<sup>286</sup> The agency may have meant that Teva could lose the exclusivity it was enjoying while marketing the authorized generic, if it did not continue to pursue the pending ANDA.

The next day, Mylan—which had an ANDA otherwise approvable and had a settlement permitting it to launch in April 2012—filed suit.<sup>287</sup> Mylan alleged that Teva USA had failed to maintain a valid paragraph IV certification, because the acquisition of Cephalon by its parent company meant that Teva USA could no longer be adverse to Cephalon; put another way, Teva USA could not infringe its own patent (or a patent that it “owns indirectly through a controlled corporate affiliate”)

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<sup>284</sup> See *Teva to Acquire Cephalon in \$6.8 Billion Transaction*, Teva Pharmaceutical Industries, Ltd. (May 2, 2011), [http://www.tevapharm.com/news/teva\\_to\\_acquire\\_cephalon\\_in\\_6\\_8\\_billion\\_transaction\\_05\\_11.aspx](http://www.tevapharm.com/news/teva_to_acquire_cephalon_in_6_8_billion_transaction_05_11.aspx).

<sup>285</sup> See Letter from Keith O. Webber, Ph.D., Deputy Director, OPS, CDER, FDA, to Marc Goshko, Vice President, Product and Patent Strategy, Legal Affairs, Teva Pharmaceuticals – Americas regarding ANDA 076596 (Apr. 4, 2012) [hereinafter *Provigil Letter Decision*]. The agency's shared exclusivity policy did not apply because Teva was the only first applicant as to both listed patents. *Id.* at 7.

<sup>286</sup> *Id.* at 7 n.21.

<sup>287</sup> *Mylan Pharm., Inc. v. Sebelius*, C.A. No. 12–524 (ESH) (D.D.C. Apr. 5, 2012) (Complaint), at 2, 7.

with a paragraph IV certification.<sup>288</sup> Moreover, Mylan argued, a federal court could not entertain the patent infringement case, because the parties would not have adverse legal interests. The statute, Mylan added, requires the NDA-holder/patent holder and the paragraph IV filer to remain independent and adverse from the time of the paragraph IV certification until exclusivity is awarded. Ultimately, permitting Teva to keep its exclusivity—that is, permitting NDA holders to themselves hold first applicant exclusivity with respect to generic versions of their own products—would “frustrate the purpose and intent of the Hatch–Waxman statute, which was designed to encourage generic competition, not to erect artificial barriers to such competition.”<sup>289</sup>

The court denied Mylan’s motion for a preliminary injunction, finding that although Mylan’s position might be sound as a policy matter, the statute did not address the issue and the appropriate remedy for the situation lay with Congress, not the court.<sup>290</sup> Mylan voluntarily dismissed its appeal before the D.C. Circuit could address the issue, presumably because it had reached an agreement with Teva that allowed it to enter the market during the 180-day exclusivity period.<sup>291</sup> In July 2012, the FTC issued a decision and order concluding its investigation of Teva Ltd’s acquisition of Cephalon.<sup>292</sup> The Director of the Bureau of Competition explained that its concerns about the delay in generic modafinil entry had been addressed. Teva had agreed that it would not challenge FDA’s determination that the 180-day exclusivity period began to run when it launched an authorized generic and would therefore end in September 2012. Also, Teva entered into a licensing agreement with subsequent filer Mylan, allowing Mylan to launch in August 2012, 45 days *before* the exclusivity term would expire.<sup>293</sup>

The impact of this dispute on future mergers and acquisitions remains uncertain. The FDA decision letter in the Provigil matter contains a comment that the agency “considered” finding that Teva’s marketing of the reference drug itself, i.e., Provigil, upon its acquisition of Cephalon triggered its 180-day exclusivity. It added that it believed “there is a strong argument for finding so.” It refrained from adopting that interpretation “in this case” because this would have meant Teva’s exclusivity would expire on April 11, 2012, and Teva had no notice. But, the agency noted, “[b]ecause of the potential for collusion between NDA holders and captive first generics, and the subversion of the statutory scheme that could result, the agency may in the future provide guidance on the effect of such a relationship between NDA holder and first applicant upon any claim for 180-day exclusivity.”<sup>294</sup>

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<sup>288</sup> *Id.*

<sup>289</sup> *Id.* at 8.

<sup>290</sup> *Mylan Pharm., Inc. v. Sebelius*, 856 F. Supp. 2d 196, 218 (D.D.C. 2012).

<sup>291</sup> *Mylan Pharm., Inc. v. Sebelius*, No. 12–5135 (D.C. Cir.). Mylan voluntarily dismissed its appeal on June 6, and it issued a press release about the settlement on June 8. See FTC, “Statement of Bureau of Competition Director Richard Feinstein on the Commission’s Final Consent Order in *In the Matter of Teva Pharmaceutical Industries Ltd. and Cephalon, Inc.*,” File No. 1110166, Docket No. C–4335” (July 2, 2012) at n.3.

<sup>292</sup> See *Mylan Pharm., Inc. v. Sebelius*, Decision and Order, Docket No. C–4335 (F.T.C. July 2, 2012).

<sup>293</sup> FTC Statement, *supra* note 291.

<sup>294</sup> Provigil Decision Letter, *supra* note 285, at 7 n.18.

### D. Triggering Exclusivity

The old scheme contained two exclusivity triggers: commercial marketing of the generic drug product by the first applicant, and a court decision declaring the patent invalid or not infringed. Under the new rules, exclusivity begins with commercial marketing; a court decision does not by itself start the 180 days. A court decision may trigger the clock for forfeiture, however, and thereby *indirectly* start the 180 days (by forcing the first applicant to launch). Most of the issues that follow relate to the court decision trigger. With one exception (private label sales) the commercial marketing trigger has not generated significant controversy.<sup>295</sup>

#### 1. What kind of court decision triggers 180-day exclusivity?

*Short answer.* As discussed in the earlier articles, the old ANDA scheme requires a decision that on its face evidences a holding on the merits of patent non-infringement, invalidity, or unenforceability. In 2003, Congress eliminated the court decision trigger for exclusivity for new ANDAs.

*Discussion.* The court decision trigger for old ANDAs referred to a “decision of a court . . . holding the patent which is the subject of the certification to be invalid or not infringed.”<sup>296</sup> FDA’s interpretation of this provision emerged after litigation involving ANDAs that referenced Pravachol® (pravastatin sodium) and earlier litigations involving generic ticlopidine and ondansetron hydrochloride.<sup>297</sup> Apotex, a subsequent applicant that referenced Pravachol®, brought suit for a declaratory judgment that the patents in question were invalid or not infringed by its product. The court dismissed the case with a stipulation and order—signed by both parties—that the innovator (Bristol-Myers Squibb) had “no intention to bring suit against Apotex for infringement.” Apparently thinking that the court decision in the ticlopidine matter<sup>298</sup> required it to treat any dismissal of a declaratory judgment action as a “court decision” triggering exclusivity, FDA agreed with Apotex that this dismissal triggered the first applicant’s exclusivity. When the first applicant, Teva, brought suit, the D.C. Circuit rejected FDA’s reading of the ticlopidine decision.<sup>299</sup> The agency “mistakenly thought itself bound,” the court concluded, which rendered the decision “arbitrary and capricious.” The statute might “preclude treating voluntary dismissals . . . as triggering events,” but the court took no view; it was “up to the agency to . . . make a reasonable policy choice.” The response was a policy articulated in an April 2006 letter to an ANDA applicant: “FDA interprets the court

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<sup>295</sup> FDA defines “commercial marketing” as “introduction or delivery for introduction into interstate commerce outside the control of the manufacturer of a drug product,” except for investigational use under part 312 of this chapter. It does not include transfer of the drug product for reasons other than sale within the control of the manufacturer or application holder. 21 C.F.R. § 314.107(c). FDA’s proposed rule would move this to section 314.3 of the regulations but not meaningfully change its substance: “Commercial marketing is the introduction or delivery for introduction into interstate commerce of a drug product described in an approved ANDA, outside the control of the ANDA holder, except for investigational use under part 312 of this chapter, but does not include transfer of the drug product for reasons other than sale to parties identified in the approved ANDA.” Proposed 21 C.F.R. § 314.3(b).

<sup>296</sup> 21 U.S.C. § 355(j)(5)(B)(iv) (1984).

<sup>297</sup> See 2009 Exclusivity Article, *supra* note 4, at 352–55.

<sup>298</sup> *Teva Pharm. USA, Inc. v. FDA*, C.A. No. 99–67(CKK), 1999 WL 1042743 (D.D.C. Aug. 19, 1999), *aff’d*, 254 F.3d 316 (D.C. Cir. 2000).

<sup>299</sup> *Teva Pharm. USA, Inc. v. FDA*, 441 F.3d 1, 3 (D.C. Cir. 2006).

decision trigger provision to require a decision of a court that on its face evidences a holding on the merits of patent non-infringement, invalidity, or unenforceability.”<sup>300</sup>

After the 2009 article, Apotex, which is a Canadian company, sought review by a NAFTA tribunal.<sup>301</sup> Apotex argued that the agency and courts committed legal error when failing to find that dismissal of its case against Bristol-Myers Squibb qualified as a triggering court decision. This asserted error included: (1) adopting and applying an interpretation of the statute that conflicts with congressional intent, the purpose of the Hatch-Waxman Amendments, and controlling federal court precedent, specifically the ticlopidine decision; (2) adopting and upholding an interpretation that runs counter to FDA’s own regulations implementing the statute in a “nontextual manner” by permitting a court decision of unenforceability to qualify as a court decision trigger; (3) construing the statute in a manner that nullifies and renders inoperable the declaratory judgment mechanism under Hatch-Waxman; and (4) failing to treat the dismissal in a similar manner to court decisions entered in certain other cases.<sup>302</sup> The tribunal dismissed the case for lack of jurisdiction on June 14, 2013.<sup>303</sup>

Also since the last article, a federal district court rejected a challenge to FDA’s application of its April 2006 policy. The dispute involved a generic application referencing Carbatrol (carbamazepine), discussed also in Section II.C.9 above. As previously discussed, Shire listed two patents in the Orange Book: the ‘013 patent and the ‘570 patent. Nostrum was the first to submit an ANDA containing a paragraph IV certification to both, thereby qualifying for exclusivity. Exclusivity under the old ANDA scheme was patent-by-patent, meaning that Nostrum had earned two exclusivity terms. The term arising from the ‘013 patent is relevant here. Shire and Nostrum settled their patent infringement litigation in March 2010, and the settlement gave Nostrum a license to market the product beginning in October 2010. FDA approved Nostrum’s product in May 2011, at which point the company launched the product. The agency denied Nostrum exclusivity in connection with the ‘013 patent, however, reasoning that a July 2009 decision involving another generic applicant had triggered the exclusivity relating to that patent, and that the exclusivity had therefore already concluded.<sup>304</sup>

The triggering decision in question was a five-page “Judgment and Order of Permanent Injunction,” which mentioned only in passing an earlier grant of summary

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<sup>300</sup> Letter from Gary Buehler, Director, OGD, CDER, FDA, to Pravastatin ANDA Applicant (Apr. 11, 2006).

<sup>301</sup> *Apotex Inc. v. United States of America*, NAFTA Arbitral Tribunal, Notice of Arbitration, (June 4, 2009).

<sup>302</sup> This included the *Granutec* case, in which the Fourth Circuit—in an unpublished opinion—found that the statute does not require the first filer to successfully defend against a patent infringement suit. *Granutec, Inc. v. Shalala*, 139 F.3d 889 (4th Cir. 1998) (unpublished). In that matter, FDA took the position that Genpharm’s exclusivity was triggered by a court decision involving another generic applicant—a partial summary judgment grounded in the patentee’s concession of non-infringement. See *Glaxo, Inc. v. Boehringer Ingelheim Corp.*, 954 F.Supp. 469 (D.Conn. 1996), judgment entered by 962 F. Supp. 295 (D.Conn. 1997), *aff’d*, No. 97-1283, 1997 WL 355339 (Fed. Cir. June 4, 1997).

<sup>303</sup> See *Apotex Inc. v. United States of America*, NAFTA Arbitral Tribunal, Award on Jurisdiction and Admissibility (June 14, 2013).

<sup>304</sup> Letter from Webber to Apotex, *supra* note 269.



judgment of noninfringement of the '013 patent.<sup>305</sup> The earlier grant of summary judgment, in turn, had been grounded in estoppel after Shire adopted irreconcilably inconsistent positions on the infringement question; the court in question had written that "[b]ecause Shire has been judicially estopped from contesting infringement of the '013 patent, Corepharma's motion for summary judgment is unopposed." Accordingly, "Corepharma is entitled to judgment of noninfringement of the 013 patent as a matter of law."<sup>306</sup> Nostrum challenged FDA's decision that the resulting judgment and order of permanent injunction had triggered its exclusivity. Noting that FDA's policy requires a decision "that on its face evidences a holding on the merits," Nostrum argued that the ruling in question was not a ruling on the merits; it was "more akin to a dismissal for lack of jurisdiction than a decision on the merits of infringement."<sup>307</sup> The district court rejected Nostrum's request for preliminary relief. FDA, the court wrote, "has never interpreted the court decision trigger provision to require a court to compare the claims of the asserted patents to the accused generic product." Instead, FDA looks for "resolution of the issues of validity, infringement and enforceability 'on the merits.'"<sup>308</sup>

Recent student notes have considered the question whether an invalidity decision in an *inter partes* review (IPR) proceeding, affirmed on appeal by the Federal Circuit, would qualify as a court decision for purposes of failure-to-market forfeiture.<sup>309</sup> IPR, made possible by 2011 amendments to the Patent Act,<sup>310</sup> is an adversarial proceeding before the Patent Trial and Appeal Board (PTAB) within the PTO. The IPR mechanism allows a third party, including a subsequent generic applicant, to mount an invalidity challenge on specific and limited grounds.<sup>311</sup> When considering invalidity, the PTAB applies a "preponderance of the evidence" standard, which is lower than the "clear and convincing evidence" standard that would apply in a district court invalidity challenge.<sup>312</sup> The statute permits any party to the proceeding to appeal the final written decision to the Federal Circuit.<sup>313</sup> If a

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<sup>305</sup> *Shire Labs., Inc. v. Corepharma LLC*, C.A. No. 06-CV-02266 (SRC) (MAS) (D.N.J. July 14, 2009) (Judgment and Order of Permanent Injunction).

<sup>306</sup> *Shire Labs. Inc. v. Corepharma LLC*, C.A. No. 06-CV-02266 (SRC) (D.N.J. Oct. 31, 2008) (Opinion).

<sup>307</sup> *Nostrum Pharms. LLC v. FDA*, C.A. No. 11-311, 2011 WL 2652147, at \*6 (D.N.J.) (unpublished).

<sup>308</sup> *Id.* The district court denied Nostrum's request for an interim injunction pending appeal, and the Third Circuit denied the company's request for an injunction pending appeal.

<sup>309</sup> See, e.g., Jaimin Shah, Comment, *Pulling the "Trigger" on the Hatch-Waxman Act's 180-Day Exclusivity Using Inter Partes Review*, 14 J. MARSHALL REV. INTELL. PROP. L. 453 (2015) (arguing that a final *inter partes* review decision should qualify as a policy matter); Brian T. Apel, Note, *An Administrative Meter Maid: Using Inter Partes Review and Post-Grant Review to Curb Exclusivity Parking Via the "Failure to Market" Provision of the Hatch-Waxman Act*, 114 MICH. L. REV. 106, 107 (2015) (concluding that *inter partes* review is unlikely to qualify).

<sup>310</sup> Leahy-Smith America Invents Act (AIA), Pub. L. No. 112-29, 126 Stat. 375 (2011).

<sup>311</sup> 35 U.S.C. § 311 (limiting the grounds to "a ground that could be raised under section 102 [novelty] or 103 [obviousness] and only on the basis of prior art consisting of patents or printed publications").

<sup>312</sup> *Id.* § 316(e). There are also significant differences between an IPR proceeding and a district court infringement case, including with respect to permissible discovery.

<sup>313</sup> *Id.* § 319. There may, however, be constitutional impediments to standing in some cases. E.g., *Consumer Watchdog v. Wisconsin Alumni Research Foundation*, 753 F.3d 1258 (Fed. Cir. 2014) (finding

court of appeals ruling affirming a PTAB written decision of invalidity qualified as a “court decision” for forfeiture purposes, the *inter partes* review mechanism might become an attractive option for subsequent applicants seeking to trigger forfeiture of the first applicant’s exclusivity. It is possible that a court would conclude that this court ruling did not qualify, because the forfeiture provision refers to a final decision “in an infringement action” or a “declaratory judgment action.”<sup>314</sup>

If the patentee did not appeal the written decision, an alternative might be for the successful petitioner (the subsequent applicant) to seek a summary judgment of invalidity in district court on the basis of the written decision cancelling the relevant claims. This might be accomplished in any ongoing patent infringement litigation brought against that subsequent applicant (whether or not the court stayed the litigation pending the outcome of the IPR), or it might be accomplished through a suit for declaratory judgment, if the district court would accept jurisdiction despite the cancellation of the claims. The subsequent applicant would then argue to FDA that a district court judgment of invalidity due to cancellation of the claims qualifies as a court decision under the forfeiture provisions.

2. *Under what circumstances may a subsequent applicant bring a declaratory judgment suit against the innovator or patent holder in order to trigger the first applicant’s exclusivity?*

*Short answer.* The court decision trigger for exclusivity under the old ANDA provisions was interpreted to permit a subsequent ANDA applicant to trigger the first ANDA applicant’s 180-day exclusivity by prevailing in its own court case, clearing the way to market after expiry of the exclusivity. Where the innovator had not sued the subsequent applicant for patent infringement on at least one of the patents for which a paragraph IV certification was submitted, that applicant sometimes sought the triggering court decision through a declaratory judgment suit against the innovator. And although there is no court decision trigger under the new provisions, there is a court decision trigger for forfeiture, which has led subsequent ANDA applicants similarly to seek declaratory judgment to cause forfeiture of exclusivity that is blocking them from the market.

*Discussion.* Prior to January 2007, courts determining whether there was jurisdiction to hear a declaratory judgment action concerning a patent applied the Federal Circuit’s “reasonable apprehension of suit” test to determine whether a declaratory judgment plaintiff satisfied the case or controversy requirement. This test required that a party seeking declaratory relief establish an explicit threat or other action by the patentee, creating a reasonable apprehension on the part of the declaratory judgment plaintiff that it would face an infringement suit.<sup>315</sup> Applying

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that petitioner, a “not-for-profit public charity” that did not allege any involvement in the relevant research or development field and that did not claim to be an actual or prospective competitor of the patentee, lacked sufficient “injury in fact” to establish standing in federal court under Article III of the U.S. Constitution).

<sup>314</sup> 21 U.S.C. § 355(j)(5)(D)(i)(I).

<sup>315</sup> E.g., *Teva Pharms. USA, Inc. v. Novartis Pharm. Corp.*, 482 F.3d 1330, 1339 (Fed. Cir. 2007), *rehear’g denied and rehear’g en banc denied*, No. 06–1181, 2007 U.S. App. LEXIS 16048 (Fed. Cir. June 20, 2007). The requirement for a reasonable apprehension of suit was part of a two-prong test formulated by the Federal Circuit to determine if an actual controversy existed in declaratory judgment actions. The other prong required present activity which could constitute infringement or concrete steps taken with the intent to conduct such activity. *Id.*

this test, courts generally took the position that in the absence of some overt action demonstrating a willingness on the part of the patent owner to enforce its patent, an ANDA applicant had no reasonable apprehension of suit, and, consequently, could not bring a declaratory judgment action.<sup>316</sup>

In the *MedImmune* case in January 2007, the Supreme Court reaffirmed that a plaintiff seeking a declaratory judgment must satisfy Article III's case or controversy requirement, and in doing so, it criticized the reasonable apprehension of suit test.<sup>317</sup> The Court directed courts to determine "whether the facts alleged, under all circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." The 2009 article noted that the Federal Circuit had decided five cases under the new standard, and that in two of the five the declaratory judgment suit was permitted to proceed. The other three cases were dismissed for lack of jurisdiction. On closer review, it appears the count should have been two and two prior to the 2009 article.<sup>318</sup> Two of the four cases discussed in the 2009 article—*Caraco Pharmaceutical Laboratories Ltd. v. Forest Laboratories Inc.* and *Janssen Pharmaceutica, N.V. v. Apotex, Inc.*— have proven to be the guideposts in subsequent cases.

*Caraco v. Forest Labs* involved generic applications referencing the antidepressant drug, Lexapro® (escitalopram oxalate). Forest Labs listed two patents with FDA: U.S. Patent No. RE34,712 (the '712 patent) and U.S. Patent No. 6,916,941 (the '941 patent). The '712 patent expired in 2012, and the '941 patent is listed as expiring in 2023. Ivax was the first applicant to file paragraph IV certifications to both patents and was therefore entitled to 180-day exclusivity. Forest Labs sued Ivax on the '712 patent, resulting in a ruling that the patent was valid and infringed and an injunction until 2012.<sup>319</sup> Caraco was a subsequent filer, blocked from entering the market by Ivax's 180-day exclusivity. This exclusivity would not be triggered until Ivax launched, unless (1) another company obtained a judgment invalidating the '712 patent, allowing FDA to approve Ivax's ANDA and allowing Ivax to launch, triggering Ivax's exclusivity, or (2) another company obtained a judgment finding *both* patents invalid or not infringed, triggering Ivax's exclusivity immediately.

Forest Labs sued Caraco on the '712 patent but not the '941 patent. Caraco then sought a declaratory judgment that its generic product did not infringe the '941 patent. Forest Labs unilaterally granted Caraco a covenant not to sue for

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<sup>316</sup> See, e.g., *Dr. Reddy's Labs., Ltd. v. Pfizer Inc.*, No. 03-cv-726, 2003 U.S. Dist. LEXIS 24351, at \*14-15 (D.N.J. July 8, 2003) ("The objective actions of the patentee must rise 'to a level sufficient to indicate an intent to enforce its patent', i.e., to initiate an infringement action.") (citation omitted) (unpublished).

<sup>317</sup> *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118 (2007).

<sup>318</sup> For cases finding jurisdiction, see *Teva Pharms. USA, Inc. v. Novartis Pharms. Corp.*, 482 F.3d 1330 (Fed. Cir. 2007); *Caraco Pharm. Labs., Ltd. v. Forest Labs., Inc.*, 527 F.3d 1278 (Fed. Cir. 2008), *petition for rehear'g and rehear'g en banc denied*, No. 2007-1404, 2008 U.S. App. LEXIS 15741 (Fed. Cir. June 24, 2008), *cert. denied*, No. 08-624, 2009 U.S. LEXIS 1482 (Feb. 23, 2009). For cases dismissing suits for lack of jurisdiction, see *Merck & Co., Inc. v. Apotex, Inc.*, 292 F. App'x 38 (Fed. Cir. 2008); *Janssen Pharmaceutica, N.V. v. Apotex, Inc.*, 540 F.3d 1353 (Fed. Cir. 2008), *rehear'g denied and rehear'g en banc denied*, No. 2008-1062, 2008 U.S. App. LEXIS 25387 (Fed. Cir. Oct. 29, 2008), *cert. denied*, No. 08-959, 2009 U.S. LEXIS 2021 (Mar. 23, 2009).

<sup>319</sup> *Forest Labs., Inc. v. Ivax Pharms. Inc.*, 501 F.3d 1263 (Fed. Cir. 2007).

infringement of the '941 patent and then moved to dismiss the declaratory judgment action on the ground that the action did not meet the "case or controversy" standard of Article III of the U.S. Constitution. The Federal Circuit found jurisdiction, relying on a "three-part framework" for justiciability: the plaintiff must have standing, the issues must be ripe for review, and the case may not be moot.<sup>320</sup> Of most relevance here, the court concluded that Caraco had standing. The company had alleged an injury in fact: its exclusion from the market with an (allegedly) non-infringing good. This injury resulted from actions taken by Forest Labs—specifically listing of the patents, "but for" which Caraco's application could have been approved.<sup>321</sup> Further, the injury was redressable by a favorable judgment, through the court decision trigger. The covenant not to sue was irrelevant, because "regardless of a covenant not to sue, a generic drug manufacturer cannot enter the market without FDA approval."<sup>322</sup> Under the circumstances, the court wrote, "even after a covenant not to sue has been granted, the dispute as to infringement or invalidity of the relevant Orange-Book-listed patents constitutes 'a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment,'" within the meaning of *MedImmune*.<sup>323</sup>

The injury alleged in the *Janssen* case, by way of contrast, did not give rise to a justiciable controversy, largely because the subsequent ANDA applicant had stipulated to the validity and infringement of the patent that was delaying the first applicant's market entry. Janssen had listed three patents in connection with Risperdal® (risperidone) Oral Solution. The first applicant, Teva, challenged two patents—U.S. Patent Nos. 5,453,425 (the '425 patent) and 5,616,587 (the '587 patent)—but filed a paragraph III certification to U.S. Patent No. 4,804,663 (the '663 patent). Janssen did not sue Teva, which meant that Teva was entitled to enter the market upon expiry of the '663 patent. Apotex, a subsequent applicant, sought a declaratory judgment of non-infringement with respect to the '425 and '587 patents but stipulated to the validity and its infringement of the '663 patent.

The court of appeals noted that in the *Caraco* case, Caraco had asserted non-infringement of *both* patents. If Caraco's non-infringement claim regarding the '712 patent was not adjudicated and another applicant established the patent's invalidity, the first applicant's exclusivity would be triggered, and Caraco would be blocked—despite having an (allegedly) non-infringing product. The harm to Caraco was that its non-infringing product was blocked by a potentially invalid patent. In that dispute, a declaratory judgment of non-infringement would trigger the first applicant's exclusivity and end the blockade. The key difference in *Janssen*, the court reasoned, was that Apotex stipulated to validity and infringement of one of the patents. Consequently, even if it obtained a declaratory judgment of invalidity of the remaining two patents, it could not obtain approval until expiry of the third patent—and the subsequent 180-day exclusivity term of the first applicant. Its harm was, in a sense, precisely the delay that the Hatch-Waxman Amendments contemplated.<sup>324</sup>

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<sup>320</sup> 527 F.3d at 1291.

<sup>321</sup> *Id.* at 1292 ("where the first Paragraph IV ANDA filer has failed to trigger its own 180-day exclusivity period, the NDA holder's listing of Orange-Book patents delays a subsequent Paragraph IV ANDA filer from entering the marketplace indefinitely").

<sup>322</sup> *Id.* at 1296.

<sup>323</sup> *Id.* at 1296-97.

<sup>324</sup> 540 F.3d at 1361.

There have been three relevant Federal Circuit rulings since the 2009 article, all finding the subsequent ANDA applicant's case justiciable.<sup>325</sup> The court found a justiciable controversies in *Dey Pharma v. Sunovion Pharmaceuticals* despite a covenant not to sue,<sup>326</sup> *Apotex v. Daiichi Sankyo* despite statutory disclaimer of the patent,<sup>327</sup> and *Teva v. Eisai* despite both a covenant not to sue and statutory disclaimers.<sup>328</sup> The analyses relating to covenants not to sue rely heavily on the court's earlier ruling and analysis in the *Caraco* case. The statutory disclaimer reasoning proceeds along similar lines. For instance, in *Apotex v. Daiichi Sankyo*, although Daiichi formally disclaimed the patent and asked FDA to remove it from the Orange Book, FDA declined to do so,<sup>329</sup> and the patent continued to support the first applicant's exclusivity. As a result, Apotex's inability to market its product resulted from Daiichi's actions (listing the patent) and was redressable by a favorable court judgment through the court decision trigger.<sup>330</sup>

### 3. What level of court decision triggers 180-day exclusivity?

For old ANDAs, exclusivity begins when a decision is rendered by "the court from which no appeal (other than a petition of the Supreme Court for a writ of certiorari) has been or can be taken."<sup>331</sup> There is no court decision trigger for exclusivity for new ANDAs, but a similar rule applies to the court-decision forfeiture event. There have been no meaningful developments since the 2009 article.<sup>332</sup>

### 4. Will marketing by the first generic of the pioneer's product under a private generic label satisfy the commercial marketing trigger?

Yes. As noted in the 2009 article, FDA decided in 2001 that private label sales could constitute commercial marketing, and this was upheld by a federal court in

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<sup>325</sup> We have not discussed district court rulings, although they are divided, with most finding justiciability and citing *Caraco*, but a few declining to exercise jurisdiction and citing *Janssen*. See *Pfizer, Inc. v. Apotex, Inc.*, C.A. No. 08-cv-7231 (N.D. Ill. June 30, 2010) (Memorandum Opinion and Order) (finding jurisdiction and relying heavily on *Caraco*); *Glenmark Generics Ltd. v. Ferring B.V.*, No. 3:14CV422-HEH, 2014 WL 5162097, at \*4 (E.D. Va. Oct. 14, 2014) (relying on *Caraco* and finding jurisdiction to hear a declaratory judgment action brought by a subsequent applicant because continued listing of disclaimed patent caused injury by obstructing FDA approval of subsequent applicant's ANDA); *Apotex Inc. v. Eisai Inc.*, No. 09-cv-00477-JAB-LPA (D.N.C. Aug. 27, 2010) (Memorandum Opinion) (dismissing the case after applying *Janssen*).

<sup>326</sup> *Dey Pharma LP. v. Sunovion Pharms. Inc.*, 677 F.3d 1158 (Fed. Cir. 2012).

<sup>327</sup> *Apotex, Inc. v. Daiichi Sankyo, Inc.*, 781 F.3d 1356 (Fed. Cir. 2015).

<sup>328</sup> *Teva Pharms. USA, Inc. v. Eisai Co., Ltd.*, 620 F.3d 1341 (Fed. Cir. 2010).

<sup>329</sup> See *supra* subsection 0.

<sup>330</sup> *Apotex*, 781 F.3d at 1364.

<sup>331</sup> The courts—reversing FDA—interpreted the original 1984 language as referring to the decision of a federal district court. *Mylan Pharm., Inc. v. Shalala*, 81 F. Supp. 2d 30 (D.D.C. 2000). Congress overruled this in 2003, providing that exclusivity for old ANDAs begins when a decision is rendered by "the court from which no appeal (other than a petition of the Supreme Court for a writ of certiorari) has been or can be taken." Pub. L. No. 108-173 § 1102(b)(3).

<sup>332</sup> See 2009 Exclusivity Article, *supra* note 4, at 355-56.

West Virginia.<sup>333</sup> Congress confirmed this in 2003 for new ANDAs with the addition of the words “including the commercial marketing of the listed drug” in the sentence describing the commercial marketing trigger.<sup>334</sup>

### *E. Use of Exclusivity and Effect of Exclusivity*

This subsection briefly addresses three issues as to which there have been no meaningful developments since 2009 and one new issue that has arisen since 2009.

#### *1. Does an ANDA applicant's 180-day exclusivity preclude the innovator from distributing an “authorized generic” version of its drug?*

No. As explained in the 2007 article, FDA concluded and two courts of appeal confirmed that the statute does not prohibit an NDA holder from marketing an unbranded version of its product—known as an “authorized generic”—during the 180-day exclusivity period.<sup>335</sup> Section 505(t) of the FDCA requires the agency to publish and update quarterly a complete list on its website of all authorized generic drugs included in the annual reports filed by NDA holders.<sup>336</sup> FDA regulations that took effect in 2010 define an “authorized generic” for this purpose and explain the annual reporting obligation.<sup>337</sup>

#### *2. Do 180-day exclusivity and pediatric exclusivity run concurrently or consecutively?*

Section 505A(m) of the FDCA, added in 2002, clarifies that if an innovator earns six months of pediatric exclusivity, the first generic applicant's ANDA is approved effective the first day after conclusion of that exclusivity, and the 180 days begin to

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<sup>333</sup> *Mylan Pharm., Inc. v. Thompson*, 207 F. Supp. 2d 476 (N.D. W.Va. 2001); 2009 Exclusivity Article, *supra* note 4, at 358-59.

<sup>334</sup> 21 U.S.C. § 355(j)(5)(B)(iv)(I) (a subsequent applicant's application “shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant”).

<sup>335</sup> See Letter from William K. Hubbard, Associate Commissioner for Policy and Planning, FDA, to Stuart A. Williams, Chief Legal Officer, Mylan Pharmaceuticals Inc. and James N. Czaban, Heller Ehrman White & McAuliffe LLP, Docket Nos. 2004P-0075 and 2004P-0261 (July 2, 2004) (stating that “FDA does not regulate drug prices and has no legal basis on which to prevent an innovator company from marketing its approved NDA product at a price that is competitive with that charged by a first generic applicant to the market”); *Teva Pharm. Indus. v. Crawford*, 410 F.3d 51 (D.C. Cir. 2005) (noting that the statute “clearly does not prohibit the holder of an approved NDA from marketing, during the 180-day exclusivity period, its own ‘brand-generic’ version of its drug”); *Mylan Pharm., Inc. v. FDA*, 454 F.3d 270 (4th Cir. 2006) (affirming that FDA lacks the power to prohibit the marketing of authorized generics during the 180-day exclusivity period).

<sup>336</sup> 21 U.S.C. § 355(t); see FDA, FDA Listing of Authorized Generics, <http://www.fda.gov/About/FDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm126391.htm>.

<sup>337</sup> 74 Fed. Reg. 37163 (July 28, 2009). Section 314.3 defines an authorized generic as a listed drug (as defined in the same section) “that has been approved under section 505(c) of the act and is marketed, sold, or distributed directly or indirectly to retail class of trade with labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trademark that differs from that of the listed drug.” *Id.* at 37164. Under 21 C.F.R. § 314.81, an NDA holder's annual report must indicate every authorized generic (and the corresponding brand name) that entered the market, or ceased being distributed, during the reporting year. Each dosage form and strength is considered a separate authorized generic drug and should be listed separately.

run at that point.<sup>338</sup> More precisely, if the two overlap, the 180-day exclusivity period is extended by the number of days of overlap. This means, as a practical matter, the terms are *consecutive*. This obviated an issue that had arisen under the old ANDA scheme, where subsequent filers were theoretically able to trigger the first applicant's exclusivity (with a court decision) while the first applicant was blocked by pediatric exclusivity.<sup>339</sup>

Although Congress eliminated the court decision trigger for exclusivity in 2003, there is now a court decision trigger for forfeiture, raising the question whether a subsequent filer may trigger the forfeiture clock while the first applicant is blocked from the market by pediatric exclusivity. There have been no rulings directly on point, but in another forfeiture situation, a federal district court declined to toll the relevant forfeiture clock during pediatric exclusivity.<sup>340</sup> In that case, the failure-to-market forfeiture clock was triggered by a combination of (1) the passage of 30 months since submission of the ANDA, and (2) delisting of the relevant patents from the Orange Book. The generic applicant was legally unable to launch, due to pediatric exclusivity on the remaining patent, and it argued that the forfeiture clock was tolled pursuant to section 505A(m). FDA found—and the court agreed—that the provision did not apply. Instead, it applies only where pediatric exclusivity and the 180-day exclusivity “overlap,” which is impossible under the new scheme—because exclusivity commences with commercial marketing.<sup>341</sup>

3. *Does 180-day exclusivity, if triggered by commercial marketing at risk, continue to run if the innovator obtains a preliminary injunction prohibiting further commercial marketing?*

*Short answer.* Although neither the agency nor a court has answered this question with respect to the new statutory language, the 180-day exclusivity probably continues to run.

*Discussion.* The issue arose once under the old ANDA scheme, in a dispute concerning a generic application that referenced Plavix® (clopidogrel bisulfate). Apotex was the first to file an ANDA with a paragraph IV certification and was therefore eligible for 180-day exclusivity. The NDA holder, Sanofi-Synthelabo, brought suit, and once the 30-month stay expired, FDA approved the ANDA. Although the patent infringement litigation was ongoing, Apotex launched at risk in August 2006, triggering its exclusivity. Several weeks later a district court preliminarily enjoined the company from further marketing pending a final decision on the merits of the patent infringement case.<sup>342</sup> Eventually the district court entered a permanent injunction,<sup>343</sup> and the Federal Circuit affirmed validity of the patent at

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<sup>338</sup> Pub. L. No. 107-109 (2002); see 21 U.S.C. § 355a(m).

<sup>339</sup> See FDA Request for Comments, 66 Fed. Reg. 27983 (May 21, 2001) (requesting comment on whether the two are concurrent or consecutive); see 2009 Exclusivity Article, *supra* note 4, at 361-62.

<sup>340</sup> *Hi-Tech Pharmacal Co., Inc. v. FDA*, 587 F. Supp. 2d 13 (D.D.C. 2008).

<sup>341</sup> *Id.* at 21-22.

<sup>342</sup> *Sanofi-Synthelabo v. Apotex, Inc.*, 488 F. Supp. 2d 317, 348 (S.D.N.Y. 2006), *aff'd*, 470 F.3d 1368, 1372 (Fed. Cir. 2006).

<sup>343</sup> *Sanofi-Synthelabo v. Apotex, Inc.*, 492 F. Supp. 2d 353, 356, 397 (S.D.N.Y. 2007).

issue.<sup>344</sup> In January 2008 FDA granted final approval to a subsequent generic applicant who had included a paragraph IV certification to the patent in question.

Apotex petitioned the agency, asking it to stay the effective date of the approved ANDA and any other pending ANDAs with paragraph IV certifications. It argued that FDA could toll its exclusivity during the injunction, because the statute provided that a subsequent applicant's ANDA should be made effective "not earlier than one hundred eighty days after" the first applicant's commercial marketing. The agency could, therefore, delay approval of the subsequent filers, in order to give Apotex the benefit of its exclusivity *after* the injunction expired. Although Apotex subsequently brought suit against the agency, its petitions for panel and *en banc* rehearing in the patent infringement litigation were denied. Once it lost the patent challenge, it lost eligibility for 180-day exclusivity. The lawsuit against FDA was, consequently, dismissed.<sup>345</sup>

Whatever the merits of Apotex's argument regarding old ANDAs, its statutory argument appears inapplicable to new ANDAs. The new statutory language provides that a subsequent application "shall be made effective on the date that is 180 days after the date of the first commercial marketing" of the first generic product. Thus it seems that once triggered, exclusivity runs, even if the holder of the exclusivity is enjoined from marketing its product.

4. *Could a subsequent ANDA applicant submit a section viii statement to a patent with both method-of-use and product claims, as to which the first applicant has submitted a split certification, and thereby cut ahead of other applicants who must wait for expiry of the first applicant's 180-day exclusivity?*

Short Answer. No. A subsequent ANDA applicant cannot avoid 180-day exclusivity by filing a section viii statement to a patent as to which the first applicant had submitted a split certification.

Discussion. As discussed earlier, an ANDA applicant must file a patent certification with respect to every patent that claims the listed drug or claims a use for the listed drug for which the applicant is seeking approval.<sup>346</sup> It may, however, file a section viii statement with respect to a method-of-use patent that does not claim a use for which it is seeking approval.<sup>347</sup> Where a patent contains both drug product claims and method-of-use claims, FDA's longstanding practice is to permit a "split certification" to the patent. That is, the applicant may submit a paragraph IV certification to the drug product claim and method of use for which the applicant seeks approval and a section viii statement for a method of use the applicant seeks to

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<sup>344</sup> *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075 (Fed. Cir. 2008).

<sup>345</sup> *Apotex Inc. v. Johnson*, No. 08-cv-00693 (D.D.C. Apr. 15, 2009) (Notice of Voluntary Dismissal Without Prejudice). In 2012, FDA denied the underlying citizen petition. Letter from Janet Woodcock, M.D., Director, CDER, FDA, to Bert W. Rein, Esq., et al., Wiley Rein LLP and Robert B. Breisblatt, Esq., Katten Muchin Rosenman LLP, Docket No. FDA-2008-P-0117 (May 17, 2012).

<sup>346</sup> 21 U.S.C. § 355(j)(2)(A)(vii)(IV); 21 C.F.R. § 314.94(a)(12)(i)(A)(4).

<sup>347</sup> 21 U.S.C. § 355(j)(2)(A)(viii); 21 C.F.R. § 314.94(a)(12)(iii).



carve out from its labeling.<sup>348</sup> FDA recently confirmed that an applicant must address all claims in the patent one way or the other and that a section viii statement is permitted only with respect to method-of-use claims.

The matter involved Actos (pioglitazone) tablets, discussed in subsection II.B.6. Three patents were at issue: the '777, the '584, and the '404. The '777 patent was slated to expire in January 2011. FDA listed the latter two with "use" codes, and because the listings predate August 2003, the Orange Book does not otherwise characterize the claims of the patent.<sup>349</sup> Sandoz, who was not a first applicant, filed a citizen petition when it appeared that two generic applicants were attempting to "cut to the front of the line" by filing section viii statements.<sup>350</sup> Specifically, Sandoz filed an ANDA with a paragraph III certification to the '777 patent and "split" certifications to the '584 and '404 patents—consisting of a section viii statement to the method-of-use claims and paragraph IV certifications to the drug product claims. Sandoz noted that three other companies—Mylan, Ranbaxy, and Watson—appeared to have submitted acceptable ANDAs with paragraph IV certifications earlier and were eligible to share 180-day exclusivity rights. Sandoz presumably would be next in the queue, approved after the exclusivity expired.

According to Sandoz, Alphapharm and Teva had submitted *only* section viii statements. In other words, they submitted paragraph III certifications to the '777 patent and section viii statements regarding the entire '584 and '404 patents. Because 180-day exclusivity precludes approval only of subsequent *ANDAs with paragraph IV certifications*, this approach meant these applications would not be affected by the 180-day exclusivity rights of the first applicants. In other words, Alphapharm and Teva would be able to receive final approval and launch in the first wave, January 2011, when the '777 patent expired. In its petition to FDA, Sandoz argued that Alphapharm and Teva sought to "cut to the front of the line," to the detriment of Sandoz and the remaining generic applicants who submitted paragraph IV certifications as well as section viii statements to the '584 and '505 patents. The NDA-holder, Takeda, filed comments confirming that the patents contained both drug product and method-of-use claims (and that its original patent submissions had said so).<sup>351</sup> FDA granted the petition in March 2010, noting that an ANDA applicant "must address all claims for which the patent was submitted."<sup>352</sup>

FDA's response in the Actos matter cited its consolidated response to two earlier citizen petitions involving Caraco's application referencing Prandin. That matter did not relate to use of section viii to circumvent exclusivity, but it did relate in part to split certifications. Among other things, FDA's decision on Prandin explained the

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<sup>348</sup> See, e.g., Letter from Janet Woodcock, Director, CDER, FDA, to Stephen R. Auten, Vice-President, Legal-Intellectual Property, Sandoz, Inc., Docket No. FDA-2009-P-0411 (Mar. 15, 2010) [hereinafter Woodcock Letter to Sandoz].

<sup>349</sup> When FDA revised its patent listing regulations in the summer of 2003, it also increased the technological capabilities of the Orange Book database. For patents submitted after August 18, 2003, the Orange Book displays the multiple types of claims (drug product, drug substance, and/or method of use) for which the patent had been submitted. The agency did not revisit listings for patents submitted before that time. *Id.* at 2.

<sup>350</sup> Sandoz Inc., Citizen Petition, Docket No. FDA-2009-P-0411 (Aug. 25, 2009).

<sup>351</sup> See Woodcock Letter to Sandoz, *supra* note 348. FDA confirmed that Takeda's original patent declarations included both types of claims.

<sup>352</sup> FDA Response, Citizen Petition FDA-2009-P-0411 (Mar. 15, 2010).

agency's practice of allowing split certifications, agreed that a section viii statement is inappropriate for drug substance and product claims, and concluded that an ANDA applicant submitting a section viii statement for a method-of-use claim must also submit a paragraph IV certification for any other claims in the patent that are not method-of-use claims.<sup>353</sup> FDA's February 2015 proposed regulations take the same approach, requiring an ANDA applicant to submit a paragraph IV certification (in addition to any section viii statements) to a patent that contains both drug substance or product claims and method-of-use claims.<sup>354</sup> The agency also noted that the first to do so would be eligible for 180-day exclusivity, if the other relevant requirements were met.<sup>355</sup>

### III. CONCLUSION

Section II of this article discusses twenty-eight discrete interpretive issues relating to the 180-day exclusivity scheme, arranged in five categories: which rules apply, earning exclusivity, forfeiture of exclusivity, commencing the exclusivity term, and enjoyment (use) of the exclusivity term. Over the years, however, stakeholders, courts, and policymakers have identified and grappled with a variety of broader policy issues relating to the 180-day exclusivity scheme. This section discusses one broad policy issue—the impact of the scheme on subsequent generic applications—and some of the scholarship, antitrust litigation, and legislative proposals that relate, directly or indirectly, to these applications.

#### A. Subsequent Applicants

Since at least the mid 1990s, FDA, the courts, and policymakers have struggled to find the right balance between the benefit that they perceive results from encouraging first applicants via the 180-day exclusivity period, on the one hand, and the harm that they perceive results from delay of subsequent applications that also contain paragraph IV certifications to patents for the same reference listed drug due to that exclusivity period, on the other hand. For instance, the agency pointed to the delay in approval of subsequent applications when justifying its original proposal that a first applicant would be entitled to exclusivity only if it had been sued.<sup>356</sup> The court in *Inwood Laboratories v. Young*, rejecting this approach, agreed that the statute as drafted might “have the effect of delaying the entry into the market of subsequent generic drugs,” and suggested the problem “warrants consideration by Congress.”<sup>357</sup> Another court made the same comment.<sup>358</sup> Notwithstanding the

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<sup>353</sup> Letter from Janet Woodcock, M.D., Director, CDER, to Rosemarie R. Wilk-Orescan, Senior Counsel, Novo Nordisk Inc. and James F. Hurst, Winston & Strawn LLP, Docket Nos. FDA-2008-P-0343 and FDA-2008-P-0411 (Dec. 8, 2008).

<sup>354</sup> Proposed 21 C.F.R. §§ 314.53(c)(2)(i)(O)(3), (ii)(P)(4).

<sup>355</sup> 80 Fed. Reg. at 6819.

<sup>356</sup> See *Inwood Labs., Inc. v. Young*, 723 F. Supp. 1523, 1527 (“FDA states that acceptance of the statute as written will lead to the ‘absurd’ result that in some cases the delay of approval of subsequent ANDAs will never end.”).

<sup>357</sup> *Id.*

<sup>358</sup> *Granutec, Inc. v. Shalala*, 139 F.3d 889, \*9 n.3 (4th Cir. 1998) (unpublished) (“As long as the pioneer prevents its captured generic from going to market and at the same time does not file an infringement suit against any generic manufacturer (captured or non-captured), the captured generic’s exclusivity period would never begin to run, and no generic could begin to sell pursuant to a Paragraph IV

*Inwood* decision, FDA finalized its proposal limiting a first applicant's entitlement to exclusivity and in fact turned it into a "successful defense" requirement—which it implemented by approving subsequent applications that were ready, unless and until the first applicant perfected its exclusivity with a successful defense. In these circumstances, the subsequent applications would remain approved. Thus, for instance, FDA approved Mylan's ANDA referencing Micronase® (micronized glyburide) even though Mova had been the first to file an ANDA with a paragraph IV certification.<sup>359</sup> The agency defended its approach in court by pointing out that, without a successful defense requirement, the first applicant "could in theory wait indefinitely to begin selling its product and thereby block all sales by later applicants."<sup>360</sup>

Although the D.C. Circuit rejected the successful defense requirement as inconsistent with the statute, it devoted considerable attention to the concern articulated by FDA. According to the court, for instance, Mylan's briefs offered "a compelling argument" for the successful defense requirement: the possibility that the first applicant might have an infringing product while the subsequent applicant has a non-infringing product. In this case, Mylan had argued, the subsequent applicant might not be sued while the first applicant's litigation might continue or even settle.<sup>361</sup> Teva suggested that this subsequent applicant could trigger the first applicant's exclusivity with a declaratory judgment action, and the court raised the question whether such a subsequent applicant could establish a case or controversy sufficient for federal court jurisdiction.<sup>362</sup> Even if the subsequent applicant could establish jurisdiction, the court noted that the first applicant would still receive its exclusivity. "It seems odd," the court wrote, "to reward the first applicant if some later applicant was the party that actually prevailed in the patent-infringement case."<sup>363</sup>

After invalidation of the successful defense requirement, FDA issued guidance stating that it expected first applicants to launch promptly upon ANDA approval.<sup>364</sup>

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certification. The 'successful defense' requirement would solve this problem, were it valid. But this problem, like many others, arises from the manner in which Congress drafted the exclusivity mechanism, and, as such, the remedy lies with Congress.").

<sup>359</sup> This decision led to *Mova v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998), and invalidation of the successful defense requirement.

<sup>360</sup> *Id.* at 1067.

<sup>361</sup> *Id.* at 1072 ("What if the first applicant does a poor job of designing its product to avoid infringing the patent-holder's patent, and the second applicant does a much better job? The first applicant would then be sued for infringement by the patent-holder, but the second applicant would not . . . . In such a situation, a literal reading of the statute admittedly produces a strange result. The second applicant, even though it has designed its product well and avoided suit, is barred from selling its product until the first applicant's lawsuit finishes (maybe years later).").

<sup>362</sup> *See id.* at 1073 ("To employ Teva's declaratory-judgment device, a party would therefore need to demonstrate a 'reasonable apprehension of facing a lawsuit.' . . . An ANDA applicant seeking to bring a declaratory judgment action might have difficulty in meeting this test, especially if the patent-holder disclaims any intention of bringing suit.")

<sup>363</sup> *Id.* at 1073.

<sup>364</sup> FDA, Guidance for Industry, *180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act* (June 1998) at 5 (indicating that first applicant approval letters will state, "The Agency expects that you will begin commercial marketing of your product promptly upon approval").

The following year, the agency proposed regulations that would have compelled this launch through a kind of regulatory forfeiture. Under the proposed regulations, once a subsequent applicant received tentative approval for its generic drug—such that the first applicant’s expected exclusivity was the only impediment to its own final approval—and assuming the 30-month stay of approval of the first applicant’s ANDA had ended, a forfeiture period would begin to run: the first applicant’s exclusivity period would need to start within 180 days. Put another way, within 180 days the first applicant would need to either obtain a favorable court decision regarding the patent it had challenged, or start marketing. If neither happened within 180 days, the first applicant would lose its exclusivity. The first applicant could, however, transfer its exclusivity to another company. Thus, a subsequent applicant with tentative approval would benefit from both a forfeiture clock and—possibly—exclusivity itself. The agency specifically noted that transfer might be useful if the subsequent applicant prevailed in its litigation. Although FDA abandoned this proposal, the failure-to-market forfeiture provision in the 2003 statute is somewhat similar at a conceptual level.

The day after President Bush signed the MMA, Senator Hatch expressed concerns about the incentives for subsequent applicants under the new scheme. He argued that it was “unfair and ill-advised” to deny exclusivity to a subsequent applicant that prevails on a patent invalidity challenge.<sup>365</sup> He also argued that, at the very least, a court decision of invalidity or non-infringement involving a subsequent applicant should lead to *immediate forfeiture*—rather than simply triggering a 75-day window for the first filer to launch and enjoy exclusivity.<sup>366</sup> Indeed, he stated that conferee staff had thought the provision as drafted, and signed into law, would have precisely that effect—that a subsequent filer’s successful invalidity challenge would lead to immediate forfeiture of the first filer’s exclusivity.<sup>367</sup> With a closer read, he realized that “the successful subsequent challenger not only does not get the 180-day benefit, but actually receives a 180-day penalty for invalidating the patent.”<sup>368</sup> He thus concluded that “the law should be changed” on this point.<sup>369</sup>

In the summer of 2003, the Congressional Budget Office (CBO) prepared, at Senator Hatch’s request, an analysis of the changes to the Hatch–Waxman Amendments that ultimately appeared in the enacted legislation.<sup>370</sup> In CBO’s view, the “failure to market” provisions did not “fully address” every situation in which 180-day exclusivity could be “parked.” The forfeiture clock requires two triggering events. The first relates to the passage of time since ANDA submission or approval. The second relates to the patents that qualified the first applicant for exclusivity. At least one of the following must occur with respect to each patent: (1) a final court decision that the patent is invalid or not infringed, (2) a settlement order or consent

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<sup>365</sup> 149 Cong. Rec. 32267 (2003).

<sup>366</sup> *Id.* He pointed out that although the successful challenger “does not get the 180-day head start, at least under this reading, the subsequent successful challenger is not penalized with respect to market entry.” *Id.*

<sup>367</sup> *Id.*

<sup>368</sup> *Id.*

<sup>369</sup> *Id.*

<sup>370</sup> Congressional Budget Office, *Analysis of Changes to the Hatch-Waxman Act As contained in S. 1, the Prescription Drug and Medicare Modernization Improvement Act of 2003, as Passed by the Senate on June 27, 2003* (Aug. 27, 2003).

decree finding that the patent is invalid or not infringed, or (3) withdrawal of the patent from the Orange Book by the NDA holder. Thus, if the relevant court decision or settlement omits a finding of invalidity or non-infringement, the forfeiture clock will not start—no matter how much earlier the ANDA was submitted and approved. FDA noted this in its 2008 decision in the generic granisetron hydrochloride controversy,<sup>371</sup> writing that “[i]nherent in the structure of the ‘failure to market’ forfeiture provisions is the possibility that a first applicant would be able to enter into a settlement agreement with the NDA holder or patent owner in which a court does not enter a final judgment of invalidity or non-infringement . . . and that subsequent applicants would be unable to initiate a forfeiture with a declaratory judgment action.”<sup>372</sup> The agency further stated that “[t]his inability to force a forfeiture of 180-day exclusivity could result in delays in the approval of otherwise approvable ANDAs owned by applicants that would market their generic drugs if they could but obtain approval.”<sup>373</sup>

Subsequent ANDA filers have argued that if they are willing to litigate to a successful conclusion, they should be permitted to market despite the first applicant’s settlement.<sup>374</sup> They can, of course, achieve a court decision on their own, but this simply triggers a forfeiture clock—precisely the result that concerned Senator Hatch in 2003. Moreover, the court decision must be one that is neither appealed nor subject to further appeal, thus requiring a significant investment of time and resources. Senator Hatch criticized the adoption of an appellate court trigger for the forfeiture clock, as well, suggesting that lower court rulings for generic applicants are “almost always” affirmed on appeal.<sup>375</sup> And while patent settlements with first applicants sometimes contain acceleration clauses so that the first applicant may launch if a subsequent challenger prevails in litigation, provided the first applicant launches within 75 days, the subsequent applicant is still subject to the first applicant’s 180-day exclusivity. In other words, a second applicant could invest in and prevail in lengthy litigation through the appellate level and then *still* be forced to wait 254 days for product launch (74 days plus 180 days of exclusivity), after which it is no better situated than other subsequent entrants who did not invest in the court decision.

Senator Hatch commented on December 9, 2003 that it would be “exceedingly difficult to reopen [the] provisions[,]” but nevertheless urged the Senate to consider changes and offered a “discussion draft” for consideration.<sup>376</sup> There has been some academic interest in the issue since the 2009 article. For instance, in 2011 Professors Hemphill and Lemley proposed a variation of the agency’s original successful defense requirement.<sup>377</sup> Under their “earned exclusivity” proposal, which they argue

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<sup>371</sup> Buehler Letter to Teva Parenteral Medicines, *supra* note 142. *See supra* section 0.

<sup>372</sup> *Id.*

<sup>373</sup> *Id.*

<sup>374</sup> *E.g.*, Apotex, Patent Settlements Between Brand and Generic Pharmaceutical Companies: Parked Exclusivity & Lack of Incentive for Subsequent Generic Filers to Fight On Are the Problems, Not “Reverse Payments,” *on file with author*.

<sup>375</sup> *Id.*

<sup>376</sup> 149 Cong. Rec. 32292 (2003).

<sup>377</sup> C. Scott Hemphill & Mark A. Lemley, *Earning Exclusivity: Generic Drug Incentives and the Hatch-Waxman Act*, 77 ANTITRUST L.J. 947 (2011); *see id.* at 968 (“Our inspiration is the successful defense regime initially maintained by the FDA.”).

could be accomplished without statutory amendment, the first applicant should receive 180-day exclusivity only if it: (1) “successfully defeats” the patent owner, for instance by proving invalidity or non-infringement, (2) “obtains a settlement that permits entry without delay,” or (3) “can enter the market without delay because the patent holder does not sue for infringement.”<sup>378</sup>

### B. Patent Settlements

There has also been continuing academic discussion of, and Congressional interest in, the relationship between 180-day exclusivity and patent settlement agreements more generally, as well as broader interest in the competitive impact of those settlements.<sup>379</sup> Several antitrust challenges to settlement agreements were winding through the courts at the time this article was written. If the FTC or any court finds an agreement to violate the antitrust laws, the result may be forfeiture of exclusivity under section 505(j)(5)(D)(i)(V).

As was noted in the 2009 article, one criticism relates to settlements in which the innovator provided something of value to the generic applicant. The 2009 article discussed a number of court decisions upholding those agreements, legislation introduced in the 109th and 110th Congresses to address this scenario, and two then-pending FTC complaints, including a lawsuit in the United States District Court for the Central District of California, challenging agreements by Watson Pharmaceuticals, Par Pharmaceuticals Companies, and Paddock Laboratories “to delay until 2015 the sale of low-cost generic versions of AndroGel, a widely prescribed branded testosterone replacement drugs, in exchange for substantial payments from Solvay.”<sup>380</sup> The 2009 article also noted that the FTC had signaled that it was trying to create a split in the circuit courts and increase chances of review of the issue by the Supreme Court.<sup>381</sup>

The Androgel complaint did, indeed, lead to a circuit split and review of the issue by the Supreme Court. In *FTC v. Actavis*, the Court ruled that an agreement in which the innovator paid cash, and generic applicants agreed not to enter the market for a portion of the remaining patent term, was neither lawful under the “scope of the

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<sup>378</sup> *Id.* at 949.

<sup>379</sup> For articles addressing 180-day exclusivity from an antitrust perspective, see Kent Bernard, *Hatch-Waxman Patent Case Settlements—The Supreme Court Churns the Swamp*, 15 MINN. J.L. SCI. & TECH. 123, 133 (2014) (recommending that the first applicant be required to pursue litigation case to conclusion or settle in a way that does not block later filers); C. Scott Hemphill, *Collusive and Exclusive Settlements of Intellectual Property Litigation*, 2010 COLUM. BUS. L. REV. 685 (2010) (arguing, prior to Actavis, that first applicants should forfeit exclusivity upon settling); C. Scott Hemphill, *Paying for Delay: Pharmaceutical Patent Settlements as a Regulatory Design Problem*, 81 N.Y.U. L. REV. 1553 (2006) (arguing that the 180-day exclusivity “bounty” makes “allocatively harmful settlements” feasible and also that its use in this manner is likely inconsistent with the innovation policy of the Hatch-Waxman Amendments); Herbert Hovenkamp, Mark Janis & Mark A. Lemley, *Anticompetitive Settlement of Intellectual Property Disputes*, 87 MINN. L. REV. 1719, 1752 (2003) (arguing that three features of the Hatch-Waxman scheme—patent listing, the 30-month stay, and 180-day exclusivity—present “opportunities for either unilateral anticompetitive behavior on the part of the pioneer or pioneer/generic collusion in the form off anticompetitive settlements”). For a discussion of legislative proposals concerning reverse payment settlements, see *infra* section 0.

<sup>380</sup> *FTC v. Watson Pharm., Inc.*, No. 09-cv-598, at 2 (C.D. Cal. Jan. 27, 2009) (Complaint).

<sup>381</sup> See *Senators, FTC Seek to Ban “Reverse Payments” Between Brands, Generics*, FDA WEEK (Feb. 6, 2009).

patent” test nor presumptively unlawful under the Sherman Act.<sup>382</sup> Instead, the Court ruled, the FTC must prove its case under antitrust law’s traditional rule of reason.

The *Actavis* decision was not a ruling on the antitrust question itself in the Androgel matter, which is still pending. Whether a particular reverse payment—including the one at issue in that case—actually brings about anticompetitive effects necessarily depends on a variety of factors, which must be assessed case by case.<sup>383</sup> The lower courts are now evaluating various challenged settlement agreements under antitrust law’s rule of reason. There have also been disputes over whether *Actavis* applies (requiring a “rule of reason” scrutiny) or another approach (such as the “scope of the patent” test) might apply, where patent settlement agreements do not include cash payments. The First and Third Circuits have concluded that the rule of reason applies.<sup>384</sup> The First Circuit will hear another reverse payment case in 2016, but the issue will not be which standard applies to agreements that lack cash payments.<sup>385</sup>

### C. Authorized Generics

As explained above, FDA and the courts have concluded that the FDCA does not preclude the holder of an approved NDA from marketing, or permitting the marketing of, an authorized generic during the exclusivity period or at any other time.<sup>386</sup> Some argue that the introduction of authorized generics is pro-competitive because it creates price competition during the 180-day period, lowering the prices of the (branded) reference product *and* the first applicant’s generic product. Others argue that authorized generics draw revenue away from the first applicant, undermining the goal of the 180-day exclusivity incentive. If this reduces incentives to challenge patents, they argue, generic competition may be delayed and prices for consumers will be correspondingly higher.

Since the 2009 article, the FTC has issued an interim and final report on the “short-term effects and long-term impact” of authorized generic drugs.<sup>387</sup> The report concludes that authorized generics have a “substantial effect” on generic revenues

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<sup>382</sup> *FTC v. Actavis*, 133 S.Ct. 2223 (2013). The “scope of the patent test” would shield an agreement from antitrust scrutiny unless (1) the patent was fraudulently obtained; (2) the patent litigation was objectively baseless; or (3) the agreement unreasonably restrains competition beyond the subject matter or temporal scope of the patent. See *In re Tamoxifen Citrate Antitrust*, 466 F.3d 187 (2nd Cir. 2006); *FTC v. Watson Pharm., Inc.*, 677 F.3d 1298 (11th Cir. 2012); *Valley Drug v. Geneva Pharm., Inc.*, 344 F.3d 1294 (11th Cir. 2003); *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 544 F.3d 1323 (Fed. Cir. 2008).

<sup>383</sup> *Id.* at 2237 (“[T]he likelihood of a reverse payment bringing about anticompetitive effects depends upon its size, its scale in relation to the payor’s anticipated future litigation costs, its independence from other services for which it might represent payment, and the lack of any other convincing justification. The existence and degree of any anticompetitive consequence may also vary as among industries. These complexities lead us to conclude that the FTC must prove its case as in other rule-of-reason cases.”).

<sup>384</sup> *E.g., King Drug Co. of Florence, Inc. v. Smithkline Beecham Corp.*, 791 F.3d 388 (3d Cir. 2015) (holding in a case involving generic applications referencing Lamictal® that the rule of reason applies even without a cash payment); *In re Loestrin 24 Fe Antitrust Litig.*, Nos. 14-CV-2071, 15-1250, 2016 WL 698077 (1st Cir. 2016) (holding in a case involving generic applications referencing Loestrin 24 Fe® that the rule of reason applies in the event of a “non-monetary reverse payment”).

<sup>385</sup> See *In re Nexium (Esomeprazole) Antitrust Litig.*, 309 F.R.D. 107, 145 (D. Mass. 2015).

<sup>386</sup> See *supra* section 0.

<sup>387</sup> FTC, *Authorized Generics: An Interim Report* (June 2009); FTC, *Authorized Generic Drugs: Short-Term Effects and Long-Term Impact* (Aug. 2011).

during the 180-day exclusivity period (reducing it as much as 52 percent) and that the impact persists after exclusivity expires. The report concludes that this would be more likely to affect the incentive to challenge patents on products with smaller sales. That said, the FTC found “no evidence that any firm has substantially abandoned its basic patent–challenge business strategy because of the proliferation of authorized generics.”<sup>388</sup> Indeed, it appears that companies “typically expect authorized generic competition during the 180-day exclusivity period and often build that assumption into their forecasts.”<sup>389</sup> Further, despite the presence of authorized generics, companies have continued to challenge patents, “even on brand–name drugs with small markets.”<sup>390</sup>

Although the FTC found little evidence that authorized generics affect the number of patent challenges, it observed that many patent litigation settlements include a provision whereby the reference product sponsor agrees not to market an authorized generic during the 180-day exclusivity period. The FTC takes the view that “agreements not to compete with an authorized generic have become a way for brand–name companies to compensate generic competitors for delaying entry,” and it alleges that this—like reverse payment settlements—causes harm to consumers.<sup>391</sup> The 2009 article noted the repeated introduction of legislation to prohibit the marketing of authorized generics during the 180-day exclusivity term as well as other legislative proposals relating to the practice.<sup>392</sup> Those have somewhat tapered off in recent years.<sup>393</sup>

#### D. Legislative Proposals

Prior to the *Actavis* decision, various members of Congress introduced bills addressing reverse payment settlements, in some instances declaring certain kinds of settlements *per se* antitrust violations.<sup>394</sup> As a general rule, these bills did not propose

<sup>388</sup> FTC, *Authorized Generic Drugs Short-Term Effects and Long-Term Impact*, *supra* note 387, at iv.

<sup>389</sup> *Id.* at v.

<sup>390</sup> *Id.*

<sup>391</sup> *Id.* at vi. *See id.* at vi-vii (“Moreover, as a consequence of an authorized generic’s significant negative impact on a generic’s revenues, some brand–name companies have used agreements not to launch an authorized generic as a way to compensate an independent generic in exchange for the generic’s agreement to delay its entry. The frequency of this practice and its profitability may make it an attractive way to structure a pay–for–delay settlement, a practice that causes substantial consumer harm.”).

<sup>392</sup> 64 FOOD & DRUG L. J., *supra* note 4, at 386.

<sup>393</sup> No relevant legislation has been introduced in the 114th Congress, nor was relevant legislation introduced in the 113th Congress. House and Senate bills pertaining to the marketing of authorized generics during the 180-day exclusivity term died in committee in both the 112th and 111th Congresses. *See* To Amend the Federal Food, Drug, and Cosmetic Act to Prohibit the Marketing of Authorized Generic Drugs, H.R. 741, 112th Cong. (2011); Fair Prescription Drug Competition Act, S. 373, 112th Cong. (2011); To Amend the Federal Food, Drug, and Cosmetic Act to Prohibit the Marketing of Authorized Generic Drugs, H.R. 573, 111th Cong. (2009); Fair Prescription Drug Competition Act, S. 501, 111th Cong. (2009). In a January 2012 Congressional Research Service report, Professor Thomas suggested that as an alternative to banning authorized generics, Congress could require innovators to file a supplemental NDA or similar application to market an authorized generic and subject that application to the first filer’s 180-day exclusivity. CRS, *Authorized Generic Pharmaceuticals: Effects on Innovation* (Jan. 27, 2012).

<sup>394</sup> *E.g.*, S. 369 (111th Cong.); H.R. 1706 (111th Cong.); S. 3677 (111th Cong.); S. 27 (112th Cong.); H.R. 3995 (112th Cong.); H.R. 3709 (113th Cong.); S. 214 (113th Cong.).



meaningful changes to the 180-day exclusivity provisions, apart from adding a forfeiture provision tied to certain reverse payment settlements. For instance, H.R. 1706 in the 111th Congress would have prohibited certain settlements and required forfeiture in the event of an order that an agreement violated the prohibition. At least three bills in the current 114th Congress address patent settlements, but none takes up the connection with 180-day exclusivity.<sup>395</sup> S. 2019, for instance, entitled the “Preserve Access to Affordable Generics Act,” creates a new section 27 of the Federal Trade Commission Act (FTC Act) that presumes a drug patent settlement is anticompetitive if: (1) the ANDA filer “receives anything of value, including an exclusive license” and (2) the ANDA filer “agrees to limit or forego research, development, manufacturing, marketing, or sales” of the ANDA product “for any period of time.” This presumption can be rebutted with “clear and convincing evidence” that (1) the value in question is “compensation” for “other goods or services” the ANDA filer promised to provide, or (2) the procompetitive benefits of the agreement outweigh the anticompetitive effects of the agreement.<sup>396</sup> H.R. 3513 and S. 2023—companion bills entitled the “Prescription Drug Affordability Act of 2015”—would also enact a new section 27 of the FTC Act, with a similar presumption. This version of section 27 would not address rebuttal of the presumption, but would add that it does not prohibit settlements in which the NDA holder provides: (1) the right to market the ANDA product prior to patent or data exclusivity expiry, (2) a payment for reasonable litigation expenses not exceeding \$7.5 million, and/or (3) a covenant not to sue on any patent infringement claim.<sup>397</sup> As noted, none of these bills addresses 180-day exclusivity.

Other legislative proposals have more directly addressed the 180-day exclusivity provisions as they relate to subsequent applicants. In the 111th Congress, for instance, Senator Nelson and Representative Hastings introduced the “Drug Price Competition Act of 2009” in the Senate and House, respectively.<sup>398</sup> Broadly speaking, this short bill seems to have been intended to allow subsequent applicants to share in the first applicant’s exclusivity if they were not sued or if they obtained a court decision (or settlement agreement) of invalidity or non-infringement. In the 112th, 113th, and the current 114th Congress, a significantly more complex proposal—known as the “Fair Generics Act”—has been offered.<sup>399</sup> The bill has not changed since its initial introduction by Senators Bingaman, Vitter, Brown, and Merkley in November 2011.

The Fair Generics Act would permit a successful subsequent applicant to launch 30 days after the first applicant and thereby enjoy the balance of the 180-day exclusivity term. A subsequent applicant would be considered a “first applicant” if certain conditions were met. First, it must submit and lawfully maintain a paragraph IV certification (or section viii statement) for each unexpired patent as to which the

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<sup>395</sup> S. 2019 (114th Cong.); S. 2023 (114th Cong.); H.R. 3513 (114th Cong.).

<sup>396</sup> S. 2019 (114th Cong.). In determining whether this showing has been made, the fact finder may not presume that entry “would not have occurred until the expiration of the relevant patent or statutory exclusivity,” nor may it presume that the agreement’s provision for generic drug entry prior to that date “means that the agreement is procompetitive.” *Id.*

<sup>397</sup> S. 2023 (114th Cong.); H.R. 3513 (114th Cong.).

<sup>398</sup> Drug Price Competition Act of 2009, S. 1315 and H.R. 3777 (111th Cong.).

<sup>399</sup> Fair And Immediate Release of Generic Drugs Act, S. 1882 (112th Cong.), S. 504 (113th Cong.), S. 131 (114th Cong.).

(first) first applicant submitted a paragraph IV qualifying it for exclusivity. Second, for each such patent—(1) it must not be sued within the 45-day period after its paragraph IV notice was received,<sup>400</sup> (2) the suit must be withdrawn or dismissed without a decision that the patent was valid and infringed, *or* (3) a court must decide that the patent is invalid or not infringed.<sup>401</sup> The (first) first applicant's exclusivity would begin, as it does under current law, with commercial marketing. But the Fair Generics Act would permit the subsequent applicant (now *also* labeled a "first applicant") to begin marketing 30 days later. The bill would not amend the forfeiture provisions, which suggests that a subsequent applicant could trigger the forfeiture clock by obtaining a court decision of invalidity or non-infringement with respect to each patent qualifying the (first) first applicant for exclusivity. A subsequent applicant could obtain this court decision through a declaratory judgment action, assuming it could satisfy the requirements for federal court jurisdiction. Or it could obtain this court decision in litigation brought by the NDA holder or patent owner. It appears that if the (first) first applicant launched at this point, the subsequent applicant could launch 30 days later and enjoy 150 days of exclusivity. The Fair Generics Act would therefore reward a "successful" subsequent applicant with 150 days of exclusivity.

Under the Fair Generics Act, either type of first applicant would lose its "first applicant" status—and thus its eligibility for exclusivity—if it entered into a "disqualifying agreement" with the NDA holder or patent owner. This would be any agreement whereby the applicant agreed "directly or indirectly" not to seek approval of its application or not to begin commercial marketing until *after* expiration of the 180-day exclusivity period awarded to another ANDA applicant. The bill also neutralizes acceleration clauses by holding a first applicant to the *latest* date—for seeking approval of its application or beginning the commercial marketing of its drug—set forth in its agreement. The latest date in the agreement for seeking approval or beginning marketing would also be the date used to determine whether the agreement is a disqualifying agreement. It remains to be seen whether this bill will move in the current Congress and whether any sponsors will introduce it in the 115th Congress.

### *E. Other Contexts*

The 2009 article noted that the FTC had convened a roundtable on biosimilars and had asked participants to consider whether a patent-challenge based incentive was warranted and whether some other type of incentive was warranted. It noted that views were mixed and that none of the bills introduced to date had included such a

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<sup>400</sup> Another provision of the bill, amending section 271(e) of the Patent Act, is—according to the sponsors—intended to require "pioneer companies to make a litigation decision within the 45 day window provided for in the Hatch-Waxman Act." Bingaman-Vitter-Brown-Merkley Fair and Immediate Release of Generic Drugs Act of 2011, *originally posted at* <http://bingaman.senate.gov/policy/FAIRGenerics.pdf>, *now available through* [web.archive.org](http://web.archive.org). It would amend section 271(e) of the Patent Act, by adding a new paragraph (7). This provision would state that the "exclusive remedy under this section" for infringement of a patent listed by FDA in the Orange Book "shall be an action brought under this subsection within the 45-day period" described in section 505 of the FDCA—that is, the 45 day period after notice of a paragraph IV certification has been received.

<sup>401</sup> This would include any substantive determination that there is no cause of action for patent infringement or invalidity, including a settlement order or consent decree signed and entered by the court stating that the patent is invalid or not infringed.

provision. Two bills had a similarly structured provision designed to encourage something else—the submission of data and information demonstrating that a proposed biological product was “interchangeable” instead of merely “biosimilar.”<sup>402</sup> A version of this language found its way into the Biologics Price Competition and Innovation Act of 2009 (BPCIA).

Under the BPCIA, the first biological product found interchangeable with a particular reference product for any condition of use receives a period of exclusivity during which no other biological product may be deemed interchangeable to that reference product for any condition of use.<sup>403</sup> This exclusivity lasts no more than one year, and the statute includes termination dates that operate as *de facto* forfeiture provisions if the sponsor does not launch in a timely fashion. In brief, if the reference product sponsor brings suit under the immediate patent litigation provisions, the exclusivity will end 18 months after a court decision (or dismissal) *or* 42 months after approval if the case is still pending, whichever is earlier. If the innovator does not bring suit under the immediate litigation provisions, exclusivity will end 18 months after the interchangeable biologic was licensed. It remains to be seen whether interchangeability determinations are valued by biosimilar sponsors; if they are, it is not unreasonable to expect that this language will trigger as many interpretive disputes and as much litigation as the 180-day exclusivity provisions of the Hatch-Waxman Amendments.

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<sup>402</sup> A biosimilar application must demonstrate that the candidate product is highly similar to its reference product and that there are no clinically meaningful differences between the two products. 42 U.S.C. § 262(i). An interchangeability determination also requires a demonstration that the candidate product can be expected to produce the same clinical result as the reference product in any given patient. If the candidate product is administered more than once to an individual, the interchangeability determination also requires a showing that the “risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.” 42 U.S.C. § 262(k)(4).

<sup>403</sup> 42 U.S.C. § 262(k)(6).