

Statutory and Regulatory Scheme¹

I. The Drug Price Competition and Patent Term Restoration Act of 1984 (aka The Hatch-Waxman Act)

In 1984 the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act, was passed into law.² The Act was intended to “strike[] a balance between two potentially competing policy interests—inducing pioneering development of pharmaceutical formulations and methods and facilitating efficient transition to a market with low-cost, generic copies of those pioneering inventions at the close of a patent term.”³

A. *Impetus for Reform*

The U.S. Court of Appeals for the Federal Circuit’s 1984 decision in *Roche Products v. Bolar Pharmaceutical*⁴ is often described as a catalyst for the passage of the Hatch-Waxman Act. But the circumstances leading to the decision in *Bolar* and the passage of the Hatch-Waxman Act shortly thereafter should be recognized as the culmination of many years of tension and shifting over how best to structure statutory incentives in the pharmaceutical industry.

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2. Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. §§ 355, 360cc; 35 U.S.C. §§ 156, 271), as amended by the Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003).

3. See *Novo Nordisk A/S, et al. v. Caraco Pharm. Labs., Ltd.*, 601 F.3d 1359, 1360 (Fed. Cir. 2010) (citing *Andrx Pharm., Inc. v. Biovail Corp.*, 276 F.3d 1368, 1371 (Fed. Cir. 2002)), rev’d on other grounds, 2012 U.S. LEXIS 3106 (U.S. Apr. 17, 2012).

4. 733 F.2d 858 (Fed. Cir. 1984).

Movement toward the Hatch-Waxman compromise developed over many years. Notably, in the late 1950s and early 1960s it became known that the use of Thalidomide, a sedative frequently prescribed to pregnant women experiencing morning sickness, significantly increased the risk of birth defects. The Thalidomide scare led to the 1962 amendments to the Federal Food, Drug, and Cosmetic Act (FDCA), requiring all new drugs to be proven safe and effective prior to approval by the Food and Drug Administration (FDA).⁵ Generic manufacturers saw the new requirements as discouraging entry.⁶ Meanwhile, branded pharmaceutical manufacturers pushed for additional protections against entry by generic manufacturers. In 1978 President Carter recommended patent term restoration for pharmaceuticals and any other products that required regulatory review, to compensate for the time lost to the review, by extending a patent's term.⁷ By 1983, debate over the Drug Price Competition Act and Patent Term Restoration raged in Congress.⁸ The *Bolar* decision in 1984 was an important event leading to the passage of the compromise Hatch-Waxman Act because the *Bolar* decision highlighted the public policy tensions for the pharmaceutical industry that only Congress could properly address.

Roche Products, a brand-name pharmaceutical company, was the maker of Valium, the formulation for which was protected by patent. Generic manufacturer Bolar Pharmaceuticals tested the chemical formulation of Valium, before the expiration of Roche's patent on that formula, to determine if Bolar's generic product was bioequivalent to Valium in order to have an FDA-approved generic ready to market upon the expiration of Roche's patent.⁹ The determination of generic bioequivalence to a previously approved drug was and is necessary to obtain FDA approval for a generic version of the drug.¹⁰

Roche brought a patent infringement suit against Bolar for this use of Roche's patented formulation, because a U.S. patent provides its owner with the right to exclude not only the unauthorized sale of a product (or practicing of a method) covered by the patent, but even the manufacture or

5. Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified at 21 U.S.C. §§ 321, 331–32, 348, 351–53, 355, 357–60, 372, 374, 376, 381).

6. G.J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54(2) FOOD & DRUG L.J. 187–94 (1999).

7. *Id.* at 187.

8. *Bolar*, 733 F.2d at 865 (citing Drug Price Competition Act of 1983, H.R. 3605, 98th Cong. (1983) (amending 21 U.S.C. § 355(b) to allow faster marketing of new generic drugs equivalent to approved new drugs); Patent Term Restoration Act of 1983, S. 1306, 98th Cong. (1983) (amending 35 U.S.C. § 155 to add to the patent grant a period of time equivalent to that lost due to regulatory delay), 129 CONG. REC. S6863 (daily ed. May 17, 1983), 26 Pat. Trademark & Copyright J. (BNA) 87–88 (May 26, 1983)).

9. *Bolar*, 733 F.2d at 860.

10. 21 U.S.C. § 355.

use of a product (or the product of a method) that is patented. In response to the suit, Bolar argued that its use of Roche's patented formulation was not infringement because it was permitted under the common-law experimental use exception to the patent laws.

It was a principle of long standing in U.S. patent law that the otherwise-infringing production and/or use of a patented product for experimental, noncommercial uses was permitted.¹¹ Nevertheless, the Federal Circuit rejected Bolar's argument, holding that the experimental use exception did not apply because Bolar intended to sell its generic product in competition with Roche's Valium after patent expiration and, therefore, Bolar's experiments had a business purpose.¹²

Bolar also pled the equities of a public policy that favors the availability of generic drugs immediately following patent expiration, which would justify the experimental use of the patented chemical.¹³ Bolar argued that denying such use would effectively extend Roche's monopoly beyond the normal expiration of its patent. In rejecting this argument, the court explained that Congress should make such policy decisions.¹⁴ In further deference to Congress on policy considerations, the court highlighted the public policy conflict between the goals of the Food and Drug Act and the Patent Act.¹⁵

Shortly after *Bolar* was decided, Congress passed the Hatch-Waxman Act, which, among many compromise elements, created a statutory exception to infringement for a generic manufacturer's use of patented products in experiments for the purpose of obtaining FDA approval.¹⁶

II. Statutory Overview and Specific Amendments

A. General Compromise

As noted earlier, the Hatch-Waxman Act was officially titled the Drug Price Competition and Patent Term Restoration Act of 1984. The "price competition" side of the Act specifically authorizes and streamlines the process of generic entry through the establishment of the Abbreviated New Drug Application (ANDA). This part of the Act is unusual in that it

11. See, e.g., *Akro Agate Co. v. Master Marble Co.*, 18 F. Supp. 305 (N.D. W. Va. 1937); *Northill Co. v. Danforth*, 51 F. Supp. 928 (D.C. Cal. 1943); *Kaz Mfg. Co. v. Chesebrough-Pond's, Inc.*, 211 F. Supp. 815 (S.D.N.Y. 1962).

12. *Bolar*, 733 F.2d at 863.

13. *Id.* at 863–64.

14. *Id.* at 864–65.

15. *Id.*

16. See 35 U.S.C. § 271(e)(1).

is more prohibitive than enabling of the actions of the FDA. Specifically, it prohibits the FDA from doing more than asking for bioavailability studies from the ANDA filer.¹⁷

On the “restoration” side, the Act provides a set of “exclusivity” incentives for patented drug manufacturers to engage in new development and testing in exchange for longer periods of market exclusivity (i.e., an FDA promise to delay the review or approval of a competing drug).

The Act also establishes the framework for addressing patent protection disputes implicated by a rival generic manufacturer’s attempt to obtain FDA approval. The framework requires that the generic ANDA filer include one of the following four certifications with its application: (1) that the drug has not been patented; (2) that the patent has already expired; (3) that the generic drug will not go on the market until after the known expiration of nonexpired patent(s); or (4) that the patent is not infringed or is invalid. These certifications are frequently referred to as the Paragraph I, II, III, and IV certifications, respectively. Paragraph IV certifications create jurisdiction for a patent dispute between the generic ANDA filer and the patented drug manufacturer to be resolved in a federal district court in the United States.

B. Subsequent Amendments

The ANDA framework created by the Hatch-Waxman Act has been augmented by subsequent legislation, most notably the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003,¹⁸ which included the Access to Affordable Pharmaceuticals Act (AAPA) that resolved certain ambiguities, attempted to close perceived loopholes, and codified important court rulings on the original Hatch-Waxman scheme. Other notable legislation involving this framework includes: Orphan Drug Act (ODA) of 1983;¹⁹ Best Pharmaceuticals for Children Act (FPCA) of 2002;²⁰ and the Food and Drug Administration Amendments Act (FDAAA) of 2007,²¹ which included the Best Pharmaceuticals for Children Act (FPCA) of 2007.²²

These legislative amendments are incorporated in the following general description of the Hatch-Waxman statutory scheme, often referred to as the ANDA statutes.

17. H.R. REP. NO. 98-857, pt. 1, at 72 (1984).

18. Pub. L. No. 108-173, 117 Stat. 2066 (MMA of 2003).

19. Pub. L. No. 97-414, 96 Stat. 2049 (ODA of 1983).

20. Pub. L. No. 107-109, 115 Stat. 1408 (BPCA of 2002).

21. Pub. L. No. 110-85, 121 Stat. 823 (FDAAA of 2007).

22. Pub. L. No. 110-85, 121 Stat. 823, 876–90 (BPCA of 2007).

III. Statutory Balancing: Incentives to Patentees and Generics

As referenced earlier, the Hatch-Waxman Act was designed to strike a balance between the patent exclusivity rights of patented drug developers and the public's right to purchase less-expensive generic drugs. New Drug Application (NDA) filers benefit by receiving a form of compensation for administrative delays caused by the FDA review process. This compensation is granted by extending the NDA filer's patent term covering the patented drug.

A. New Drug Application Filers

1. Patent Term Extension and Exclusivity

a. Extension Based on FDA Review

The Hatch-Waxman Act specifies that the term of a patent covering NDA inventions can be extended to make up for patent life lost during the approval process for the patented drug.²³ The patent term extension provisions of the Hatch-Waxman Act provide an extension of up to five years for drugs, medical devices, and food additives that have premarket delays caused by administrative and regulatory evaluations. The rationale for patent extension is that the lengthy approval process under the FDCA affects the useful life of an NDA filer's patent term because the new drug cannot be marketed until after completion of FDA review.

NDA patents that qualify for term extension include those claiming products, methods of manufacturing, and methods of use for human and veterinary drugs, medical devices, and food additives. The patent must be issued prior to FDA approval for the patent to be eligible for term extension. In addition, the patent must not have been extended for another reason. Further, the regulatory approval must be the first such approval for a commercial use of the product.

The U.S. Patent and Trademark Office (USPTO) and the FDA jointly administer the patent term extension provisions of the Hatch-Waxman Act. The FDA identifies the period of extension by calculating the period of regulatory review of the drug product. Two periods of regulatory review are included in the calculation. According to 35 U.S.C. § 156(g)(1)(B), subsections (i) and (ii), there are two relevant regulatory review periods—the “testing phase” and the “approval phase.” These two regulatory phases

23. See 35 U.S.C. § 156.

correspond to the Investigational New Drug (IND) application period and the NDA review period, respectively.²⁴

The Federal Circuit has interpreted 35 U.S.C. § 156 as entitling patentees to patent term extensions for a single approved product, but not for all potential products covered by the patent claims.²⁵ The statute states that the grant of a patent extension is both patent-specific and product-specific. Accordingly, only one extension may be granted for each patent and only one patent extension is granted per active ingredient, even if multiple patents claim the ingredient. Further, the extension is specific to a single NDA (i.e., only one extension is permitted), even if other approved NDAs for alternative indications had additional administrative delays.

The Federal Circuit has also clarified that patent term extensions under 35 U.S.C. § 156 are only intended for patented inventions that are subject to FDA pre-market approval.²⁶

b. “New Data” Exclusivity

Hatch-Waxman Amendments and other subsequent acts incentivize drug companies to discover and test drugs by offering periods of exclusivity.

i. New Chemical Entity

Five-year exclusivity for new chemical entity (NCE) with a novel active moiety.

The Hatch-Waxman Amendments also created another type of competition-protection for NDA approvals of new chemical entities (NCE). Under the Amendments, for five years after an NDA covering an NCE is approved, the FDA will not consider a request by another party for approval of that NCE either alone or in combination with other active molecules. Thus, more than five years of exclusivity is effectively possible. If made with a certification of patent invalidity or noninfringement, an application for approval of that NCE by another party may be submitted after four years.

The five-year exclusivity period applies only to novel chemical entities. The NCE that must not have been previously approved is the active moiety.²⁷ The FDA has described an active moiety as “the part of the drug that makes the drug work the way it does.”²⁸ The FDA’s regulations define

24. See *id.* § 156(g)(1)(B)(i)–(ii); 21 C.F.R. § 60.22; 37 C.F.R. § 1.775(b).

25. See, e.g., *Merck & Co. v. Kessler*, 80 F.3d 1543, 1547 (Fed. Cir. 1996) (“the restoration period of the patent does not extend to all products protected by the patent but only to the product on which the extension was based”).

26. *Proveris Scientific Corp. v. Innovasystems, Inc.*, 536 F.3d 1256, 1265 (Fed. Cir. 2008).

27. 21 C.F.R. § 314.108.

28. 64 Fed. Reg. 47,719, 47,721 (Sept. 1, 1999).

active moiety as “the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.”²⁹

This narrow interpretation of the statutory term “active ingredient” was adopted to avoid overcompensating drug makers who had made “minor variations of previously approved chemical compounds.”³⁰ However, the statute does not expressly limit “active ingredients” eligible for NCE exclusivity to “active moieties.” Before the FDA officially adopted the narrow definition of “active ingredient,” the District of Columbia district court rejected the active moiety restriction as contrary to the plain meaning of the statute. However, the district court’s ruling was vacated by the D.C. Circuit, which remanded the question to the FDA for further consideration.³¹ Moreover, the Federal Circuit recently held that the interpretation of active moiety by the USPTO was incorrect, and that the phrase “active ingredient” is unambiguous in the statute.³²

ii. Three-Year New Clinical Investigation Exclusivity

Three-year exclusivity for applicants conducting essential new clinical investigations on previously approved active ingredients.

The Hatch-Waxman Act also includes a three-year period of exclusivity for a drug product that contains an active ingredient that has been previously approved, when the application contains reports of new clinical investigations conducted or sponsored by the applicant that were essential to approval of the application. For example, if the applicant provides support showing changes in an approved drug product that affect its active ingredient(s), strength, dosage form, route of administration, or conditions of use, then the applicant may be granted exclusivity if new clinical investigations were essential for approval of the application containing those changes.³³

The FDA interprets the term “new clinical investigations” to mean safety or efficacy studies in humans. Bioavailability studies do not qualify.³⁴ Although the statute requires that the studies be “new,” the regulations require only that the studies be “new” to the FDA; the studies should not

29. See 21 C.F.R. § 314.108(a).

30. 54 Fed. Reg. 28,872, 28,898 (July 10, 1989).

31. See *Abbott Labs. v. Young*, 691 F. Supp. 462 (D.D.C. 1988), *vacated and remanded*, 920 F.2d 984 (D.C. Cir. 1990).

32. *PhotoCure ASA v. Kappos*, 603 F.3d 1372 (Fed. Cir. 2010).

33. 21 U.S.C. § 355(j)(5)(F)(iii), (iv); 21 C.F.R. § 314.108(a).

34. See 21 U.S.C. § 355(j)(5)(F)(iii), (iv); 21 C.F.R. § 314.108(a).

have been previously relied upon to support the safety or efficacy of a drug.³⁵ Further, the new clinical investigations must have been conducted or sponsored by the NDA applicant or holder, who must ordinarily have contributed at least 50% of the study's cost.³⁶ Finally, the new studies must be essential to the FDA's approval of the application. This aspect can be disputed because opinions can differ on data that are "essential" to the application or merely "confirmatory" of previously submitted studies.³⁷

Importantly, a generic manufacturer may submit an ANDA during the three-year new clinical investigation exclusivity period, but the FDA is prohibited from approving the application. In addition, the three-year exclusivity only covers the indication(s) approved in the supplemental NDA approval. Consequently, a generic manufacturer may seek and obtain approval for other indications not covered by the exclusivity period (i.e., the exclusivity covered indications are "carved out" of the ANDA-filers' application).³⁸

iii. Orphan Drug Exclusivity

Seven-year exclusivity for drugs treating or preventing rare but serious diseases (aka orphan drugs).

The ODA was enacted to encourage drug manufacturers to develop drugs for rare but serious diseases.³⁹ The FDA will designate a drug candidate as an "orphan drug" after review of the "sponsor's" request. The request must describe the rare disease or condition for which the drug is being investigated, explain why the drug is thought to have potential for treating or preventing the disease, and provide documentation that the disease is "rare."

The ODA prohibits the FDA from approving another application for approval for such drug for such disease or condition for seven years from the date on which the FDA approves the NDA for the designated orphan drug.⁴⁰ In contrast to Hatch-Waxman exclusivities, the ODA bars approval of subsequent NDAs. However, the FDA has strictly construed the statutory phrase "for such disease or condition" as limiting exclusivity to applications that seek approval for treating the same disease or condition that the orphan designation was made. Consequently, a competitor can obtain approval for the drug for treating other diseases or conditions. Further, the

35. See 21 C.F.R. § 314.108(a) (2006).

36. *Id.*

37. See *Upjohn Co. v. Kessler*, 938 F. Supp. 439 (W.D. Mich. 1996).

38. 21 C.F.R. § 314.94(a)(8)(iv).

39. See 21 U.S.C. § 360aa-cc.

40. See *id.*

statute does not indicate when a subsequent drug is the same as an exclusive orphan drug. FDA regulations, however, state that drugs are similar if they have the same active moiety (for small molecules) or “contain[] the same principal molecular structural features” (for large molecules like proteins or nucleic acids).⁴¹ The FDA, however, will not deem a subsequent drug as the “same” as an approved orphan drug, even if it is structurally the same, if the latter drug is “clinically superior” or provides a “significant therapeutic advantage.”⁴²

iv. Pediatric Exclusivity

Six-month exclusivity, based on remaining patent life or data exclusivity protection, for pediatric studies on the safety, effectiveness, and conditions of use of approved drugs.

Congress created an incentive for drug makers to determine the safety, effectiveness, and conditions of use of their drug products in children by enacting the BPCA of 2002.⁴³ Pediatric exclusivity is obtained by submitting the results of pediatric studies and the FDA’s acceptance of those studies. Typically, the FDA makes a written request (WR) for an NDA holder sponsor and studies the pediatric use of its approved drug product. The WR will identify the “indication” of the drug that the FDA wants studied, the population to be studied, and the period for completion of the studies.⁴⁴ In 2007 the BPCA was amended to clarify that the FDA’s WR may include more than one indication, which may be “on-label” or “off-label,” and which may include nonclinical studies.⁴⁵ Other changes implemented through the BPCA of 2007 include: (1) the requirement that an applicant submit a report of all adverse events with the final pediatric study report, (2) the requirement that final exclusivity determination based on new WRs be made within 180 days of a response to the WR, (3) the restriction of exclusivity only to applicants with at least nine months of data exclusivity or patent protection remaining at the time of determination, and (4) the prioritization of FDA review of applications submitted in response to a WR. In addition, under the BPCA of 2007, a sponsor must submit its application (or supplement) for pediatric exclusivity fifteen months prior to expiration of adult exclusivity.

41. 21 C.F.R. § 316.3(b)(13)(ii).

42. *Id.* § 316.3(b)(3).

43. Pub. L. No. 107-109, 115 Stat. 1408. (BPCA of 2002); 21 U.S.C. § 355a.

44. *Id.* § 355a(c).

45. Best Pharmaceuticals for Children Act of 2007, Pub. L. No. 110-85, 121 Stat. 823 (BPCA of 2007).

The BPCAs benefit manufacturers who conduct pediatric studies by providing an additional six-month extension of FDA exclusivity, based on existing patent life or data exclusivity, to which the manufacturer is already entitled. Importantly, the manufacturer must have at least nine months of existing patent term or data exclusivity remaining for which “pediatric exclusivity” can attach. If not, then pediatric exclusivity provides it no additional term-extension benefit. Pediatric exclusivity does not actually extend the patent term, as many courts have misstated. Pediatric exclusivity extends by six months a bar to the FDA’s approval to a generic version of the drug. Unlike other data-based exclusivities, the scope of the pediatric extension is not limited to the particular drug product that was the subject of the pediatric studies. The FDA interprets the extension as applying to all drug products, in all dosage forms, that contain the same active moiety that was present in the product studied for pediatric use.

2. Artificial Act of Infringement Based on ANDA Filing

Patent Suit Standing Before Generic Launch: 35 U.S.C. § 271(e)(2) deems ANDA filing and certification an act of “infringement” against the listed patents (aka artificial infringement).

a. 35 U.S.C. § 271(e)(2)

The Hatch-Waxman Act was enacted to encourage patent owners and prospective generic drug makers to identify and resolve patent disputes before a generic product reaches the market. The Act also established a new procedure for resolving patent infringement issues prior to patent expiration. Generic manufacturers were obligated to notify patent owners respecting possible infringement, and patent owners were given the right to litigate their claims of patent infringement prior to the time the generic drug is put on the market. However, this procedure also created a conundrum for adjudicating potential infringement claims. In the premarket stage, the generic manufacturer does not sell the patented invention. Further, the Hatch-Waxman Act “safe harbor” immunizes the generic manufacturer from infringement for the use of the patented product in studies directed to FDA approval.⁴⁶ Accordingly, if the patentee attempted to sue the generic manufacturer for infringement prior to product launch, justiciability issues would arise because there has not been an actual act of infringement, and the patentee would lack standing to sue in federal court.

The Hatch-Waxman Act overcomes this issue by making the filing of an ANDA application an act of artificial infringement that satisfies the case or controversy requirements and gives the patentee standing to file

46. 35 U.S.C. § 271(e)(1).

suit against the generic manufacturer. Thus, the artificial act of infringement accomplished by filing an ANDA application serves “to create case or controversy jurisdiction to enable a court to promptly resolve’ a dispute concerning an infringement that will happen in the future.”⁴⁷ The Hatch-Waxman Act amended the basic infringement section of the Patent Act, 35 U.S.C. § 271, to add subsection (e), which provides in pertinent part:

It shall be an act of infringement to submit—

...

an application under Section 505(j) of the [Food, Drug and Cosmetic Act] or described in Section 505(b)(2) of such act for a drug claimed in a patent or the use of which is claimed in a patent . . .

if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.⁴⁸

b. Orange Book Listing

Patents covering NDA drug must have been listed in FDA’s Orange Book.

The Hatch-Waxman Act requires that an NDA applicant or holder list patent rights applicable to a drug in an official FDA publication entitled *Approved Drug Products with Therapeutic Equivalence Evaluations*—more commonly called the “Orange Book” owing to its original orange-colored cover. The Orange Book lists all commercial drug products approved for safety and effectiveness in the United States together with patents relevant to the active drug substances as well as drug formulations, inert ingredients, and their uses.⁴⁹ The Orange Book is published annually with quarterly supplements; it is accessible on the FDA’s website in an electronic version that is updated daily to provide all newly listed patents and newly approved generic drugs.⁵⁰

Submission of a patent for Orange Book listing is the responsibility of the patent owner. The Act specifies two types of patents that can be listed in the Orange Book: any patent that (1) “claims the drug for which the

47. *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1249 (Fed. Cir. 2000) (quoting *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997)).

48. 35 U.S.C. § 271(e).

49. 21 U.S.C. § 355(b)(1), (j)(7).

50. U.S. Food & Drug Admin., *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations* (Oct. 28, 2011), <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>.

applicant submitted the application”; or (2) “claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.”⁵¹ Thus, the typical types of patents listed in the Orange Book are compound claims, formulations, and methods of use or treatment claims. Process patents are not eligible for Orange Book listing.

c. Orange Book “Delisting” Counterclaim

The MMA permits a generic manufacturer who has been sued under 35 U.S.C. § 271(e)(2) to assert a counterclaim seeking an order requiring the NDA drug manufacturer/patent owner to correct or delete patents listed in the Orange Book listing.⁵² The generic manufacturer may assert that the listed patent either does not claim the drug for which the application was approved or does not claim an approved method of using the drug. This section does not provide an independent cause of action, and no damages are available under such a counterclaim.

d. Paragraph IV Certification

35 U.S.C. § 271(e)(2) triggered ANDA filer’s “certification” that the listed patents are not infringed or are invalid (aka Paragraph IV certification).

When an ANDA is filed, the ANDA applicant must certify to the FDA that for each patent applicable to the patented drug, the proposed generic drug would not infringe the patent because the ANDA filer will not market the generic drug until after the applicable patents expire⁵³ or the patent is believed to be invalid, or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA applicant seeks approval.⁵⁴ The certification of invalidity or noninfringement is commonly called a “Paragraph IV certification.” The patent owner and/or NDA holder are then given notice by the generic applicant that an ANDA has been filed with a Paragraph IV certification. The Paragraph IV certification constitutes the only required notice to the patent owner that someone seeking to market before patent expiration has filed an ANDA. The notice required to be sent to a patented drug manufacturer following a generic manufacturer’s Paragraph IV certification must explain in detail the legal and factual reasons

51. 21 U.S.C. § 355(b)(1)(G).

52. *Id.* § 355(j)(5)(C)(ii). The Supreme Court’s unanimous decision in *Caraco Pharm Labs., Ltd. v. Novo Nordisk A/S et al.*, 2012 U.S. LEXIS 3106 (U.S. Apr. 17, 2012), reversing the Federal Circuit’s narrow view of the counter claim to preclude its use where at least one proper method patent “use code” is designated, may open the door to considerably more “delisting” counter claims.

53. *Id.* § 355(j)(2)(A)(vii)(III).

54. *Id.* § 355(j)(2)(A)(vii)(IV).

why the patent is believed invalid or not infringed.⁵⁵ However, the ANDA application itself is not required to include any details beyond the labeling and certification elements listed in 21 U.S.C. § 355(j)(2)(A).⁵⁶

e. Method of Use Statement and Carve-Outs

Where an ANDA filer seeks approval for a use that is outside the scope of a method of use patent listed for the drug, the ANDA filer must submit a method of use statement to this effect.⁵⁷ It is not an act of infringement to submit an ANDA for marketing approval of a drug for a use when neither the drug nor that use is covered by an existing patent, and the patent at issue is for a use not approved under the NDA.⁵⁸

The ANDA filer must “carve out” any mention of the patented method of use from the proposed label for the generic drug.⁵⁹ Unlike Paragraph III or IV certifications, the filing of a method of use or “section viii” statement will not by itself delay approval of an ANDA.⁶⁰

A generic manufacturer cannot infringe by filing an ANDA where the generic manufacturer’s intended (and NDA approved) use of the drug is not covered by an existing patent, even if there are patents listed in the Orange Book that cover other uses for the drug.⁶¹ Likewise, inducement to infringe can only be found where the patented drug manufacturer’s patented use is FDA-approved.⁶² When the proposed instructions on a generic label will, however, allow some users to practice the drug manufacturer’s patented and FDA-approved method of use, a claim for inducement to infringement may be established.⁶³

f. Declaratory Judgment by ANDA Filer

Under MMA, if a patent/NDA holder does not sue the ANDA filer for patent infringement within forty-five days of receiving notice of the ANDA filer’s Paragraph IV patent challenge, then the ANDA filer may bring a declaratory judgment action for patent invalidity or noninfringement under the following conditions: (a) the forty-five-day period following notice of the ANDA filing has expired; (b) the ANDA filer was not sued

55. *Id.* § 355(j)(2)(B).

56. *See id.* § 355(j)(2)(A) (“The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii)[.]”).

57. *Id.* § 355(j)(2)(A)(viii).

58. *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1362 (Fed. Cir. 2003).

59. *See* 21 C.F.R. § 314.92(a)(1); *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.*, 601 F.3d 1359, 1361 (Fed. Cir. 2010), *rev’d on other grounds*, 2012 U.S. LEXIS 3106 (U.S. Apr. 17, 2012).

60. *AstraZeneca, LP v. Apotex, Inc.*, 633 F.3d 1042, 1046 (Fed. Cir. 2010).

61. *Warner-Lambert Co.*, 316 F.3d at 1362.

62. *Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322 (Fed. Cir. 2003).

63. *AstraZeneca*, 633 F.3d at 1060–61.

for infringement within the forty-five-day period; and (c) the ANDA filer asserting noninfringement provided notice to the NDA holder/patent owner which included an offer of confidential access to the ANDA application.⁶⁴ While the offer of confidential access is necessary to trigger declaratory judgment rights for the ANDA filer asserting noninfringement, it is not an otherwise mandatory obligation of the ANDA filer. The NDA holder/patent owner recipient of this confidential information may only use it to evaluate possible infringement by the ANDA filer of the patents over which a Paragraph IV certification was made, and the ANDA filer may redact extraneous information from their disclosure.⁶⁵

3. The Thirty-Month Stay

Final FDA approval of generic is stayed for thirty months pending timely filed patent litigation.

a. Litigation Within Forty-Five Days of Notice

The thirty-month stay applies only when a patent infringement suit is brought on an Orange Book listed patent within forty-five days of notice of ANDA filing.

Once the ANDA Paragraph IV certification is filed, a patent owner has forty-five days to sue the generic ANDA filer. FDA rules provide that a thirty-month statutory stay period begins to run when the patent owner receives notice from the ANDA filer that it has made a Paragraph IV certification.⁶⁶ The FDA begins the forty-five-day period on the date of receipt of the notice by the patent owner and NDA holder's mailroom. The FDA requires strict compliance with the forty-five-day period.⁶⁷ If the patent owner does not respond to the ANDA filing challenge, the FDA may approve the ANDA "immediately" without regard to any unresolved patent or exclusivity issues. If, however, the patent owner sues, the FDA must not approve the ANDA for thirty months.⁶⁸ The thirty-month stay is terminated if a district court determines that the patent is invalid or not infringed.⁶⁹ A patent owner can sue the ANDA filer outside the forty-five-day period but the patent owner will not have the benefit of the thirty-month statutory stay. In addition, the court has the power to modify the

64. MMA § 1101(a)(2)(C); 21 U.S.C. § 355(j)(5)(C)(i)(I); 35 U.S.C. § 271(e)(5).

65. MMA § 1101(a)(2)(C); 21 U.S.C. § 355(j)(5)(C)(i)(III).

66. 21 U.S.C. § 355(j)(4)(B); 21 C.F.R. § 314.707(b)(3).

67. See *Mylan Labs. v. Thompson*, 332 F. Supp. 2d 106, 113 (D.D.C. 2004), *aff'd*, 389 F.3d 1272 (D.C. Cir. 2004) (45-day time limit not expanded for unintentional error).

68. See *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 261 F. Supp. 2d 188, 195 n.8 (S.D.N.Y. 2003) (recognizing that a longer period resulted for NCE).

69. 21 U.S.C. § 355(j)(5)(B)(iii)(I).

thirty-month stay if a party is not reasonably cooperating in expeditiously processing the case, although this rarely occurs.⁷⁰

b. Generic Must Give Notice Within Twenty Days

Prior to the AAPA, an ANDA filer had no time limit on when to provide notice to the patent holder and NDA holder of a Paragraph IV certification that triggers the patent/NDA holder's forty-five-day period to file the patent infringement suit to obtain the benefit of the automatic thirty-month stay. Under the AAPA, the ANDA filer must now give notice to the patent holder and NDA holder within twenty days of receiving notice from the FDA that the ANDA application has been filed.⁷¹

The AAPA also changes the ANDA filer's notice obligations when filing application amendments or supplements. Prior FDA regulations did not require ANDA filers to give notice to the patent/NDA holder when an application is amended to add an additional Paragraph IV certification. Under the AAPA, the ANDA filer must give notice of a Paragraph IV certification at the time of the amendment or supplement, regardless of whether the ANDA filer had provided a previous notice.⁷²

c. Timing of Final FDA Approval

Final FDA approval of generic occurs upon earliest of expiration of last listed patent, final judgment, or expiration of thirty-month stay.

If the patentee sues the ANDA-filer within the forty-five-day period, the FDA's evaluation of the ANDA will go forward in its normal fashion, but final approval permitting market launch of the generic cannot be effective until the earlier of (1) the expiration of the Orange Book listed patent(s); (2) a final judicial determination favorable to the ANDA applicant; or (3) expiration of the thirty-month stay, unless the court determines that the patent owner has not been diligent in prosecuting the matter.⁷³ The typical period for evaluation and approval of an ANDA by the FDA is about eighteen to twenty-four months.⁷⁴

If a federal district court invalidates the patent or holds the patent not infringed, before expiration of the thirty-month period, the ANDA approval date is the date of the final court decision.⁷⁵ Importantly, a final

70. *Id.* § 355(j)(5)(B)(iii).

71. MMA of 2003, § 1101(a)(1)(B); 21 U.S.C. § 355(j)(2)(B).

72. Pub. L. No. 108-173, MMA § 1101(c).

73. 21 U.S.C. § 355(j)(5)(B)(iii).

74. *Bristol-Myers Squibb Co. v. Royce Labs.*, 69 F.3d 1130, 1131–32 (Fed. Cir. 1995), *cert. denied*, 516 U.S. 1026 (1995).

75. 21 U.S.C. § 355(j)(4)(B)(iii)(I).

decision is made by the Court of Appeals for the Federal Circuit. Thus, the legislative scheme permits litigation respecting validity and infringement to begin before FDA approval and allows the litigation to proceed simultaneously with the FDA's evaluation of the ANDA. The patent owner can litigate the patent issues before the generic copy reaches the market.⁷⁶

At the expiration of the thirty-month period (or a shorter or longer period as a court may order), an ANDA filer that has received FDA approval may commence marketing immediately, or it may delay such activities until the conclusion of the litigation. The Federal Circuit has affirmed the trial court's authority to extent the thirty-month stay based on perceived litigation delays caused by the generic manufacturer.⁷⁷ Even where an FDA-approved ANDA filer is free to begin marketing prior to the termination of the suit, it may still be subject to infringement damages if it ultimately loses the infringement suit (*see Section III.A.3.e "At Risk? Launches" below*).

The settlement of ANDA litigation can also terminate the thirty-month stay, because a settlement eliminates the rationale for the stay by permitting the parties an opportunity to resolve the patent challenge in court prior to FDA approval.

d. Changes to Thirty-Month Stay Under 2003 Amendments

The most significant change brought by the AAPA is the limitation of only one statutorily prescribed automatic thirty-month stay per product in ANDA litigation.⁷⁸ Prior to this change, the manufacturer/patent owner could obtain the benefit of an additional, automatic thirty-month stay upon the later listing of an additional patent in the Orange Book for a product already subject to ANDA litigation, which required a new Paragraph IV certification by the ANDA filer and a new ANDA litigation. Under the AAPA, an ANDA applicant need only make a certification as to those patents listed in the Orange Book at the time of the ANDA filing.

The AAPA also prevents an ANDA applicant from shortening the thirty-month stay of approval by amending a previously filed ANDA to include a different drug, although ANDA amendments to include different strengths of the same drug are permitted.

The AAPA also clarifies that the thirty-month stay automatically terminates upon the entry of a district court judgment of patent invalidity or noninfringement. A patent invalidity or noninfringement ruling by the Court of Appeals following a district court determination of infringement terminates the stay upon the date of the Court of Appeals decision.

76. *See* Glaxo, Inc. v. Novopharm, Ltd., 110 F.3d 1562, 1569 (Fed. Cir. 1997).

77. *Eli Lilly & Co. v. Teva Pharm. USA, Inc.*, 557 F.3d 1346, 1351 (Fed. Cir. 2009).

78. 21 U.S.C. § 355(j)(2), (5).

e. “At Risk” Launches

Post-stay launch by generic may be “at risk” of damages liability to patent owner.

The thirty-month stay is not the only consideration that keeps the generic company from marketing the generic copy while the litigation is still pending. When the drug product in suit is an important one, a generic company could be financially destroyed by the patent infringement damages incurred for lost profits of a blockbuster drug.

In order for a company to collect infringement damages for a patent on an important drug, the company that is marketing the patented drug must also be the patent owner or have an exclusive license to the listed patent. A nonexclusive licensee of a patent does not have standing to sue for damages from infringement.⁷⁹ In contrast, a subsidiary corporation that owns a patent, but does not market any product, has a patent infringement damages claim limited to a reasonable royalty. In addition, the obligation to pay a reasonable royalty is not likely to be a deterrent against a generic ANDA filer marketing “at risk” before the patent has been determined noninfringed or invalid. It also leaves the potentially enormous harm caused to the patent owner by an infringing generic drug launch beyond the reach of any effective legal remedy.

B. ANDA Filers

The Hatch-Waxman Act established several incentives for a drug manufacturer to file an ANDA for a generic drug. Creation of these incentives was intended to meet the policy goal of accelerating the introduction of generic drugs to the market. The statutory incentives to file an ANDA can be divided into three main categories:

- Simplification of application requirements for an ANDA, as compared to the requirements for an NDA;
- Broad-based immunity from patent infringement for the generic developer for activities related to the development and approval of the generic drug; and
- Market exclusivity rights for the first ANDA filer making a Paragraph IV certification, and risking a patent infringement action from the patent owner.

79. See *Ortho Pharm. Corp. v. Genetics Inst.*, 52 F.3d 1026, 1031 (Fed. Cir. 1995), *cert. denied*, 516 U.S. 907 (1995) (“A holder of such a nonexclusive license suffers no legal injury from infringement and, thus, has no standing to bring suit or even join in a suit with the patentee.”).

1. Abbreviated Process for Bioequivalence

Statute simplifies (abbreviates) FDA filing and approval requirements for new drugs that are therapeutically equivalent to a previously approved new drug.

As its name indicates, the filing requirements for a generic drug under the ANDA scheme are simplified in comparison to the application process for the corresponding drug. It is presumed that a generic drug will function in the same manner as the drug if the two drugs are identical. Thus, the major difference in application requirements for a drug and its generic is that the generic applicant is permitted to rely on the safety and efficacy testing data of the NDA drug application.⁸⁰ The generic applicant is not required to submit new preclinical and clinical testing data in an ANDA.

In place of safety and efficacy data for the drug, a generic applicant must provide in the ANDA information showing that the active ingredient in the generic is identical to that in the NDA drug and that the generic drug is bioequivalent to the NDA drug. By showing active ingredient identity and bioequivalence in the generic, the generic drug is presumed to be as safe and effective as the NDA drug. Reliance on the safety and efficacy information contained in the NDA drug application allows the generic developer to avoid the costs associated with generating preclinical and clinical test data.

a. Establishing Bioequivalence

ANDA filer must demonstrate that the active ingredient is identical to the previously approved drug.

Instead of the preclinical and clinical testing data previously submitted by the NDA applicant to demonstrate the safety and efficacy of a drug, the generic must include in the ANDA evidence that the generic drug contains the same active ingredient and is bioequivalent to the previously approved NDA drug. The active ingredient of a drug “is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the body[.]”⁸¹ The requirement for active ingredient identity is generally applied to the chemical composition of the generic drug. The active ingredient of the generic can be permitted to differ in physical characteristics from the NDA drug active ingredient and still be considered identical (for example, differences in crystalline structure between the active ingredient of the generic drug and the NDA drug).

80. 21 U.S.C. § 355(j).

81. 21 C.F.R. § 210.3(b)(7) (2006).

For the purposes of an ANDA application, bioequivalence is established by showing that the generic drug does not significantly differ in the rate and extent to which the active ingredient becomes available in the body or at the site of action as compared to the NDA drug. Thus, a generic applicant can meet this requirement by submitting data relating to the absorption of the drug into the bloodstream.

b. Other ANDA Requirements

ANDA filing must mirror the previously approved drug application with respect to labeling; usage, dosage, and administration; and manufacturing information.

The ANDA application mirrors the previously approved drug application by requiring that the generic drug match the approved drug in labeling, usage, dosage, and route of administration. Additionally, the generic developer must disclose drug manufacturing information in the ANDA.

An ANDA application must include copies of the labeling of the previously approved drug and proposed labeling of the generic drug, along with an annotated comparison identifying differences between the two labels. An ANDA applicant can comply with the requirement for identical labeling by using for the generic a verbatim copy of the NDA drug labeling with necessary differences in manufacturing information, expiration date, formulation (e.g., permitted differences in active ingredient as noted above, and differences in inactive ingredients), bioavailability, patent markings, and any deviations from the NDA drug labeling necessitated by changes in FDA labeling requirements. As an additional incentive to copy the previously approved label, generics cannot be sued for a failure to warn under state tort law, as long as their labeling complies with the FDA mandated labeling for the NDA drug.⁸²

An ANDA application must also include information demonstrating that the usage, dosage, and route of administration of the generic drug are the same as the NDA drug. “Dosage form” is defined neither in statute nor regulations and is typically evaluated based on a comparison of the physical appearance and method of administration of the drugs. An ANDA filer can petition the FDA for permission to deviate from the NDA drug’s active ingredient (from a plurality of active ingredients in the NDA drug), usage, dosage, route of administration, and/or strength.⁸³

82. *Pliva, Inc. v. Mensing*, 131 S. Ct. 2567, 2581 (2011).

83. 21 U.S.C. § 355(j)(2)(C).

2. Safe Harbor

Generics are immune from infringement for drug uses related to FDA approval process.

The Hatch-Waxman Act provides infringement immunity to the ANDA applicant for activities related to its development of the generic drug. This exemption from infringement actions is codified at 35 U.S.C. § 271(e)(1) and the scope of the exemption is clarified by the Supreme Court in *Merck KGaA v. Integra Lifesciences I, Ltd.*⁸⁴

a. 35 U.S.C. § 271(e)(1)

35 U.S.C. § 271(e)(1) exempts from patent infringement all uses of a patented invention “reasonably related” to the pursuit of FDA drug approval. Commonly referred to as the “safe harbor” provision, Section § 271(e)(1) specifically provides that:

[i]t shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

As noted earlier in this chapter, one of the two principal policy concerns addressed by the Hatch-Waxman Act was the distortion of protection at the end of the patent term protecting a patented drug. As shown in the decision of the Federal Circuit in *Bolar*, prior to the enactment of the Hatch-Waxman Act and the safe harbor provision provided in Section 271(e)(1), generic applicants could avoid infringement only by beginning development activities for the generic drug after expiration of the patent protecting the patented drug. Despite the stated goal of providing protection for the development of generic drugs during the patent term of corresponding patented drugs, the statutory language and lack of legislative history fail to define and provide guidance for several key terms, including “solely for uses reasonably related.” For over two decades after passage of the Hatch-Waxman Act, it was unclear which types of activities by the generic applicant and at which stages of research and development were immune from infringement claims by the patented drug developer. Upon considering the issue, the Supreme Court provided a broad scope for “reasonably related” activities.

84. 545 U.S. 193 (2005).

b. Scope of Exemption

Broad judicial interpretation: Merck v. Integra.

Judicial interpretation of the safe harbor provision has set broad definition for “reasonably related” in 35 U.S.C. § 271(e)(1). The Supreme Court set the current standard for determining “reasonably related” in *Merck KGaA v. Integra Lifesciences I, Ltd.*⁸⁵ In its decision, the Court considered whether “uses of patented inventions in preclinical research, the results of which are not ultimately included in a submission to the FDA are exempted from infringement by 35 U.S.C. § 271(e)(1).”⁸⁶

The case arose from Merck’s activities in developing cancer treatments using RGD peptides in order to identify potential drug candidates for further development and possible submission for regulatory approval. Integra owned patents relating to the RGD peptides and sued Merck for infringement on the basis that because Merck’s activities focused on research, rather than clinical testing, the safe harbor provision did not protect Merck.

At trial, Merck was found liable for infringement and the Federal Circuit affirmed the trial decision on appeal. The Federal Circuit found that Merck’s drug development activities were not meant to produce clinical testing information to provide to the FDA, but amounted only to general research to identify new pharmaceutical compounds. The Federal Circuit indicated that the safe harbor provision of Section 271 does not exempt all activities that may eventually lead to an FDA submission.

The Supreme Court reversed, holding that “the statutory text makes clear that it [the safe harbor provision] provides a wide berth for the use of patented drugs in activities related to the federal regulatory process.”⁸⁷ The Court found that the research outside of the direct scope of development of a generic drug for an ANDA approval falls within the Section 271 safe harbor provision. The Court acknowledged that the safe harbor provision provides for “experimentation and failure on the road to regulatory approval” and that the infringement exemption applies to all phases of research, including preclinical studies using patented compounds. The Court noted that a generic developer is exempt from infringement even if an ANDA application is never filed, as long as the developer has a reasonable basis for believing that a patented compound will be effective for use and could be used in an ANDA.

85. *Id.*

86. *Id.* at 195.

87. *Id.* at 202.

In addition to the broad interpretation of “reasonably related” activities, the generic developer is not barred from using any patented invention in developing the generic drug. Thus, the generic developer, in addition to using the patented drug, can also use patented research tools in uses reasonably related to the production of data for the ANDA without infringing the patents that claim those tools.

In 2008, the Federal Circuit further clarified the scope of safe harbor under Section 271(e)(1), confining its application to products subject to FDA premarket approval.⁸⁸

3. 180-Day Exclusivity

First ANDA filer receives 180-day exclusivity over subsequent generics.

The Hatch-Waxman Act establishes a 180-day exclusivity period for the first ANDA filer including a Paragraph IV certification. This portion of the Act was intended to promote development of generic drugs, especially those generics copying patented NDA drugs considered to have weak or vulnerable patent protection. Since the filing of an ANDA with Paragraph IV certification is a technical act of patent infringement, the market exclusivity period is designed, in part, to reward the ANDA filer’s risk of provoking an infringement suit by filing a Paragraph IV certification.

The language of the Hatch-Waxman Act setting forth the exclusivity period was vague, and FDA implementation of the exclusivity period served as the impetus for litigation relating to who is entitled to the exclusivity period, when the exclusivity period commences, and how the exclusivity period can be forfeited. The MMA of 2003 revised the portion of the statute relating to the 180-day exclusivity period.⁸⁹ The MMA provisions relating to market exclusivity apply to ANDA applications filed with a first Paragraph IV certification after December 8, 2003. The following section addresses the current statutory framework of the exclusivity period.

a. First to File

“First to file” is the first to make Paragraph IV certification (i.e., first to challenge the validity of the listed patent(s)).

The MMA of 2003 makes clear that the first generic company to submit a substantially complete ANDA with a Paragraph IV certification is considered the “first applicant” for purposes of enjoying the 180-day market exclusivity. Under this provision, it is possible for more than one company

88. *Proveris Scientific Corp. v. Innovasystems, Inc.*, 536 F.3d 1256, 1265 (Fed. Cir. 2008).

89. MMA § 1102; 21 U.S.C. § 355.

to obtain the benefit of the market exclusivity in the event multiple companies file on the same day a substantially complete ANDA with a Paragraph IV certification for a drug for which a substantially complete ANDA with a Paragraph IV certification has not previously been filed. For the purposes of this requirement, a “substantially complete” ANDA contains all required information for a substantive review.⁹⁰

b. Subsequent Filers

First ANDA filer’s exclusion applies against a subsequent generic filing an ANDA on the same drug, dosage strength, and Paragraph IV certification.

The 180-day exclusivity period delays market entry over subsequent ANDA applicants with a Paragraph IV certification for the same drug. There are three exceptions to the exclusivity period for the first applicant: (1) the later ANDA application does not include a Paragraph IV certification, (2) the later ANDA application is for a different dosage, and (3) the patented NDA drug manufacturer produces an authorized generic.

The first Paragraph IV filer has market exclusivity only over subsequent ANDA applicants who include a Paragraph IV certification for any patents listed in the first-filed ANDA. A subsequent ANDA filer avoids the exclusivity period of the first filer by not including a Paragraph IV certification.

For purposes of drug applications, the FDA considers a variation in dosage strength in drugs having the same active ingredient(s) as a new drug. Thus, the first Paragraph IV certifier enjoys exclusivity over later applicants only for the same drug at the same dosage strength. The first applicant cannot use its market exclusivity period against a subsequent applicant for a generic for the same NDA drug who gains approval for a petition to vary dosage strength from the NDA drug.

Finally, the first Paragraph IV certifier cannot enjoy market exclusivity over the patented NDA manufacturer’s authorized generic. A patented NDA drug manufacturer is permitted to market an unbranded version of its drug based on the information of the original NDA.

c. Commercial Marketing

First filer’s 180-day exclusivity period commences when first filer begins commercial marketing.

The 180-day exclusivity period is calculated from the first date of “commercial marketing” of the generic drug by the first filer.⁹¹ This is a modification from the Hatch-Waxman Act under which commenced the exclusivity period

90. 21 U.S.C. 355(j)(2)(A).

91. MMA §1102(a)(1); 21 U.S.C. § 355(j)(5)(B)(iv)(1).

from the date of a favorable district court decision for the generic applicant. Thus, the generic producer has some control over the start date of the exclusivity period and the opportunity to undertake product launch activities after the approval of the ANDA and termination of infringement litigation.

d. Losing Exclusivity

Failure to timely commence marketing results in forfeiture of first filer's exclusivity.

The first Paragraph IV ANDA filer can forfeit its exclusivity rights for failing to bring the generic drug to market within certain time limits. The first Paragraph IV ANDA filer will forfeit its exclusivity rights for failure to market the generic drug by within any one of: seventy-five days after FDA approval of the ANDA or thirty months after filing the ANDA; seventy-five days after a nonappealable favorable district court or favorable Federal Circuit decision; seventy-five days after a favorable settlement; and seventy-five days after the patent protecting the drug expires or is withdrawn. These timing requirements were established in the MMA of 2003. The Hatch-Waxman Act did not include the requirement to bring the generic to market or risk forfeiture of the exclusivity period. Additionally, a first filer can lose the exclusivity rights by amending or withdrawing the Paragraph IV certification from its ANDA.

e. Change and Clarifications to 180-Day Exclusivity

As noted above, the MMA instituted a forfeiture policy, regarding the 180-day exclusivity period, for first filers failing to timely market the approved generic. The new legislation also applies forfeiture to the following acts: (1) withdrawal of an ANDA, (2) failure to obtain tentative approval within thirty months of filing, (3) the ANDA filer's entry into an anticompetitive agreement; and (4) expiration of all patents subject to the Paragraph IV certification.

The MMA also codifies certain FDA policies regarding the 180-day exclusivity, specifically:

- Exclusivity is determined on a drug-by-drug basis, rather than for each separate patent challenged under a Paragraph IV certification.
- Exclusivity is shared by all ANDAs with Paragraph IV certifications filed on the same day that the first ANDA with a Paragraph IV certification is filed.

A forfeited 180-day exclusivity period does not pass to a subsequent ANDA filer (i.e., there is no rolling exclusivity).