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The Conflict Between the FDA's Pre-Launch Activities Importation Request Program and the Hatch-Waxman Act

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The Conflict Between the FDA’s Pre-Launch Activities Importation Request Program and the Hatch-Waxman Act

by ALEX CHENG AND MATTHEW AVERY*

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Introduction

In 2008, the Food and Drug Administration (FDA) implemented the Pre-Launch Activities Importation Request (PLAIR) program.¹ The FDA exercises its enforcement discretion under the guise of the PLAIR program to permit the importation of unapproved finished drug products into the United States based on anticipated approval of a New Drug Application (NDA) or an Abbreviated New Drug Application (ANDA).² In other words, the FDA gives drug manufacturers permission to import unapproved drugs into the United States so the manufacturers can expedite their commercial launches when they finally receive official FDA approval.³

The FDA developed the PLAIR program with an eye toward the globalization of the pharmaceutical industry.⁴ In particular, the intense competition and relatively small margins in the generic

1. Annual Guidance Agenda, 73 Fed. Reg. 153 (Jul. 30, 2008).

2. Food and Drug Administration, Draft Guidance for Industry on Pre-launch Activities Importation Requests (PLAIR), at 1 (2013) [hereinafter FDA, PLAIR Draft Guidance], available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM362177.pdf> (“Historically, when applicants sought to import unapproved finished dosage form drug products in preparation for market launch, FDA considered such requests, informally referred to as Pre-Launch Activities Importation Requests (PLAIRs), on a case-by-case basis. FDA has decided to create a more formal program . . .”).

3. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 1; Kurt R. Karst, *PLAIRs—What are They and What are FDA’s Current Policies?*, FDA LAW BLOG (Apr. 11, 2010), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2010/04/plairs-what-are-they-and-what-are-fdas-current-policies.html.

4. Karst, *supra* note 3.

industry mean that generic companies often must manufacture their drugs in foreign countries where production costs are lower.⁵ While generic companies may be able to produce cheaper goods by manufacturing in foreign countries, they face additional burdens when they import their drugs into the United States, a process which is heavily regulated by the FDA.⁶ One such burden is seeking PLAIR approval from the FDA to import a drug prior to FDA marketing approval.⁷ But the ability to import unapproved finished drug products into the United States ahead of anticipated FDA approval conflicts with certain provisions of the Hatch-Waxman Act that permit brand-name companies to use permanent injunctions to prevent the importation of generic equivalents of their drugs before patent expiration.⁸

Sanofi-Synthelabo v. Apotex, Inc. is the first case under Hatch-Waxman in which a generic company, notwithstanding a permanent injunction, has requested to take advantage of the PLAIR program to import a generic drug into the United States before the expiration of the pioneer's patent.⁹ Although arguments were made on both sides regarding whether Apotex should be allowed to take advantage of the PLAIR program despite the permanent injunction, *Sanofi v. Apotex* was dismissed for not being timely, and neither the District Court nor the Federal Circuit addressed the conflict between PLAIR and Hatch-Waxman.¹⁰ However, it is likely that more generic manufacturers will attempt to take advantage of the PLAIR program

5. Compare World Health Organization, Pharmaceutical Industry, <http://www.who.int/trade/glossary/story073/en/> (noting that some of the largest pharmaceutical companies have profit margins of about 30%) with THE HENRY FUND, GENERIC DRUG MANUFACTURERS (2013), <http://tippie.uiowa.edu/henry/reports13/generics.pdf> (showing that the profit margins for the five largest generic manufacturers range from 0.89% to 18.93%). See also Christelle Laot, *FedEx and Generic Drugs: Connecting Global Manufacturers to Consumer Markets*, FEDEX BLOG (Mar. 14, 2011), <http://blog.fedex.designcdt.com/generic-drugs-markets>.

6. See 21 U.S.C. § 355(a) (2012).

7. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 1.

8. 35 U.S.C. § 271(e)(4) (2012).

9. *Sanofi-Synthelabo v. Apotex, Inc.*, (nonprecedential order) 1, 2 (Fed. Cir. 2012).

10. See Brief of Petitioner-Appellant at 5-6, *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS (Fed. Cir. May 9, 2012); see also Brief of Respondent-Appellee at 3-6, 8-9 *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS (Fed. Cir. May 9, 2012); *Sanofi-Synthelabo v. Apotex, Inc.*, (nonprecedential order) 1, 3 (Fed. Cir. 2012).

to overcome injunctions and import their drugs prior to FDA marketing approval.¹¹

This Article analyzes the conflict between the PLAIR program and the Hatch-Waxman Act and discusses solutions to the conflict. Part 1 of this Article provides an overview of the Hatch-Waxman Act and the regulation of generic drugs. Part 2 provides an overview of the PLAIR program. Part 3 analyzes the validity of the PLAIR program. Part 4 analyzes the conflict between the PLAIR program and the Hatch-Waxman Act and provides a description of the *Sanofi v. Apotex* case. Part 5 discusses balancing the goals of the PLAIR program with the intent of the Hatch-Waxman Act. Part 6 discusses modifying the current regulatory regime to resolve the conflict between the PLAIR program and the Hatch-Waxman Act. Finally, Part 7 provides strategic considerations for practitioners in this area.

1. Overview of the Hatch-Waxman Act and the Regulation of Generic Drugs

1.1. The Regulation of Drugs Under the Food, Drug, and Cosmetic Act

In order to market a new drug, or to import it for marketing, a pharmaceutical company must first obtain FDA approval.¹² Section 355(a) of the Food, Drug, and Cosmetic Act (FDCA) provides that “[n]o person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application . . . is effective with respect to such drug.”¹³ Because section 355(a) only prohibits importation of finished drug products (i.e., products that are ready for sale), the FDA has long allowed the importation of *unfinished* drug products into the United States, and has issued specific regulations to permit the importation of unfinished bulk products ahead of FDA approval.¹⁴ Unfinished bulk products can undergo further manufacturing, processing, and repackaging in the United States prior to regulatory approval, so the finished drug product will be ready for an immediate market launch when the FDA

11. Kurt R. Karst, *FDA's PLAIR Program Collides with Hatch-Waxman*, FDA LAW BLOG (May 23, 2011), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2012/05/fdas-plair-program-collides-with-hatch-waxman.html.

12. See 21 U.S.C. § 355(a).

13. 21 U.S.C. § 355(a).

14. 21 C.F.R. § 314.410(a)(2) (2008) (“A drug substance intended for use in the manufacture, processing, or repackaging of a new drug may be imported into the United States if it complies with the labeling exemption in § 201.122 pertaining to shipments of drug substances in domestic commerce.”).

finally grants approval.¹⁵ While FDA regulations allow the importation of unfinished bulk products, no such regulations exist for *finished* drug products. Consequently, finished drug products cannot be imported into the United States ahead of FDA approval, and therefore, will not be ready for market launch upon regulatory approval. This effectively places generic companies that manufacture in foreign countries at a competitive disadvantage to those who manufacture generics domestically.¹⁶

Despite the absence of such regulations, the FDA has historically exercised enforcement discretion to permit the importation of finished drug products into the United States ahead of anticipated FDA approval.¹⁷ As the authority for this enforcement discretion, the FDA has cited section 336 of the FDCA,¹⁸ which provides that the FDA is not required “to report for prosecution, or for the institution of . . . injunction proceedings, *minor violations* . . . whenever [it] believes that the public interest will be adequately served”¹⁹ By allowing preapproval importation, the FDA seeks to promote competition and lower prices of drugs as quickly as possible.²⁰

1.2. The Regulation of Generic Drugs Under the Hatch-Waxman Act

Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act, to amend section 355(j) of the FDCA and section 271(e) of the Patent Act to create the statutory scheme to regulate the modern generic pharmaceutical industry.²¹ The intent of Hatch-Waxman was to “strike a balance between ‘two conflicting policy objectives: to induce name-brand pharmaceutical firms to make the investments necessary to research and develop new drug products, while

15. 21 C.F.R. § 201.122(c) (2012) (“A new drug application . . . has been submitted but not yet approved, disapproved, granted, or denied, the bulk drug is not exported, and the finished drug product is not further distributed after it is manufactured until after the new drug application . . . is approved . . .”).

16. Although it is beyond the scope of this article, it is worth noting that domestic manufacturers may also be at a disadvantage, since they likely cannot even begin to manufacture their generic products until the pioneer’s patent expires.

17. Karst, *supra* note 3.

18. *Id.*

19. 21 U.S.C. § 336 (emphasis added); *see also* Karst, *supra* note 3.

20. E-mail from Peter Barton Hutt, Senior Counsel, Covington & Burling LLP, to Author (Feb. 18, 2014, 08:40 PST) (on file with author).

21. Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355(j) (2012), 35 U.S.C. §§ 156, 271(e) (2012)).

simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market.”²²

In order to enable competitors to bring generic copies of pioneer drugs to market, Hatch-Waxman provides for an Abbreviated New Drug Application (ANDA).²³ An ANDA applicant is only required to provide proof that its generic copy of the pioneer drug: (1) has the same active ingredient and the basic pharmacokinetics as the pioneer drug, (2) is bioequivalent to the pioneer drug and (3) the dosage form and strength of the pioneer and generic are the same.²⁴ However, unlike drug pioneers, an ANDA applicant is not required to provide independent proof of either the safety or the efficacy of the generic copy, and instead can rely on the clinical trial data of the pioneer drug.²⁵

An ANDA applicant must make one of the following certifications with respect to *each* patent which claims the pioneer drug that it seeks to copy: (I) the drug is not patented or the patent information has not been filed; (II) the patent has expired; (III) the date when the patent expires and that the generic drug will not go on the market until that date passes; or (IV) that the patent is invalid or will not be infringed by the manufacture, use, or sale of the generic drug.²⁶

Patent challenges pursuant to Paragraph IV are a frequently deployed mechanism for the early introduction of generic competition.²⁷ When an applicant files an ANDA with Paragraph IV certification, two features of Hatch-Waxman apply: (1) thirty-month stay, and (2) 180-day marketing exclusivity. In addition, if the pioneer successfully sues the Paragraph IV challenger for patent infringement, then the Act allows the pioneer to get a permanent injunction against the generic challenger.

22. *aaiPharma Inc. v. Thompson*, 296 F.3d 227, 230 (4th Cir. 2002).

23. H.R. Rep. No. 98-857, pt. 1, at 16.

24. 21 U.S.C. § 355(j)(2)(A)(ii)–(iv).

25. 21 U.S.C. § 355(j)(2)(A).

26. 21 U.S.C. § 355(j)(2)(A)(vii)(I)–(IV).

27. See FED. TRADE COMM’N, *GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY* (July 2002) (reporting challenges involving 130 drugs between 1984 and 2000); *Examining the Senate and House Versions of the “Greater Access to Affordable Pharmaceuticals Act” Before the S. Comm. on the Judiciary*, 108th Cong. 117 (2003) (statement of Timothy Muris, Chairman, FTC) (noting challenges involving more than eighty drugs between January 2001 and June 2003).

1.2.1. Thirty-Month Stay

The Hatch-Waxman Act also provides that making a Paragraph IV certification is itself an act of patent infringement.²⁸ An applicant who files an ANDA with Paragraph IV certification must provide notice of the ANDA to the patent holder.²⁹ After receiving such notice, the NDA holder has forty-five days to bring an infringement action against the ANDA applicant.³⁰ If suit is not filed within that time, then the FDA can approve the ANDA immediately.³¹ But if suit is brought during that time, then FDA is barred from approving the ANDA for thirty months.³²

During the thirty-month stay, the FDA can only “tentatively approve” the ANDA, such that the ANDA can become effective immediately upon the expiration of the thirty-month stay.³³ The exceptions to the thirty-month stay are if either: (1) the patent expires, or (2) the district court finds that the patent is invalid or is not infringed during the thirty-month stay. In either case, the ANDA can be approved immediately.³⁴

1.2.2. 180-Day Marketing Exclusivity

The statute provides that the first applicant to file a Paragraph IV ANDA with the FDA will be granted 180 days of market exclusivity upon entering the market with their generic equivalent.³⁵ The FDA is barred from approving later-filed ANDAs for the same drug until 180 days after the first filer begins marketing its generic copy of the pioneer drug.³⁶ The purpose of 180-day marketing exclusivity is to encourage Paragraph IV challenges by rewarding the first filer: “[i]n exchange for undertaking the costs and risks of patent litigation, the successful challenger is given [six] months of marketing without any other generic competition.”³⁷ This marketing exclusivity

28. 35 U.S.C. § 271(e)(2)(A) (“It shall be an act of infringement to submit . . . an [ANDA] for a drug claimed in a patent or the use of which is claimed in a patent . . .”).

29. 21 U.S.C. § 355(j)(2)(B).

30. 21 U.S.C. § 355(j)(5)(B)(iii).

31. *Id.*

32. *Id.*

33. 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd).

34. 21 U.S.C. § 355(j)(5)(B)(iii)(I)–(IV).

35. 21 U.S.C. § 355(j)(5)(B)(iv).

36. *Id.*

37. Representative Henry Waxman, *Speech at the Generic Pharmaceutical Association’s First Annual Policy Conference: Securing the Future of Affordable Medicine*

period is valuable to generic companies because they can sell their generic drugs at a price significantly higher than if multiple generic drugs were on the market.³⁸

1.2.3. Permanent Injunction

Section 271(e)(4) of the Patent Act, which was added as part of the Hatch-Waxman amendments, allows courts to order the FDA to delay ANDA approval until a patent expires and to grant an injunction to prevent the manufacture, use, sale, or importation of a drug.³⁹ A patent holder is entitled to a permanent injunction pursuant to section 271(e)(4) if: (1) the patent holder brings an infringement action, and (2) the district court finds that the patent is both valid and infringed.⁴⁰ But Hatch-Waxman does not include any provisions that allow for a permanent injunction to be ignored for pre-launch importation purposes. And because the injunction provisions are part of the Patent Act, the FDA does not have discretion to interpret or enforce these injunctions.⁴¹

2. Overview of PLAIR Program

2.1. Pre-Launch Importation of Drugs Before the PLAIR Program

The FDA has long allowed drug manufacturers to import unfinished bulk products into the United States ahead of FDA approval.⁴² Despite Section 355(a) of the FDCA, the FDA has issued regulations to permit the importation of unfinished bulk products into

(Sept. 20, 2005), available at http://www.house.gov/waxman/news_files/news_statements_generic_pharmaceutical%20association_9.20.05.htm.

38. Matthew Avery, *Continuing Abuse of the Hatch-Waxman Act by Pharmaceutical Patent Holders and the Failure of the 2003 Amendments*, 60 HASTINGS L.J. 171, 178 n.56 (2008) (“For example, when generic Prozac (Fluoxetine) entered the market, the first generic challenger sold it at \$1.91/capsule, or 12% below the cost of brand-name Prozac. Two months after the exclusivity period expired, multiple generics had entered the market and the price of generic Prozac had dropped to \$0.32/capsule.”).

39. 35 U.S.C. § 271(e)(4) (“For an act of infringement [caused by filing a Paragraph IV ANDA] (A) the court shall order the effective date of any approval of the drug . . . to be a date which is not earlier than the date of the expiration of the patent which has been infringed, (B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product. . .”).

40. 21 U.S.C. § 355(j)(5)(B)(iii)(II).

41. *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 161 (2000); see also discussion *infra* Part 3.3.

42. 21 U.S.C. § 355(a); 21 C.F.R. § 314.410(a)(2) (2008); 21 C.F.R. § 201.122(c) (2012).

the United States ahead of regulatory approval.⁴³ The only restriction on such importation is that the label of a drug in a bulk package must bear the statements “Caution: For manufacturing, processing, or repackaging” and “Rx only.”⁴⁴ These unfinished bulk products can then undergo further processing in the United States.

However, despite the absence of such regulations for the importation of finished drug products into the United States ahead of FDA approval, the Agency has historically exercised enforcement discretion to also permit such importation.⁴⁵ But this historical enforcement discretion was exercised informally and there is no record of how it was used by the FDA.⁴⁶

2.2. The PLAIR Program

In 2008, the FDA launched the PLAIR program by issuing guidance documents describing its policy for exercising enforcement discretion with respect to the importation of unapproved drugs into the United States.⁴⁷ PLAIR formalizes the FDA’s historical exercise of enforcement discretion to permit the importation of finished drug products into the United States ahead of anticipated FDA approval.⁴⁸

Based on a PLAIR request, the FDA will decide on a case-by-case basis whether to permit importation of unapproved finished drug products.⁴⁹ An applicant should make a PLAIR request no more than two months prior to its expected launch date, but at least one month prior to the expected importation to allow the Agency time to process the request.⁵⁰ A PLAIR applicant is required to submit, among other things, information on: (1) the drug product name, and (2) the warehouse in United States where it will be stored pending FDA

43. 21 C.F.R. § 314.410(a)(2) (2008); 21 C.F.R. § 201.122(c) (2012).

44. 21 C.F.R. § 201.122 (2012).

45. Karst, *supra* note 2.

46. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 1 (“Historically, when applicants sought to import unapproved finished dosage form drug products in preparation for market launch, FDA considered such requests, informally referred to as Pre-Launch Activities Importation Requests (PLAIRs), on a case-by-case basis.”)

47. Annual Guidance Agenda, 73 Fed. Reg. 153 (July 30, 2008); *see also* REGULATIONS.GOV (last visited Feb. 8, 2014) (The FDA published its annual guidance agenda, which included a notice that it was planning to publish a guidance document for the PLAIR program. No comments were submitted by the public in response to this agenda.), <http://www.regulations.gov/#!documentDetail;D=FDA-2004-N-0056-0003>.

48. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 1; *see also* Karst, *supra* note 3.

49. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 1.

50. *Id.* at 4-5.

approval.⁵¹ In addition, a PLAIR applicant must also submit a letter signed by an authorized representative certifying that it will not sell the finished drug product before receiving regulatory approval.⁵² Notably, the PLAIR applicant does not need to submit any information identifying injunctions that may prohibit the applicant from importing the finished drug product. The Agency has previously stated that it will respond to a PLAIR request within two weeks,⁵³ however the current draft guidance does not specify how long the Agency will take to respond. If the FDA approves the request, then the applicant may immediately begin importing the finished drug product, notwithstanding any injunctions.⁵⁴

3. Validity of the PLAIR Program

Because there is no explicit statutory basis for the PLAIR program, it is unclear whether the FDA has the legal authority to allow the importation of unapproved finished drug products. The constitutional validity of the PLAIR program and the FDA's ability to exercise enforcement discretion under the FDCA are discussed in more detail below. In short, the FDA has the authority to regulate the importation of drugs into the United States and the right to exercise enforcement discretion to not prosecute a violation of section 355(a) of the FDCA. However, that authority is limited to the extent that the importation of finished drug products is not subject to restrictions by other regulatory schemes, including the Patent Act, outside the control of the FDA.

3.1. Constitutional Validity Under *Chevron v. NRDC*

The scope and extent of a federal agency's authority is limited by Congress.⁵⁵ Section 706 of the Administrative Procedure Act provides that a court must "hold unlawful and set aside agency action, findings, and conclusions found to be . . . arbitrary, capricious, an

51. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 2-4.

52. *Id.* at 3-4.

53. FOOD AND DRUG ADMINISTRATION, PRE-LAUNCH ACTIVITIES IMPORTATION REQUEST (PLAIR) FREQUENTLY ASKED QUESTIONS (FAQS) 1, 2 (July 2013) [hereinafter FDA, PLAIR FAQ], available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/ImportsandExportsCompliance/UCM297907.pdf>.

54. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 5-6.

55. See *Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842-43 (1984); *Marbury v. Madison*, 5 U.S. (1 Cranch) 137 (1803).

abuse of discretion, or otherwise not in accordance with law.”⁵⁶ When an agency acts in a way that is allegedly arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law, the reviewing court must evaluate the agency’s actions using the two-step analysis described in *Chevron v. NRDC*. First, the court must review the agency’s authorizing statute de novo to determine “[i]f the intent of Congress is clear.”⁵⁷ If Congress clearly intended to allow the agency to act in the way challenged, then the challenge must be rejected and the action allowed.⁵⁸ However, if Congress did not clearly intend to allow the agency to so act, then the court should only defer to the agency when it appears that Congress delegated authority to the agency generally to make rules carrying the force of law (e.g., if the agency has the power to engage in notice-and-comment rulemaking).⁵⁹

Section 355(a) of the FDCA requires a pharmaceutical company to first obtain FDA approval in order to market, or to import to market, a new drug.⁶⁰ However, section 336 of the FDCA permits the FDA to exercise enforcement discretion with respect to “minor violations” of the FDCA if the “public interest will be adequately served.”⁶¹ As discussed in Part 1.1 above, the FDA has historically exercised enforcement discretion to permit the importation of finished drug products into the United States ahead of anticipated FDA approval, classifying these preapproval importations

56. 5 U.S.C. § 706 (2012) (“To the extent necessary to decision and when presented, the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall—(2) hold unlawful and set aside agency action, findings, and conclusions found to be—(A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law . . . In making the foregoing determinations, the court shall review the whole record or those parts of it cited by a party, and due account shall be taken of the rule of prejudicial error.”).

57. *Chevron*, 467 U.S. at 842.

58. *Id.* at 842-43.

59. *United States v. Mead Corp.*, 533 U.S. 218, 226-27 (2001) (“[A]dministrative implementation of a particular statutory provision qualifies for *Chevron* deference when it appears that Congress delegated authority to the agency generally to make rules carrying the force of law . . . Delegation of such authority may be shown . . . by an agency’s power to engage in . . . notice-and-comment rulemaking.”).

60. 21 U.S.C. § 355(a) (“No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.”).

61. 21 U.S.C. § 336 (“Nothing in this chapter shall be construed as requiring the Secretary to report for prosecution, or for the institution of libel or injunction proceedings, minor violations of this chapter whenever he believes that the public interest will be adequately served by a suitable written notice or warning.”).

as “minor violations.”⁶² However, Congress failed to define what constitutes “minor violations” or the “public interest,” and therefore, it is not at all clear how far the Agency’s enforcement discretion extends under Section 336 of the FDCA.

As required by the Administrative Procedure Act, the FDA has engaged in notice-and-comment rulemaking with respect to its regulations that permit the importation of unfinished bulk products into the United States ahead of FDA approval.⁶³ Under the second step described in *Chevron*, if a reviewing court determines that Congress delegated authority to the FDA generally to make rules carrying the force of law, and “if the statute is silent *or ambiguous* with respect to the specific issue, the question for the court is whether the agency’s answer is based on a permissible construction of the statute.”⁶⁴ As such, because the statute is ambiguous with respect to the scope of “minor violations,” the FDA’s regulations interpreting the FDCA to allow for preapproval importation of unfinished bulk product are valid and should be given deference by a reviewing court.

However, with respect to the importation of finished bulk product, the Agency has issued no regulations. And the FDCA is not silent with respect to the issue of the importation of new drugs—section 355(a) is quite explicit that marketing approval is needed before a sponsor may import new drugs into the country.⁶⁵

Section 355 of the FDCA was intended to ensure the safety and efficacy of new drugs.⁶⁶ For example, section 355(b)(1) of the FDCA provides that an NDA or ANDA applicant is required to submit information, including “full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use”⁶⁷ While the PLAIR program permits the importation of finished drug products into the United

62. Karst, *supra* note 3.

63. 1 C.F.R. § 314.410(a)(2) ; 21 C.F.R. § 201.122(c).

64. *Chevron*, 467 U.S. at 843.

65. 21 U.S.C. § 355(a).

66. Richard S. Fortunato, *FDA Disclosure of Safety and Efficacy Data: The Scope of Section 301(j)*, 50 FORDHAM L. REV. 1280 n.2-3 (1984) (“A new drug” is defined as a drug whose composition is not generally recognized “as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling,” or a drug whose composition has been so recognized as a result of investigations, but which has not “been used to a material extent or for a material time.” 21 U.S.C. § 321(p) (1982). . . . The Act provides that no person shall introduce into interstate commerce any new drug without premarket approval from the Secretary of Health and Human Services certifying that the drug is safe and effective for use. 21 U.S.C. § 355(a), (b) (1982)”).

67. 21 U.S.C. § 355(b)(1).

States ahead of anticipated FDA approval, a pharmaceutical company is still prohibited from marketing its new drug ahead of actual FDA approval.⁶⁸ If the FDA does not grant approval, then a pharmaceutical company risks having to destroy or export its inventory.⁶⁹ The PLAIR program still prohibits pharmaceutical companies from marketing new drugs without actual FDA approval, so that even if a drug has been imported, the public is still protected from consuming potentially unsafe or ineffective drugs. Consequently, because the intent of the FDCA is to protect the public health by ensuring citizens are not exposed to adulterated or misbranded drugs,⁷⁰ and because the PLAIR program still prevents such exposure, it is not, at the very least, arbitrary, capricious, or an abuse of discretion under a *Chevron* analysis.

However, as previously noted, section 271(e)(4) of the Patent Act allows an NDA holder that has prevailed in a patent litigation to obtain a permanent injunction against a generic challenger to prevent it from importing its infringing drug product.⁷¹ These injunctions seem absolute—there is no exception allowing the FDA or anyone else to disregard a permanent injunction for public interest reasons or otherwise. The Patent Act does not include a provision corresponding to section 336 of the FDCA granting enforcement discretion. Even if there were such a provision, it would likely apply to the agency having general authority over the Patent Act, the United States Patent and Trademark Office, not the FDA, which has no authority to interpret the Patent Act, and thus has no authority to issue regulations regarding permanent injunctions obtained under section 271(e)(4). Because the intent of Congress with respect to section 271(e)(4) seems clear, and because the FDA has no authority to say otherwise, courts performing a *Chevron* analysis should hold as unlawful and set aside any FDA action under the PLAIR program that would allow importation of an infringing drug product in violation of a permanent injunction. But if there are no permanent injunctions prohibiting importation, then per the second step of the *Chevron* analysis courts should defer to the FDA's decision to allow preapproval importation as a "minor violation" of section 355(a) of the FDCA.

68. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 2.

69. *Id.* at 6 ("the finished dosage form drug product should be exported or destroyed within 90 days of the refusal"); Laot, *supra* note 5.

70. 21 U.S.C. § 393(b).

71. 21 U.S.C. § 355(j)(5)(B)(iii)(II); 35 U.S.C. § 271(e)(4).

3.2. Prosecutorial Discretion

Although PLAIR allows for the type of behavior that both section 355(a) of the FDCA and section 271(e)(4) of the Patent Act prohibit, it is important to distinguish between lawful and unlawful activity. PLAIR does not declare the importation of finished drug products into the United States ahead of anticipated FDA approval to be lawful. When the FDA grants a PLAIR request, the Agency is simply exercising its enforcement discretion to not prosecute a violation of section 355(a) of the FDCA. But it is also important to highlight that the FDA's determination to not prosecute an unlawful activity is well within its discretion.⁷²

In the landmark case on prosecutorial discretion, *Heckler v. Chaney*, the Supreme Court affirmed the FDA's right to determine for itself how to enforce the FDCA.⁷³ For practical reasons, the FDA cannot act against each technical violation of the FDCA.⁷⁴ An agency decision not to enforce often involves a complicated balancing of a number of factors that are peculiarly within its expertise, including: (1) whether a violation has occurred, (2) whether the agency has sufficient resources to take action, (3) whether prosecuting the violation is an efficient use of agency resources, (4) whether the agency is likely to succeed if it acts, and (5) whether taking action aligns with the Agency's overall policies.⁷⁵ The *Heckler* court reasoned that the FDA is far better equipped than the courts to deal with the many variables involved in the proper ordering of its priorities.⁷⁶

The Supreme Court subsequently reiterated in *Buckman Co. v. Plaintiffs Legal Committee* that the FDA has "complete discretion" to decide how and when to enforce the FDCA, and must exercise its prosecutorial discretion to balance statutory objectives.⁷⁷ The *Buckman* decision suggests that the FDA essentially has unlimited

72. *Heckler v. Chaney*, 470 U.S. 821 (1985); *Buckman Co. v. Plaintiffs Legal Committee*, 531 U.S. 341, 348-49 (2001).

73. *Heckler*, 470 U.S. at 837-38 ("The general exception to reviewability provided by [the Administrative Procure Act] § 701(a)(2) for action "committed to agency discretion" remains a narrow one . . . but within that exception are included agency refusals to institute investigative or enforcement proceedings, unless Congress has indicated otherwise. In so holding, we essentially leave to Congress, and not to the courts, the decision as to whether an agency's refusal to institute proceedings should be judicially reviewable.").

74. *Id.* at 831.

75. *Id.*

76. *Id.* at 831-32.

77. *Buckman*, 531 U.S. at 348.

discretion to prosecute or excuse violations of the FDCA as it sees fit.⁷⁸ Notwithstanding *Heckler* and *Buckman*, a recent decision from the Court of Appeals for the District of Columbia shows that the FDA's enforcement discretion is not be entirely shielded from judicial review.⁷⁹ In *Cook v. Food and Drug Administration*, the D.C. Circuit held that where there are clear statutory guidelines for the FDA to follow in exercising its enforcement discretion, the FDA's compliance with such guidelines is subject to judicial review under the Administrative Procedure Act.⁸⁰ Consequently, *Cook* suggests that, because section 355(a) clearly prohibits importation of finished drug products "unless an approval of an application . . . is effective with respect to such drug," the FDA's decision not to prosecute violations of section 355(a)—as it does under PLAIR—may be subject to judicial review.⁸¹ However, even if allowing preapproval importation under PLAIR is subject to judicial review, the Agency's allowance of such importations is not necessarily an abuse of discretion.

In light of *Heckler* and *Buckman*, the PLAIR program's allowance for "minor violations" of section 355(a) to permit the importation of finished drug products ahead of anticipated FDA approval is consistent with the scope of the Agency's enforcement discretion. Furthermore, even if the PLAIR program is subject to judicial review under *Cook*, allowing for preapproval importations is likely not an abuse of the FDA's prosecutorial discretion. Note, however, that this allowance is limited to the extent that the importation of finished drug products is not subject to restrictions by other regulatory schemes, including injunctions under the Patent Act, outside the control of the FDA.

3.3. Authority to Regulate

In a modern case on the scope of the FDA's regulatory power, *FDA v. Brown & Williamson Tobacco Corp.*, the Supreme Court held that where Congress enacts a regulatory scheme outside the control of the FDA, the Agency may not regulate that area.⁸² The power of the FDA to regulate must always be grounded in a valid grant of

78. James M. Beck et al., *Don't Forget FDA Prosecutorial Discretion*, DRUG AND DEVICE LAW (Oct. 5, 2012), <http://druganddevicelaw.blogspot.com/2012/10/dont-forget-fda-prosecutorial-discretion.html>.

79. See *Cook v. Food & Drug Admin.*, 733 F.3d 1, 10 (D.C. Cir. 2013).

80. *Id.*

81. 21 U.S.C. § 355(a); see *Cook*, 733 F.3d at 10.

82. *Brown & Williamson Tobacco Corp.*, 529 U.S. at 161.

authority from Congress.⁸³ In other words, the FDA may only regulate in areas specified by its authorizing statute.

The FDCA grants the Agency the authority to regulate, among other things, drugs and devices.⁸⁴ In particular, pursuant to section 355(a), the FDA possesses the authority to regulate the importation of drugs into the United States.⁸⁵ However, such authority to regulate must be squared with the fact that the importation of drugs into the United States might also be subject to regulation by other regulatory schemes outside the control of the FDA, such as the Patent Act.

Under the Patent Act, the power to regulate patents is granted to the Secretary of Commerce.⁸⁶ The FDA is not granted any general authority with respect to the Patent Act. However, the Patent Act does grant the FDA authority to do one thing—the FDA has the power to determine the period of extension of patent terms for drugs, devices, and additives that are subject to regulation by the FDCA.⁸⁷

There is no evidence that Congress intended to authorize the FDA to regulate patent-related issues beyond the specifically recited power to determine the period of extension of patent term for the limited class of items. Therefore, if a generic drug is subject to a permanent injunction pursuant to section 271(e)(4) of the Patent Act, it is not eligible for pre-launch importation. The FDA cannot ignore the statutory mandate of the Patent Act.

The foregoing discussion leads to the conclusion that, subject to the limitations discussed above, PLAIR is a valid regulatory program. The FDA has the authority to regulate the importation of drugs into the United States and the right to exercise enforcement discretion to not prosecute a violation of section 355(a) of the FDCA. However, that authority is limited to the extent that the importation of finished drug products is not subject to restrictions by other regulatory schemes, including the Patent Act, that are outside the control of the FDA.

83. *Brown & Williamson Tobacco Corp.*, 529 U.S. at 161.

84. 21 U.S.C. §§ 301, 321(g)-(h), 393.

85. 21 U.S.C. § 355(a).

86. 35 U.S.C. § 2(a).

87. 35 U.S.C. §§ 156(e)(d)(1)(C), 156(c)(4)(d)(2)(A)(ii)-(B)(ii) (“The term of a patent eligible for extension . . . shall be extended by the time equal to the regulatory review period for the approved product which period occurs after the date the patent is issued”).

4. The Conflict Between the PLAIR Program and the Hatch-Waxman Act

4.1. The Conflict

When the FDA grants a PLAIR request, it does not declare the importation to be lawful—instead, the Agency simply exercises its enforcement discretion to not prosecute a violation of section 355(a) of the FDCA. However, importation under PLAIR may nevertheless violate a permanent injunction granted pursuant to section 271(e)(4) of the Patent Act, which was added as part of the Hatch-Waxman amendments.⁸⁸ Regardless of whether the FDA chooses not to prosecute a violation of section 355(a), it has no power to abrogate the Patent Act amendments added by Hatch-Waxman.⁸⁹

If a generic company files an ANDA with a Paragraph IV certification, the brand-name company can respond by bringing an infringement action within forty-five days.⁹⁰ If the brand-name company does not file suit within that time, then the FDA can approve the ANDA immediately.⁹¹ Here, there is no conflict between PLAIR and Hatch-Waxman since the brand-name company never asserted its patent rights, and thus the generic company can take advantage of an approved PLAIR request to import its generic drug ahead of anticipated ANDA approval.

However, if the brand-name company files suit within that time, then the FDA is barred from approving the ANDA until the expiration of a thirty-month stay.⁹² The only exceptions to the thirty-

88. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355(j) (2012), 35 U.S.C. §§ 156, 271(e) (2012)).

89. *Brown & Williamson Tobacco Corp.*, 529 U.S. at 120. Although it is beyond the scope of this Article, there is an alternative argument that the FDA has authority to abrogate injunctions issued under section 271(e)(4) by virtue of its authority to regulate all aspects of the Hatch-Waxman Act. Hatch-Waxman was created as a tool to allow the FDA to regulate generic drug marketing. Even though the permanent injunction provision of section 271(e)(4) was inserted into the Patent Act, by virtue of originating from Hatch-Waxman, the FDA may be able to abrogate permanent injunctions granted by 271(e)(4) by virtue of its arguable authority to regulate *all* aspects of the Hatch-Waxman Act (regardless of whether the amendments ended up in Title 21 or 35). Thus, generic manufacturers could use a PLAIR request to overcome an injunction under 271(e)(4) to import prior to final ANDA approval. However, if an injunction is issued under 271(a) (i.e., during a typical patent infringement action), then a PLAIR request could not be used to allow importation during the term of the injunction.

90. 21 U.S.C. § 355(j)(5)(B)(iii).

91. 21 U.S.C. § 355(j)(5)(B)(iii).

92. 21 U.S.C. § 355(j)(5)(B)(iv)(II)(dd).

month stay are if the patent expires, or if the district court finds that the patent is either invalid or not infringed, at which point the FDA can approve the ANDA immediately.⁹³ If one of these exceptions occurs, there is again no conflict between PLAIR and Hatch-Waxman since the brand-name company has no valid patent rights to assert against the ANDA filer. In this case, the generic company can take advantage of an approved PLAIR request to import its generic drug ahead of anticipated ANDA approval.

The conflict between PLAIR and Hatch-Waxman arises only when a district court finds that the patent is both valid and infringed.⁹⁴ In this case, the FDA cannot approve the ANDA until the patent expires.⁹⁵ Furthermore, the brand-name company is entitled to seek a permanent injunction against the generic pursuant to section 271(e)(4) of the Patent Act, which can be used to stop the generic company from importing its infringing drug product before the date that the patent expires.⁹⁶ Therefore, under Hatch-Waxman, the generic company should not be able to take advantage of PLAIR to import its generic drug into the United States ahead of anticipated ANDA approval.⁹⁷

The problem with the PLAIR program is that it does not consider the Hatch-Waxman Act, notwithstanding the fact that Hatch-Waxman essentially serves as the statutory basis for regulating the entire generic pharmaceutical industry.⁹⁸ Under the PLAIR program, a generic company could theoretically import its generic drug ahead of anticipated ANDA approval, regardless of whether there is a permanent injunction barring such importation.⁹⁹ This is precisely what occurred in *Sanofi v. Apotex*, discussed below, where

93. 21 U.S.C. § 355(j)(5)(B)(iii)(I)–(IV).

94. Note that the conflict also likely only arises when the generic challenger is the first Paragraph IV ANDA filer. Later filers typically cannot launch their products until after the first filer's 180-day exclusivity period has expired. Depending on when the first filer begins marketing its generic drug, later filers have at a minimum 180 days after the patent expires to import their generic drugs. Since the patent has expired, later filers who take advantage of PLAIR to import during the 180-day exclusivity period to be ready to launch when the 180-day exclusivity period expires will not conflict with section 271(e)(4) of the Patent Act.

95. 21 U.S.C. § 355(j)(5)(B)(iii)(II).

96. *Id.*

97. 35 U.S.C. § 271(e)(4)(B).

98. See FDA, PLAIR DRAFT GUIDANCE, *supra* note 2.

99. *Id.*

the FDA did not consider a prior permanent injunction and approved the PLAIR request.¹⁰⁰

4.2. Sanofi v. Apotex

Sanofi v. Apotex is the first Hatch-Waxman case in which the conflict with the PLAIR program has been raised as an issue. Sanofi-Synthelabo (Sanofi) is the owner of U.S. Patent No. 4,847,265 (the '265 patent), which expired on November 17, 2011, with a period of pediatric exclusivity that expired on May 17, 2012.¹⁰¹ The '265 patent covers Plavix (clopidogrel bisulfate), a blockbuster drug used to treat heart attacks and strokes.¹⁰²

On November 16, 2001, Apotex filed an ANDA for Plavix that included a Paragraph IV certification against '265 patent.¹⁰³ Since Apotex was the first applicant to file a Paragraph IV ANDA, it was entitled to 180 days of marketing exclusivity against later-filing applicants.¹⁰⁴

In response to the ANDA filing, Sanofi brought an infringement action against Apotex in the District Court for the Southern District of New York in March 2002.¹⁰⁵ More than five years later, the Court held that the '265 patent was both valid and infringed, and that Sanofi was entitled to a permanent injunction against Apotex per section 271(e)(4) of the Patent Act.¹⁰⁶ In December 2008, the Court of Appeals for the Federal Circuit affirmed.¹⁰⁷

In January 2006, while the infringement action was still pending in the District Court, the FDA approved the ANDA.¹⁰⁸ Before the District Court could render its decision on the validity of the '265 patent, Apotex initiated an at-risk launch on August 8, 2006, (which also triggered the start of its 180-day exclusivity period).¹⁰⁹

100. See Brief of Petitioner-Appellant at 2-3, *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS (Fed. Cir. May 9, 2012).

101. *Sanofi-Synthelabo v. Apotex, Inc.*, 492 F. Supp. 2d 353, 356 (S.D.N.Y. 2007).

102. *Id.*

103. *Id.* at 357.

104. *Id.*

105. *Id.*

106. *Id.* at 397.

107. *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F. 3d 1075, 1090 (Fed. Cir. 2008).

108. *Apotex clopidogrel at-risk launch costs US\$442 million*, GABI ONLINE – GENERIC AND BIOSIMILARS INITIATIVE (Feb. 3, 2012), <http://www.gabionline.net/Generics/News/Apotex-clopidogrel-at-risk-launch-costs-US-442-million>; *Sanofi-Synthelabo*, 492 F. Supp. 2d at 357.

109. *Sanofi-Synthelabo v. Apotex Inc.*, 488 F. Supp. 2d 317, 344 (S.D.N.Y. 2006) *aff'd sub nom.* *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368 (Fed. Cir. 2006). On August 8,

However, just three weeks later, the District Court issued a preliminary injunction ordering Apotex to stop its sales of generic Plavix (and subsequently issued a permanent injunction, as mentioned above).¹¹⁰

Then in April 2012, notwithstanding the permanent injunction, Apotex filed a PLAIR request with the FDA to import its generic product ahead of anticipated ANDA approval on May 17, 2012, which was the date of the expiration of the '265 patent.¹¹¹ On May 7, 2012, the FDA approved the PLAIR request.¹¹²

Just a few days before the PLAIR request was approved by the FDA, Apotex filed a motion pursuant to Fed. R. Civ. P 60(b)(6) to amend the 2007 permanent injunction to include the underlined text:

[Apotex is] hereby permanently enjoined from engaging in the commercial manufacture, use, offer to sell or sale within the United States, or importation into the United States of drug products as claimed in [the '265 patent], until the expiration of [the '265 patent] and any period of pediatric exclusivity that may be granted, *except for importation by Apotex to its own warehouse facilities prior to the expiration of the pediatric exclusivity period to the extent such importation is permitted by [the FDA] pursuant to a [PLAIR request] made by Apotex and granted by the FDA.*¹¹³

Apotex argued that because it initiated an at-risk launch and forfeited its 180-day marketing exclusivity, it must be permitted to take advantage of PLAIR so as not to be placed at a competitive disadvantage.¹¹⁴ Other manufacturers of generic Plavix would be able to use the PLAIR program to import their products ahead of

2006, Apotex initiated an at-risk launch of its generic product, in advance of a determination on the merits of its invalidity defense against the '265. *Id.* Sanofi moved for a preliminary injunction prohibiting Apotex from distributing its generic product. *Id.* On August 31, 2006, the District Court for the Southern District of New York granted a preliminary injunction, but denied a recall on the approximately six-month supply of generic product that had already been shipped to distributors in the United States. *Id.*

110. GABI ONLINE – GENERIC AND BIOSIMILARS INITIATIVE, *supra* note 108. Note that by launching at-risk, Apotex triggered the start of its 180-day exclusivity period, but then lost the benefit of the exclusivity period when it was enjoined shortly thereafter. *Sanofi-Synthelabo*, 488 F. Supp. 2d at 344-45. However, this was a small loss, since when Apotex lost in litigation it was forced to amend its Paragraph IV certification to a Paragraph III certification, which would have caused an immediate forfeiture under 35 U.S.C. § 355(j)(5)(D)(III).

111. *Sanofi-Synthelabo v. Apotex, Inc.*, No. 2012-1383 (Fed. Cir. May 15, 2012) (order denying motion).

112. *Id.*

113. Brief of Petitioner-Appellant at 2-3, *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS (Fed. Cir. May 9, 2012) (emphasis in original).

114. *Id.*

anticipated ANDA approval, and therefore Apotex's competitors would be ready to launch the minute after Sanofi's exclusivity expired on May 17, 2012.¹¹⁵ In contrast, the permanent injunction would bar Apotex from even importing its generic product until May 17, 2012.¹¹⁶ Because the first-mover advantage is critical in generic drug sales, even the slight marketing delay caused by the permanent injunction would unfairly present Apotex with "extreme and undue hardship."

On May 10, 2012, the District Court denied Apotex's motion to amend the 2007 permanent injunction, holding that the five-year delay in bringing the motion was not reasonable.¹¹⁷ Unfortunately, the District Court did not address whether the proposed amendment to allow importation under PLAIR would have been granted if it had been brought in a timely manner. A few days later, the Court of Appeals for the Federal Circuit affirmed, also without addressing the substance of the proposed amendment.¹¹⁸ Then on May 18, 2012, the day Sanofi's exclusivity expired, the FDA approved the ANDAs of Apotex and six other generic companies.¹¹⁹ Apotex's competitors were able to immediately launch their generic products.¹²⁰ Although Apotex also launched its own generic version of Plavix, as evidenced by the fact that it is currently marketing the product in the United States, the company has not publicized the specific date on which it launched its version following the FDA's en masse approval.¹²¹

The *Sanofi* case shows how conflict between the Hatch-Waxman Act and the PLAIR program stems from the fact that the FDA and the courts are enforcing two different sets of rules. The policies of the PLAIR program only require the FDA to review a limited set of information, which does not include possible injunctions

115. Brief of Petitioner-Appellant at 2-3, *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS (Fed. Cir. May 9, 2012).

116. *Id.* at 5-6.

117. *Sanofi-Synthelabo*, No. 2012-1383 (order denying motion).

118. *Id.*

119. *Drug In Focus April 2012: Clopidogrel*, GENERICSWEB (Apr. 2012), <http://www.genericsweb.com/download/DIF%20Clopidogrel.pdf>. The six other generic companies were Dr. Reddy's Laboratories Ltd., Mutual Pharmaceuticals Co., Mylan Inc., Roxane Laboratories, Inc., Sun Pharma USA, and Torrent Pharmaceuticals Ltd.

120. *Dr Reddy's Laboratories, Mylan Launch Clopidogrel Tablets in US Market*, ECONOMIC TIMES (May 18, 2012), http://articles.economictimes.indiatimes.com/2012-05-18/news/31765607_1_paragraph-iv-tablets-generic-version.

121. *Clopidogrel Tablets USP, 75MG, 30 TABLET (BOTTLE) - Apotex Products: United States*, APOTEX CORP., <http://www.apotex.com/us/en/products/detail.asp?m=45969> (last visited Apr. 11, 2014).

against the requester.¹²² In *Sanofi v. Apotex*, Apotex did not submit information on the permanent injunction against it, and the FDA presumably was not aware of it when approving the PLAIR request.¹²³ The courts, in contrast, refused to allow Apotex to insert PLAIR-related language into the permanent injunction. As shown in *Sanofi*, the courts reviewed the entire record before it, which included the 2007 permanent injunction.¹²⁴

Because the courts did not address the substance of Apotex's motion, we do not know whether a court would allow a permanent injunction issued under section 271(e)(4) of the Patent Act to be abrogated by a PLAIR request. However, as discussed in Part 3, *supra*, while the FDA has the authority to regulate the importation of drugs into the United States and the right to allow preapproval importation via the PLAIR program, the Agency does not have any authority to regulate with respect to the Patent Act. As such, the courts should not allow PLAIR-based importations during the pendency of a permanent injunction.

5. The PLAIR Program and the Intent of the Hatch-Waxman Act

The goal of the PLAIR program is to allow pharmaceutical companies to import unapproved finished drug products in preparation for market launch.¹²⁵ Here we discuss how this goal does not conflict with the intent of the Hatch-Waxman Act, which is to strike a balance between conflicting policy objectives—enabling generic companies to bring low-cost drugs to the market while maintaining incentives for pioneers to develop and launch innovative new drugs.¹²⁶ These objectives are reflected in the two parts of the Hatch-Waxman Act: Title I, the Drug Price Competition Act, which amended section 355 of the FDCA, and Title II, the Patent Term Restoration Act, which amended section 271 of the Patent Act.¹²⁷ The intent of each part is separate and distinct, and therefore, the

122. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 1.

123. See Brief of Petitioner-Appellant at 2-3, *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS (Fed. Cir. May 9, 2012). Interestingly, even if the FDA were aware of the permanent injunction, it is not clear that this would have had any effect on its decision to approve Apotex's PLAIR request.

124. *Sanofi-Synthelabo*, No. 2012-1383 (order denying motion).

125. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 2-3.

126. *aaPharma Inc.*, 296 F.3d at 230; *Abbott Labs. v. Young*, 920 F.2d 984, 991 (D.C. Cir. 1990); see also H.R. REP. NO. 98-857, pt. I, at 14-15 (1984).

127. H.R. Rep. No. 98-857, pt. 1, at 20; pt. 1, at 37.

PLAIR program and its effects will be discussed in the context of Title I and Title II in Parts 5.1 and 5.2, respectively.¹²⁸

5.1. Title I and Making Generic Drugs Available to the Public

The intent of the Drug Price Competition Act is to make more generic drugs available to the public.¹²⁹ It is in the public interest that generic drug manufacturers bring their products to market as soon as possible because the price of generic drugs is significantly discounted from the price of brand-name drugs.¹³⁰ In addition, it is in the public interest that there be as many generic competitors in the marketplace as possible, since the more generic competitors there are in the marketplace, the cheaper the generic drugs become.¹³¹ The PLAIR program aligns with the intent of Title I by helping generic manufacturers expedite the commercial launch of their products.¹³² As such, from this policy standpoint, Apotex arguably should have been permitted to take advantage of its approved PLAIR request.

As discussed in Part 1.2, *supra*, the Hatch-Waxman Act primarily helps bring generics to market via the ANDA process, which most notably allows generic competitors to use Paragraph IV certifications to seek market entry prior to the expiration of the patents covering the brand-name drug.¹³³ Additionally, in order to encourage Paragraph IV challenges, Hatch-Waxman provides that the first applicant to file an ANDA with a Paragraph IV certification will be granted 180 days of market exclusivity upon market launch, in

128. H.R. Rep. No. 98-857, pt. 1, at 14; pt. 2, at 11.

129. H.R. Rep. No. 98-857, pt. 1, at 14 (“The purpose of Title I of the Bill is to make available more low cost generic drugs by establishing a generic drug procedure for pioneer drugs first approved after 1962.”).

130. FOOD AND DRUG ADMINISTRATION, GENERIC DRUGS: QUESTIONS AND ANSWERS, <http://www.fda.gov/drugs/resourcesforyou/consumers/questionsanswers/ucm100100.htm> (last visited Mar. 11, 2013) (According to the FDA, “[a]lthough generic drugs are chemically identical to their branded counterparts, they are typically sold at substantial discounts from the branded price.”).

131. Avery, *supra* note 38, at 179 n.56 (“For example, when generic Prozac (Fluoxetine) entered the market, the first generic challenger sold it at \$1.91/capsule, or 12% below the cost of brand-name Prozac. Two months after the exclusivity period expired, multiple generics had entered the market and the price of generic Prozac had dropped to \$0.32/capsule.”).

132. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2, at 1; Kurt R. Karst, *PLAIRs—What are They and What are FDA’s Current Policies?*, FDA LAW BLOG (Apr. 11, 2010), http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2010/04/plairs-what-are-they-and-what-are-fdas-current-policies.html.

133. H.R. Rep. No. 98-857, pt. 1, at 16; *see also* 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

exchange for assuming the costs and the risks associated with litigation.¹³⁴

In *Sanofi v. Apotex*, Apotex was the first applicant to file an ANDA with Paragraph IV certification, and therefore secured the 180-day exclusivity period.¹³⁵ However, Apotex lost in litigation, lost the exclusivity period, and was enjoined from importing generic Plavix until the expiration of Sanofi's patent.¹³⁶ In contrast, Apotex's competitors were able to import and stockpile their products prior to patent expiry via the PLAIR program.¹³⁷ Consequently, these other generic manufacturers were ready and able to ship generic Plavix to their customers the minute Sanofi's patent expired.¹³⁸ Apotex argued that it would not be able to compete in the marketplace against its competitors because by being delayed in market launch by even a single day, it risked losing profits forever because it would not be able to match the delivery schedules of its competitors.¹³⁹

While this result for Apotex was legally correct, it was also contrary to the intent of the Hatch-Waxman Act to encourage generic manufactures to bring more of their products to the market. By challenging Sanofi's patents, Apotex assumed the costs and risks associated with litigation. However, just because Apotex lost in litigation does not mean that it should be placed at a competitive disadvantage compared to later filing applicants who did not face the costs and the risks associated with litigation. But this is precisely what occurred in *Sanofi v. Apotex*.¹⁴⁰ After Sanofi successfully sued Apotex for patent infringement, Apotex converted its Paragraph IV certification to a Paragraph III certification, in which it certified it would not launch its generic product until after Sanofi's patent expired.¹⁴¹ Apotex was able to manufacture its generic product in a

134. 21 U.S.C. § 355(j)(5)(B)(iv); Representative Henry Waxman, *Speech at the Generic Pharmaceutical Association's First Annual Policy Conference: Securing the Future of Affordable Medicine* (Sept. 20, 2005), available at http://www.house.gov/waxman/news_files/news_statements_generic_pharmaceutical%20association_9.20.05.htm.

135. *Sanofi-Synthelabo*, 492 F. Supp. 2d at 357.

136. 35 U.S.C. § 271(e)(4); *Sanofi-Synthelabo*, 492 F. Supp. 2d at 397; *Sanofi-Synthelabo*, 550 F.3d at 1090.

137. Brief of Petitioner-Appellant at 3, 5 *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS (Fed. Cir. May 9, 2012).

138. *Id.*

139. *Id.* at 5-6.

140. *Id.* at 3, 5.

141. Letter from Keith Webber, Deputy Director, Office of Pharmaceutical Science, Center for Drug Evaluation and Research, to Kiran Krishnan, Director, North American

foreign country prior to the expiry of Sanofi's patent, but it was not able to import this product into the United States.¹⁴² Apotex's competitors were not similarly restrained. Consequently, even though there was effectively no difference between Apotex and its competitors—no one was going to launch a generic prior to the expiration of Sanofi's exclusivity period—Apotex was placed at a competitive disadvantage merely for taking the risk of filing the first Paragraph IV challenge. This should not be the result. Instead, keeping with the intent of Hatch-Waxman, Apotex should have been permitted to take advantage of its approved PLAIR request to expedite its product launch.

5.2. Title II and Incentivizing Research and Development by Brand-Name Manufacturers

The intent of the second part of Hatch-Waxman, the Patent Term Restoration Act, is to induce brand-name companies to make the investments necessary to research and to develop new drugs by restoring some of the patent term lost during the FDA approval process.¹⁴³ Title II permits the extension of the term of a patent for a definite period of time provided that certain requirements are met, where this period of time is primarily based on marketing delays created while the product is awaiting FDA approval.¹⁴⁴ Congress was explicit that the extension of the patent term should be a definite period of time with no other direct or indirect method of extending patent term, and thereafter, *immediate* competition should be encouraged.¹⁴⁵ For that reason, Title I, the Drug Price Competition Act, permits the filing and tentative approval of ANDAs before

Regulatory Affairs, Apotex Corp. (May 12, 2012) (on file with the Food and Drug Administration).

142. 35 U.S.C. 271(e)(4)(b) (emphasis added) (“For an act of infringement . . . injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale *within the United States* or importation into the United States of an approved drug, veterinary biological product, or biological product. . .”).

143. H.R. Rep. No. 98-857, pt. 2, at 11 (“Title II of the Bill encourages drug manufacturers to assume the increased costs of research and development of certain products which are subject to premarketing clearance by restoring some of the time lost on patent life while the product is awaiting FDA approval.”).

144. H.R. Rep. No. 98-857, pt. 1, at 46.

145. *Id.* (“Article 1, Section 8, Clause 8 of the Constitution empowers Congress to grant exclusive rights to an inventor for a limited time. That limited time should be a definite time, and thereafter, immediate competition should be encouraged. For that reason, Title I of the Bill permits the filing of Abbreviated New Drug Applications before a patent expires and contemplates that the effective approval date will be the expiration date of the valid patent covering the original product.”).

patent expiration, and contemplates that the *effective* approval date will be the expiration date of the valid patent.¹⁴⁶ In practice, there should be no lag between patent expiration and competition, and the generic drug should be able to enter the market the minute after the brand-name manufacturer's patent expires. But if the first applicant to file an ANDA with Paragraph IV certification loses in litigation, pursuant to section 271(e)(4) of the Patent Act, it can be enjoined from importing its generic product into the United States before patent expiration, causing such a lag.¹⁴⁷ This is precisely what happened in *Sanofi v. Apotex*. Sanofi's marketing exclusivity expired on May 16, 2012 and Apotex's competitors were able to start shipping their generic products to customers at 12:01 a.m. on May 17.¹⁴⁸

However, this result is contrary to the intent of the Hatch-Waxman Act. By delaying importation of generic drugs until after patent expiration, section 271(e)(4) of the Patent Act effectively grants a *de facto* patent term extension, which is in direct conflict with Congress' explicit intent to allow generic competition immediately after patent expiration. PLAIR allows generic companies to warehouse their drugs in the United States prior to FDA approval so that they can expedite their market launches once they receive final approval from the Agency. The PLAIR program aligns with the intent of Title II by ensuring that there is immediate competition after patent expiration. Thus, from a policy standpoint, Apotex arguably should have been permitted to take advantage of its approved PLAIR request.

6. Solutions to the Conflict Between the PLAIR Program and Hatch-Waxman and Guidance for Practitioners

Although PLAIR does not conflict with the goals of the Hatch-Waxman Act, and regardless of whether the FDA chooses to exercise enforcement discretion to not prosecute a violation of the FDCA, the Agency has no power to abrogate the statutory mandates of Hatch-Waxman. Under the current laws, pharmaceutical patent holders should be able to use permanent injunctions to prevent any importation prior to patent expiration, including preapproval importations via PLAIR requests. Ultimately, whether to allow

146. H.R. Rep. No. 98-857, pt. 1, at 46 (emphasis added). Note that this aligns with the Patent and Copyright Clause of the Constitution, which empowers Congress to grant exclusive rights to inventors "for limited times." U.S. CONST. art. I, § 8, clause 8.

147. 35 U.S.C. § 271(e)(4).

148. Brief of Petitioner-Appellant at 3, 5 *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS.

generic companies to take advantage of PLAIR despite the conflict with Hatch-Waxman comes down to a policy choice that is up to Congress to make—it must choose whether to protect the patent rights of innovators or to speed generic drug competition.

6.1. Protecting Patent Rights

As discussed in Part 3, the FDA's enforcement discretion does not give the Agency the power to override injunctions under section 271(e)(4) of the Patent Act that prohibit importation of a generic drug. To ensure that the FDA does not approve PLAIR requests during the term of a patent injunction, the FDA should amend the PLAIR process so that an applicant is required to submit information identifying any injunctions that may prohibit importation of its product. For example, the FDA could amend the PLAIR Draft Guidance¹⁴⁹ to require the following be included with all PLAIR requests:

- (j) A letter signed by an authorized representative of the applicant certifying under 18 U.S.C. § 1001 that the applicant is not a party to a court order subject to an injunction prohibiting importation of the drug product.

This requirement will save both the FDA and the courts resources. Such a requirement would allow the FDA to reject PLAIR requests that seek to illegally import products during the term of an injunction (or to summarily deny such requests if they fail to submit this required information). In turn, this would prevent courts from having to weigh in on whether importation under the PLAIR request is proper.

Requiring PLAIR applicants to notify the FDA of injunctions prohibiting importation of their product would avoid the issue raised in *Sanofi v. Apotex*, where the FDA has approved Apotex's PLAIR request without considering the permanent injunction against Apotex that prohibited importation before the expiration of Sanofi's patent. The conflict between PLAIR and Hatch-Waxman is a waste of resources for both the FDA and the courts, and revision of the PLAIR process is necessary.

6.2. Accomplishing the Intent of Hatch-Waxman

Given that PLAIR accomplishes the intent of Hatch-Waxman, one solution to resolving the conflict between them is to incorporate language into the Hatch-Waxman Act permitting PLAIR-based

149. FDA, PLAIR DRAFT GUIDANCE, *supra* note 2 at 2-4.

importation. Congress could revise section 271(e)(4) of the Patent Act with an amendment of subsection (B), adding similar language to the underlined text below:

For an act of infringement [caused by filing an ANDA with a Paragraph IV certification]

(A) the court shall order the effective date of any approval of the drug . . . to be a date which is not earlier than the date of the expiration of the patent which has been infringed,

(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product, *except importation into the United States shall be allowable to the extent that such importation is permitted by the Food and Drug Administration pursuant to a Pre-launch Activities Importation Request.*¹⁵⁰

Such an amendment to subsection (B) would allow generic companies to import their products during the term of an injunction, while still prohibiting them from actually marketing their products until the brand-name manufacturer's patent expires, thereby protecting the pioneer's patent rights. Furthermore, section 271(e)(4) could be further amended to only allow importation if the PLAIR applicant submits a letter signed by an authorized representative certifying under 18 U.S.C. § 1001 that it will not sell, offer to sell, or distribute its product prior to receiving final marketing approval from the FDA.¹⁵¹ Requiring such a letter would ensure that PLAIR still prohibits pharmaceutical companies from marketing new drugs without actual FDA approval, so that even if a drug has been imported, the public is still protected from consuming potentially unsafe or ineffective drugs.

7. Strategic Considerations for Practitioners

Until Congress or the FDA acts, practitioners are left with flawed statutory and regulatory schemes. If a district court issues a permanent injunction pursuant to section 271(e)(4) of the Patent Act to prohibit the generic company from importing its infringing drug product before the date that the patent expires, then the generic should not be able to take advantage of PLAIR to import its generic drug into the United States ahead of anticipated ANDA approval. The following sections discuss strategic considerations and

150. 35 U.S.C. § 271(e)(4) (emphasis added).

151. This would codify one of the current requirements for submitting PLAIR requests. See FDA, PLAIR DRAFT GUIDANCE, *supra* note 2 at 3-4.

precautions for lawyers representing both generic manufacturers filing PLAIR requests and brand-name manufacturers seeking to stop preapproval importation of generics.

7.1. Guidance for Generic Companies

In order for a generic company to take advantage of the PLAIR program, it may wish to avoid the possibility of being enjoined under section 271 (e)(4) by filing its ANDA with a Paragraph III certification rather than a Paragraph IV certification. Since filing a Paragraph III certification is not an act of patent infringement, the pioneer will not be able to sue the ANDA applicant to seek an injunction.¹⁵² Of course, the disadvantage of filing a Paragraph III certification is the generic applicant must wait until the pioneer's patent expires to enter the market, but this may be a moot point in certain cases.

For example, the first generic company to file an ANDA will likely include a Paragraph IV certification in order to secure the 180-day exclusivity period.¹⁵³ However, if during litigation it appears that the pioneer may prevail in proving both validity and infringement of its patent, the first filer may want to amend its Paragraph IV certification to a Paragraph III certification before the court can rule and issue an injunction. While this will cause the first filer to forfeit its 180-day exclusivity period,¹⁵⁴ it will also prevent the first filer from being enjoined from importing infringing product during the patent term.¹⁵⁵ In this case, the generic challenger will not be able to enter the market until the pioneer's patent expires, but this is no different from if the generic lost in litigation and was enjoined. But by switching over to a Paragraph III certification before a court can issue an injunction, the generic manufacturer will preserve its ability to use the PLAIR program to import finished drug product prior to patent expiry, allowing it to launch immediately thereafter.¹⁵⁶

This strategy may also be useful for later ANDA filers. The first ANDA filer will typically enter into a reverse-payment settlement with the pioneer, where it agrees to delay marketing its generic product (typically until several months before the patent

152. 21 U.S.C. § 355(j)(2)(A)(vii)(III).

153. 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

154. 21 U.S.C. § 355(j)(5)(D)(III); *see also* Avery, *supra* note 38, at 186.

155. 21 U.S.C. § 355(j)(5)(B)(iii)(II).

156. Brief of Petitioner-Appellant at 2-3, 5, *Sanofi-Synthelabo v. Apotex, Inc.*, No. 1:02-cv-02255-SHS.

expires).¹⁵⁷ This means that any later filers will be prevented from entering the market until the first filer's 180-day exclusivity period runs, which may be no sooner than the expiration of the pioneer's patent.¹⁵⁸ If the later ANDA filer includes a Paragraph IV certification, it will pointlessly risk an infringement suit and a possible injunction with little chance of entering the market before the first filer's exclusivity period is over. Since an injunction would prevent the later filer from utilizing the benefits of the PLAIR program, it may be advantageous for the later filer to simply file a Paragraph III certification from the start.

7.2. Guidance for Brand-Name Companies

In order for a brand-name company to prevent a generic manufacturer from using the PLAIR program to import finished drug product prior to the expiration of its patents, the pioneer must prevail in showing both validity and infringement of its patents, and then successfully secure an injunction barring the generic manufacturer from importing its product during the term of the patent. Furthermore, the pioneer should ensure that the injunction bars all importation into the United States, with no exceptions for PLAIR-based importations.

If the pioneer becomes aware of a PLAIR request filed by a generic challenger that has been previously enjoined under section 271(e)(4), the pioneer may consider filing a citizen petition with the FDA requesting that it deny the PLAIR request.¹⁵⁹ In such a petition, the pioneer should inform the FDA of the injunction and argue that the FDA should deny the PLAIR request because the Agency does not have the authority to contravene the injunction by authorizing importation of the generic product prior to patent expiry. Alternatively, the pioneer may wish to be more aggressive and sue the FDA directly, seeking to enjoin the Agency from approving the PLAIR request. While the authors are not aware of any such petitions or lawsuits, these strategies may allow a pharmaceutical patent holder to stop the FDA from approving a PLAIR request and prevent any importation prior to the expiration of its patents.

157. Matthew Avery & Mary Nguyen, *The Roadblock to Generic Drugs: Declaratory Judgment Jurisdiction for Later Generic Challengers*, 15 N.C. J.L. & TECH. 1, 8-9 (2013).

158. *Id.* at 10-11.

159. See Matthew Avery et al., *The Antitrust Implications of Filing "Sham" Citizen Petitions with the FDA*, 65 HASTINGS L.J. 113, 122-23 (2013).

Conclusion

A conflict arises between the PLAIR program and the Hatch-Waxman Act when the FDA allows preapproval importation notwithstanding an injunction against a generic manufacturer prohibiting such importation. While the FDA has the authority to regulate the importation of drugs into the United States and the right to allow preapproval importation via the PLAIR program, it does not have the authority to abrogate patent injunctions issued under section 271(e)(4) of the Patent Act (which was added as part of the Hatch-Waxman amendments).

Nevertheless, the PLAIR program does not conflict with the objectives of the Hatch-Waxman Act of facilitating generic market entry while preserving incentives for pioneer's to develop innovative new products. Under the current laws, pharmaceutical patent holders should be able to use permanent injunctions to prevent any importation prior to patent expiration, including preapproval importations via PLAIR requests. However, if Congress decides that speeding generic competition is more important than protecting the patent rights of pioneers, then it could resolve this conflict by amending section 271(e)(4) to include language permitting PLAIR-based importations. In the meantime, the FDA should amend the requirements of PLAIR requests so that applicants are required to notify the FDA of any injunctions prohibiting importation of their products. Doing so would help the Agency to avoid violating the patent rights of pioneers and approving illegal importations.