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FDA's Proposed Rules on Patent Listing Requirements for New Drug and 30-Month Stays on ANDA Approval (Proposed Oct. 24, 2002)

*Yuk Fung Hui**

I. INTRODUCTION

Drug cost constitutes a large portion of health care expenses in the United States.¹ Accordingly, many people choose to use lower priced generic drugs instead of brand-name drugs.² In order to make generic drugs more available, Congress enacted the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act of 1984.³ Amending various provisions of the Food, Drug, and Cosmetic Act ("FDCA"), the Hatch-Waxman Act intended to balance the interest in encouraging pharmaceutical research and innovation via exclusive patent rights, with the public interest of making generic drugs more readily available.⁴

Under the Hatch-Waxman Act, the Food and Drug Administration ("FDA") may approve a new drug entity under a New Drug Application ("NDA") if the applicant shows that the drug is safe and effective.⁵ Together with the NDA file, the applicant must provide the patent number and expiration date of any patent that claims the pioneer drug, or a method

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1. Dana P. Goldman & Geoffrey F. Joyce, *Congress Must Find a Way to Provide Drug Benefits*, SAN JOSE MERCURY NEWS, Dec. 16, 2002, at OP2 (reporting that Medicare spending on drugs will exceed \$400 billion in the year 2002).

2. *Medication Muddle*, COLUMBUS DISPATCH, Oct. 19, 2000, at 10A (quoting a study that reports national savings of \$112.5 billion between 1985 and 1997 through the use of generic drugs instead of brand-name drugs).

3. Pub. L. No. 98-417, 98 Stat. 1585 (codified in scattered sections of 15, 21, 28 and 35 U.S.C., with the primary provisions at 21 U.S.C. § 355 (2000)).

4. W. Lindsey Wilson, *Antitrust Solutions to Pharmaceutical Abuses: An Examination of Agreements Between Brand-Name and Generic Pharmaceutical Manufacturers*, 2001 LAW REV. MICH. ST. U. – DETROIT C.L. 1227, 1230.

5. 21 U.S.C. § 355(b)(1) (2000).

of using the drug in 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.”⁶ After the FDA approves the NDA, the patent information will be published in *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the *Orange Book*, due to its orange-colored cover.⁷

A generic drug entity, on the other hand, could gain approval from the FDA under an Abbreviated New Drug Application (“ANDA”) by showing merely that the generic drug is a bio-equivalent to the pioneer drug.⁸ There is no need to submit any independent data on the safety and efficacy of the generic drug.⁹ However, an ANDA applicant must include certifications regarding the patents related to the corresponding pioneer drug that are listed in the *Orange Book*.¹⁰ Originated from the four paragraphs of 21 U.S.C. § 355(j)(2)(A)(vii), these certifications are dubbed as “Paragraph I, II, III, and IV Certifications,” respectively stating that:

- (I) no patent related to the pioneer drug has been filed;
- (II) the relevant patent has expired;
- (III) the patent will expire on certain date; or
- (IV) the patent is invalid or will not be infringed by the manufacture, use, or sale of the generic drug entity.¹¹

If the ANDA applicant issues a Paragraph IV Certification stating that the patent involved is invalid or will not be infringed, the Hatch-Waxman Act requires the ANDA applicant to notify the owner of the patent and the holder of the approved NDA.¹² If the pioneer drug manufacturer or the patent holder initiates a patent infringement suit within forty-five days of this notice, the FDA may not approve the ANDA until either the court rules that there is no patent infringement or until the expiration of thirty months counted from the date of receipt of the notice, whichever comes first.¹³ But

6. If the patent information could not have been submitted together with the NDA, e.g., because the patent is not issued until after the NDA is approved, the NDA applicant must provide the patent information to the FDA within thirty-days after the patent is issued. 21 C.F.R. § 314.53(d)(3) (2002).

7. CTR. FOR DRUG EVALUATION & RESEARCH, U.S. DEP’T OF HEALTH & HUM. SERVS. (2002), <http://www.fda.gov/cder/ob/default.htm> (last modified Jan. 29, 2003) (last visited Mar. 22, 2003). The hardcopy of *Orange Book* is published annually, with a monthly supplement that contains the cumulative changes since the annual edition was published.

8. 21 U.S.C. § 355(j)(2)(A)(iv) (2000). Two drugs are considered bioequivalent if the rate and extent of absorption are significantly the same under similar circumstances. *Id.* at § 355(j)(8)(B).

9. *See id.* at § 355(j)(2).

10. *Id.* at § 355(j)(2)(A)(vii).

11. *Id.*

12. *Id.* § 355(j)(2)(B)(i).

13. *Id.* § 355(j)(5)(B)(iii). *See also* *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661,

if the ANDA applicant is the first to challenge the patent and FDA approves the ANDA, the applicant will have 180 days to sell the generic drug exclusively, during which time no other generic companies may enter the market.¹⁴

These measures were designed to protect the patent right of the pioneer drug, while promoting the introduction of generic drugs into the market.¹⁵ However, recent high profile litigations show that the Hatch-Waxman Act has a loophole. For example, a pioneer drug company can pay the holder of an approved ANDA not to market the generic version of the drug, thus delaying the initiation of the 180-day exclusive period.¹⁶ If the 180-day exclusive period never begins, other generic companies cannot enter the market, effectively giving an indefinite patent term to the pioneer drug.¹⁷

Pioneer drug companies may also take advantage of the thirty-month stay of ANDA approval by adding a new patent in the Orange Book shortly before other listed patents for the same drug are about to expire.¹⁸ Because of the lack of expertise in patent law among the FDA officials, the FDA often accepts the pioneer drug company's patent listing request at face value.¹⁹ As explained above, the ANDA applicant must provide certifications on all listed patents that claimed rights to the drug at issue.²⁰ If the ANDA applicant addresses this new patent with a Paragraph IV

677-78 (1990) (summarizing the approval process for generic drugs).

14. 21 U.S.C. § 355(j)(5)(B)(iv) (2000).

15. See Laura Giles, *Promoting Generic Drug Availability: Reforming the Hatch-Waxman Act to Prevent Unnecessary Delays to Consumers*, 75 ST. JOHN'S L. REV. 357, 361-62 (2001) (stating that the Hatch-Waxman Act serves to encourage innovation in drug treatments, to reduce health care costs by making generic drugs available, and to increase competition).

16. See e.g., Julia Rosenthal, *Hatch-Waxman Use or Abuse? Collusive Settlements Between Brand-Name and Generic Drug Manufacturers*, 17 BERKELEY TECH. L.J. 317, 320-327 (2002) (discussing three recent cases: *In re Buspirone Patent Litig.*, 176 F. Supp. 2d 1377 (J.P.M.L. 2001); *In re Terazosin Hydrochloride Antitrust Litig.*, 164 F. Supp. 2d 1340 (S.D. Fla. 2000); and *In re Cardizem CD Antitrust Litig.*, 105 F. Supp. 2d 682 (E.D. Mich. 2000)), each of which involved anti-competitive agreements between pioneer and generic drug manufacturers by taking advantage of the 180-day exclusive period for the marketing of the generic drug).

17. Rosenthal, *supra* note 16, at 327.

18. Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 67 Fed. Reg. 65,448-49 (Oct. 24, 2002) (to be codified at 21 C.F.R. pt. 314) (laying out the events that led to the proposed changes in regulations relating to ANDA) [hereinafter Proposed Rules].

19. *Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1080 (D.C. Cir. 2002) (indicating that FDA is reluctant to get involved in patent listing disputes and accepts "at face value the accuracy of NDA holder's patent declarations and following their listing instructions.").

20. 21 U.S.C. § 355(j)(2)(A)(vii) (2000).

Certification and a second patent infringement claim ensues, the pioneer drug company will be entitled to another 30-month stay on the ANDA.²¹ In other words, once the pioneer drug company initiates a patent infringement lawsuit and receives the first thirty-month stay, it could submit another patent to the Orange Book immediately before the thirty months expired. By adding new patents to the Orange Book at the “right” time, a pioneer drug company can obtain multiple stays on the ANDA, adding years to the patent term of the pioneer drug.²²

In light of the abuses discussed above, the Federal Trade Commission (“FTC”) submitted a citizen petition to the FDA in May 2001, requesting guidance on patent listing criteria.²³ The FTC also initiated an industry-wide study in April 2001 (“FTC Study”) to investigate whether the thirty-month stay and the 180-day exclusive period provisions in the Hatch-Waxman Act are appropriate in facilitating the introduction of generic drugs into the market.²⁴ Based on the results of this study, the FTC recommended a limitation on the number of thirty-month stay grants to one per ANDA, and a requirement that certain agreements between pioneer and generic drug companies be submitted to the FTC.²⁵

On October 24, 2002, the FDA responded by proposing new operational rules related to the drug approval process (“Proposed Rules”).²⁶ The new rules clarify the patent listing requirements, modify the patent declaration statement that must be submitted as part of a NDA file, and restrict the number of thirty-month stays allowable per ANDA to one.²⁷ At the time of

21. *Andrx Pharm., Inc. v. Biovail Corp.*, 276 F.3d 1368, 1376 (Fed. Cir. 2002) (holding that the pioneer drug company is entitled to a second thirty-month stay when it listed a new patent in the Orange Book shortly before the first thirty-month stay expired). *See also, American Bioscience*, *supra* note 19, at 1080 n.2 (noting that the FDA did not adopt the generic drug company’s argument that the statute would not allow for consecutive thirty-month stays).

22. Steven Lee, *Third Party Without Remedy in Orange Book Case 4th Circuit Holds That FDA’s Refusal To List a Patent Was Not Arbitrary Or Capricious*, NAT’L L.J., Nov. 11, 2002, at C6 (indicating that a pioneer drug company could potentially extend the patent indefinitely by listing a new patent every couple of years).

23. Letter from Seth C. Silber, Attorney, Federal Trade Commission, to the Food and Drug Administration (May 16, 2001), <http://www.fda.gov/ohrms/dockets/dailys/01/May01/052901/cpa.pdf> (last visited Mar. 22, 2003) (requesting the FDA to clarify issues relating to patent listing in the Orange Book in light of the increasing number of antitrust litigations involving pioneer and generic drug companies).

24. FED. TRADE COMM’N, *GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION* (July 2002) [hereinafter F.T.C. REPORT], <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf> (last visited Mar. 22, 2003).

25. *Id.* at ii, vi.

26. Proposed Rules, *supra* note 18, at 65,448.

27. *Id.* at 65,449. The FDA published its own operational rules for the enactment of FDCA in Title 21 of the Code of Federal Regulations. The Proposed Rules discussed in this

this writing, the Proposed Rules have completed the mandatory sixty-day comment period.²⁸ This article will discuss the details of the Proposed Rules and provide a brief analysis of the proposal in view of its legality, implications under patent law, and its impact on pharmaceutical industry and efficacy.

II. THE PROPOSED RULES

The Proposed Rules address two weaknesses of the Hatch-Waxman Act: the ambiguity of the patent listing requirements, and the possibility of multiple thirty-month stays.²⁹ The FDA intends to revise its policies on patent listing, patent declaration statements, and the imposition of automatic thirty-month stays in the event of patent infringement litigation.³⁰

A. Patent Listing Requirements

Under current FDA regulations, a holder of a NDA has to submit information on a patent if: (1) the patent claims the drug or a method of using the drug that is the subject of the NDA; and (2) the patent infringement could reasonably be asserted if other people make, use, or sell the drug.³¹ In view of the recent disputes over the types of patents that should be listed in the Orange Book,³² the Proposed Rules reaffirm the two-pronged criteria for patent listing and clarify the listing requirements by mandating the documentation of all patents that claim the:³³

- (1) drug substance (ingredient),³⁴

article are the subject of 21 C.F.R. §§ 314.52, 314.53, and 314.95.

28. News Release, Dep't of Health & Human Services, HHS Moves to Speed the Availability of Generic Drugs: New Regulation Would Help to Reduce Drug Costs for Consumers (Oct. 21, 2002), at <http://www.os.dhhs.gov/news/press/2002pres/20021021a.html> (last visited Mar. 22, 2003).

29. Proposed Rules, *supra* note 18, at 65,449.

30. *Id.* at 65,448.

31. 21 C.F.R. § 314.53(b) (2002).

32. *See, e.g.*, Ben Venue Lab., Inc. v. Novartis Pharm. Corp., 10 F. Supp. 2d 446, 450 (D.N.J. 1998) (involving a dispute whether a patent claiming a pentahydrate form of the drug should be listed even when the approved NDA is of an anhydrous form); Zenith Lab., Inc. v. Abbott Lab., Inc., 1996 WL 33344963, at *9 (D.N.J. 1996) (disputing whether patents claiming different anhydrous polymorphs of the drug were properly listed when the approved NDA is a dehydrate form).

33. Proposed Rules, *supra* note 18, at 65,464.

34. The FDA reinterprets the listing requirements under the Hatch-Waxman Act to include patents claiming a drug substance that is of a different form than the drug substance that is approved under the NDA so long as the two forms demonstrate the same dissolution, solubility, and bioavailability. Under the Proposed Rules, for example, a patent claiming an anhydrate form of a drug should be listed, even though the FDA-approved drug substance is of a dihydrate form. *Id.* at 65,452-53.

- (2) drug product (formulation and composition),
- (3) product by process, or
- (4) method of using the drug.

The Proposed Rules also explicitly prohibit the listing of patents that claim:

- (1) packaging,
- (2) metabolites, or
- (3) intermediates of the drug.³⁵

These are prohibited because such patents do not claim the drug or a method of using the drug that is the subject of the NDA.³⁶

B. Patent Declaration Statement

As admitted by the FDA, the agency does not have the expertise and resources to decide patent issues.³⁷ Instead, the FDA relies on the NDA applicant or the NDA holder to determine which patent should be listed in the Orange Book.³⁸ Under the current regulations, a NDA applicant has to submit a patent declaration statement as part of the application file.³⁹ The declaration states that, “[t]he undersigned declares that Patent No. _____ covers the formulation, composition, and/or method of use of (name of drug product). This product is (currently approved under section 505 of the Federal Food, Drug and Cosmetic Act) [or] (the subject of this application for which approval is being sought): _____.”⁴⁰ So long as the NDA applicant declares that the patent is “listable,” the FDA is required by law to publish the patent in the Orange Book.⁴¹ In practice, this declaration statement renders the FDA defenseless when the patents submitted are inappropriate for listing.⁴²

To increase the compliance with patent listing requirements,⁴³ the FDA

35. *Id.* at 65,464.

36. *Id.* at 65,451-52. The proposed amendments on the patent listing requirement provisions can be found on 67 Fed. Reg. 65,464-465.

37. *Id.* at 65,453 (admitting that the FDA “lack[s] the patent expertise, resources, and statutory mandate to scrutinize patent listings”).

38. *See, e.g.,* *Watson Pharm., Inc. v. Henney*, 194 F. Supp. 2d 442, 445 (D. Md. 2001) (concluding that “it is entirely appropriate and reasonable for the FDA to rely on the patentee’s declaration as to the coverage.”).

39. 21 C.F.R. § 314.53(c)(2)(i) (2002).

40. *Id.*

41. 21 U.S.C. §§ 355(b)(1), (c)(2) (2000) (stating that upon submission of the patent information, the FDA shall publish it).

42. F.T.C. REPORT, *supra* note 24, at 40 (pointing out that “many of the later-issued patents do not appear to claim the approved drug product or an approved use of the drug.”).

43. *See infra* Part II.A (requiring the submission of patent information by the NDA holder if the patent claims the drug or a method of using the drug that is the subject of the NDA, and a patent infringement could be reasonably asserted if other people make, use, or

proposes to replace the current declaration statement with a detailed multi-page "check-list" type declaration, to prompt the NDA applicants and holders to submit only appropriate patent information.⁴⁴ Instead of utilizing a general statement that identifies the patent, this proposed declaration emphasizes identifying the relevant patent claims, thereby facilitating parties to assess patent infringement matters and expediting the approval of ANDAs.⁴⁵

C. 30-Month Stay

The FDA has consistently allowed multiple thirty-month stays to an ANDA under the Hatch-Waxman Act.⁴⁶ Still, the FTC Study indicated that the number of thirty-month stays for each ANDA is on the rise.⁴⁷ Before 1998, one thirty-month stay at most was imposed per ANDA when a pioneer drug company initiated a patent infringement suit against a generic drug company, with the majority of the suits involving one or two patents per ANDA.⁴⁸ Since 1998, however, the infringement suits have involved more patents,⁴⁹ some of which were listed in the Orange Book after an ANDA has been filed. This has resulted in multiple thirty-month stays and delays in the introduction of generic drugs.⁵⁰

To close this loophole, the FDA proposes requiring an ANDA applicant who is amending an application to include a new Paragraph IV Certification to notify the patent owner and NDA holder only if the original ANDA did not previously include a Paragraph IV Certification.⁵¹ If no notice is given to the NDA holder, no additional stays on the ANDA can be asserted.⁵² The

sell the drug).

44. Proposed Rules, *supra* note 18, at 65,453-54.

45. *Id.* The proposed amendments on the patent declaration provision can be found at 67 Fed. Reg. 65,464-65.

46. *See, e.g.*, F.T.C. REPORT, *supra* note 24, at 49 (noting that at least seven NDAs captured in the FTC Study successfully obtained multiple thirty-month stays, while one NDA obtained as many as five stays).

47. *Id.* at 39-40.

48. *Id.* at 39 (stating that infringement was alleged on one or two patents in eight out of nine suits that involved drugs with substantial annual revenues).

49. *Id.* at 39-40 (reporting that infringement was alleged on at least three patents in five out of eight suits that involved drugs with substantial annual revenues).

50. Since 1998, eight pioneer drug companies listed new patents in the Orange Book after an ANDA was filed. Because of these new patents, as many as forty months were added to the holding period beyond the initial thirty-month stay, delaying the approval of ANDA even further. *Id.* at 40.

51. Proposed Rules, *supra* note 18, at 65,464-65 (proposing to revise 21 C.F.R. §§ 314.52(a)(3), 314.95(a)(3) (2002)). The corresponding federal statutory provisions are published in 21 U.S.C. §§ 355(c)(3)(C) (2000), (j)(5)(b)(iii) (2000).

52. Proposed Rules, *supra* note 18, at 65,455.

exemption of additional notice in this situation is based on the argument that further notice to the patent owner and NDA holder is required by the statute only if the ANDA is amended to “include” a Paragraph IV Certification.⁵³ According to the FDA, if a Paragraph IV Certification was previously filed, any subsequent Paragraph IV Certification attached with an amended ANDA could not be “included” in the application, because the ANDA has already contained a Paragraph IV Certification.⁵⁴ If the additional Paragraph IV Certification is not considered “included” in the amended ANDA, the notice requirement under the statute is never triggered and hence no further thirty-month stay could be imposed.⁵⁵

To illustrate the impact of the Proposed Rules on the number of thirty-month stays asserted, consider the following examples:

Example 1: An ANDA applicant files a Paragraph IV Certification on a patent and notifies the patent owner and NDA holder. In response, the pioneer drug company initiates a patent infringement suit and thus is entitled to a 30-month stay.⁵⁶ While the lawsuit is pending, the pioneer drug company obtains a new patent and lists it in the Orange Book.⁵⁷ Under the Proposed Rules, if the ANDA applicant amends the application and files a new Paragraph IV Certification to this second patent, she is not required to give another notice of certification of invalidity or non-infringement to the NDA holder.⁵⁸ As a result, the pioneer drug company will not receive another thirty-month stay.⁵⁹

Example 2: Two generic drug companies file two different ANDAs involving the same pioneer drug. Generic drug company #1 (G1) files a Paragraph IV Certificate to a patent, whereas generic drug company #2 (G2) files a Paragraph III Certificate to the same patent. After receiving notice from G1, the pioneer drug company brings a patent infringement suit against G1 and obtains an automatic thirty-month stay on G1’s

53. 21 U.S.C. § 355(j)(5)(B)(iii) (2000).

54. Proposed Rules, *supra* note 18, at 65,455.

55. *Id.* The proposed amendments on the relevant provisions can be found at 67 Fed. Reg. 65,464-65.

56. 21 U.S.C. § 355(j)(5)(B)(iii) (2000) (mandating a thirty-month stay on approval of ANDA that is under the attack of patent infringement by the pioneer drug company); *see also* Proposed Rules, *supra* note 18, at 65,455.

57. If the patent is issued after the NDA is approved, the NDA holder is obligated to provide listing information to the FDA within thirty days of patent issuance. *See* 21 C.F.R. § 314.53(d)(3) (2002).

58. Proposed Rules, *supra* note 18, at 65,464 (exempting the notification requirement if a Paragraph IV Certification has been filed previously for a separate patent).

59. *Id.* at 65,455 (explaining that, if the ANDA applicant is not required to submit another notification, “the pre-requisites to trigger the thirty-month stay in an ANDA’s approval date are not met, so the thirty-month stay would not be available.”).

ANDA.⁶⁰ Assume further that the pioneer drug company now obtains a new patent and has it listed in the Orange Book, and that both G1 and G2 respond by filing new Paragraph IV Certifications to the second patent with their amended ANDAs. The Proposed Rules mandate G2, but not G1, to provide a notice of certification of invalidity or non-infringement.⁶¹ A thirty-month stay with respect to the second patent is thus applicable only on G2's ANDA.⁶² In sum, at most a single thirty-month stay will be applicable to each of the ANDAs.

III. ANALYSIS

A. Legality

The Proposed Rules express the FDA's interpretation of certain provisions in the Hatch-Waxman Act.⁶³ In determining the legality of statutory construction by an administrative agency, the courts have consistently relied on the two-step test laid out in *Chevron U.S.A., Inc. v. Natural Resource Defense Council, Inc.*,⁶⁴ which states:

- (1) If congressional intent is clear, the court will follow the intent in construing the statute.
- (2) If the Congress is silent or ambiguous with respect to the issue, the court will adopt the agency's statutory construction so long as it is permissible under the statute.⁶⁵

60. 21 U.S.C. § 355(j)(5)(B)(iii) (2000) (stating that the approval of ANDA will be stayed for thirty months, or such shorter or longer period as the court may order if an infringement action is brought within forty-five days from the date of notice); *see also* Proposed Rules, *supra* note 18, at 65,455.

61. Since G2 has not previously filed any Paragraph IV Certification, G2 must notify the patent owner and the NDA holder of its ANDA. G1, however, is exempted from notifying the pioneer drug company again. Proposed Rules, *supra* note 18, at 65,464.

62. *Id.* at 65,456-57.

63. The patent listing requirements, patent declaration statement, and the imposition of 30-month stay were covered in Titles I and II of the Hatch-Waxman Act, now codified in 21 U.S.C. §§ 355(b), (c), (j) (2000). Proposed Rules, *supra* note 18, at 65,448-49.

64. *Chevron v. Natural Res. Def. Council*, 467 U.S. 837, 842 (1984). *See, e.g.*, *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 132 (2000) (adopting the *Chevron* test to determine whether the FDA has the authority to regulate the tobacco industry under the Federal Food, Drug, and Cosmetic Act); *Nat'l R.R. Passenger Corp. v. Boston & Maine Corp.*, 503 U.S. 407, 418 (1992) (upholding the interpretation of the Rail Passenger Service Act by the Interstate Commerce Committee under the *Chevron* test); and *Pauley v. BethEnergy Mines, Inc.*, 501 U.S. 680, 697 (1991) (giving deference to the Department of Labor in interpreting the Federal Coal Mine Health and Safety Act as directed under the *Chevron* test).

65. If the statute does not specifically address the issue, the court will then consider whether the agency's interpretation "is based on a permissible construction of the statute." *Id.* at 843.

In construing the patent listing requirements, the FDA looked at the statutory provision that requires the listing of any patent that “claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted[.]”⁶⁶ The FDA’s allowance of listing patents that claim the drug substance, drug product, product by process, and method of use compared to the disallowance of listing patents that claim packaging, metabolites, and intermediates seem to fall within the boundary of the statute. After all, there is no indication that Congress intended to have the FDA approve of the packaging design, the entity derived during the process of metabolism (metabolite), or the substance formed in the course of reaction involving the drug claimed in the NDA (intermediate).⁶⁷ Since it is unambiguous that the statute permits only patents that claim the drug or the method of using the drug to be listed,⁶⁸ it is permissible under *Chevron* for the FDA to amend the patent listing requirements as proposed.⁶⁹

On the other hand, patent declarations are not required by the statutes.⁷⁰ However, the FDA is endowed with the authority to “promulgate regulations for the efficient enforcement” of the FDCA.⁷¹ Since the congressional intent is to list patents claiming only the drug or method of using the drug, it is permissible for the FDA to impose a patent declaration requirement that is designed to encourage compliance with the patent listing requirements.⁷² As explained by the FDA, the proposed checklist type declaration would ensure the submission of only appropriate patent information for listing purposes, thus satisfying the goal of efficient enforcement of the FDCA.⁷³ Therefore, the patent declaration statement of the Proposed Rules sustains scrutiny under the *Chevron* test.⁷⁴

Some question the legality of the revised regulations’ limitation on the

66. 21 U.S.C. § 355(b)(1) (2000).

67. Proposed Rules, *supra* note 18, at 65,451-52 (stating that the Hatch-Waxman Act does not “identify a listed drug’s packaging or container as an element for . . . review,” and concluding that metabolites and intermediates are not considered “approved drugs”).

68. 21 U.S.C. § 355(b)(1) (2000).

69. With the clear congressional intent that only patents that claim the drug or the method of using the drug should be listed, FDA’s construction of the patent listing requirements passes the *Chevron* test. *See infra* Part III.A.

70. 21 U.S.C. § 321 (2000).

71. *Id.* at § 371(a).

72. *See* Proposed Rules, *supra* note 18, at 65,453 (stating that the original declaration statement is designed to “help ensure that appropriate patents are listed.”).

73. *See id.* (concluding that the proposed declaration “would ensure that applicants submit only appropriate patent information and stand behind the accuracy of that information”).

74. *See supra* note 65 and accompanying text.

number of thirty-month stays.⁷⁵ As stated above, unless the congressional intent is clear and unambiguous, a court will uphold an agency's statutory interpretation, so long as it is permissible under the statute.⁷⁶ Finding that the statute is ambiguous,⁷⁷ the FDA relied on the legislative history to support its argument that a maximum of one thirty-month stay period per ANDA is a reasonable compromise between the competing interests of pioneer drug companies and generic manufacturers.⁷⁸ However, while it may be true that many members of Congress were concerned about pioneer drug companies obtaining multiple patent term extensions and inhibiting competition from generic drug companies by stacking one patent on top of another to extend protection,⁷⁹ there is no evidence that imposing a maximum of one thirty-month stay per ANDA is the preferred way of preventing unfair patent term extensions.⁸⁰ In fact, it could easily be argued that two thirty-month stays per ANDA would be a "reasonable compromise." Unless the FDA can establish a stronger argument, the proposed limit on the number of thirty-month stays is likely to invite legal challenge on its statutory permissibility.⁸¹ Moreover, because the FDA has consistently allowed multiple thirty-month stays in the past,⁸² it may now be difficult to convince the public that there should be a 180-degree shift on the issue.

B. The Proposed Rules and Patent Law

It has long been recognized that patent rights are defined by the language in a patent claim.⁸³ The claim sets forth to what extent the patent owner can exclude others from making, using, or selling the invention.⁸⁴ In other

75. Steve Seidenberg, *Rule on Generics Faces Hurdles as Proposed by Bush, the Regulation Would Change Provisions of Hatch-Waxman*, 26 NAT'L L.J. 12, Nov. 11, 2002, at C1 (commenting that the legal right of the FDA to limit the automatic stay to one time only was questionable).

76. *See infra* Part III.A.

77. Proposed Rules, *supra* note 18, at 65,456 n.1 (justifying the reliance on legislative history because the statute is ambiguous on the maximum number of thirty-month stay).

78. *Id.*

79. Proposed Rules, *supra* note 18, at 65,456.

80. *Id.*

81. If the language of the statute is ambiguous, the next question is whether the agency's interpretation is permissible under the statute. *See Chevron*, 467 U.S. at 843.

82. *See* F.T.C. REPORT, *supra* note 46.

83. ROBERT P. MERGES ET AL., *INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE* 239 (2d ed. 2000) (analogizing the patent claim as the "metes and bounds" of a real property deed).

84. Sean T. Moorhead, *The Doctrine of Equivalents: Rarely Actionable Non-Literal Infringement or the Second Prong of Patent Infringement Charges?*, 53 OHIO ST. L.J. 1421, 1423 (1992).

words, a patent claim is the bedrock of a patent infringement suit.⁸⁵ If the Hatch-Waxman Act allows the listing of patents in the Orange Book only if infringement of such patents could be reasonably alleged, then the FDA regulations on patent listing should be aimed at individual patent claims instead of the entire patent.

This is exactly what the FDA recommended. In the Proposed Rules, the FDA suggested a revision of the patent declaration statement into a checklist format, which would prompt the NDA applicants to submit patent information that emphasizes patent claims.⁸⁶ Instead of giving a general statement declaring that the patent should be listed,⁸⁷ NDA applicants are now asked to identify which patent claim, if any, they believe would be infringed.⁸⁸ This amendment brings the patent listing requirements in step with patent law. More importantly, the amendment to patent declarations will aid the FDA in promulgating the congressional intent of listing only patents against which infringement could reasonably be asserted.⁸⁹

On the other hand, the proposal of limiting the number of thirty-month stays on an ANDA while an infringement suit is pending only disturbs the patent rights of the innovator.⁹⁰ As the FTC pointed out, the government has an interest in protecting the patent rights of the pioneer drug companies who have invested an enormous amount of money into the innovation.⁹¹ Under the Patent Act, a plaintiff in an infringement suit can obtain a preliminary injunction on the alleged infringing activity by establishing: (1) a reasonable likelihood of success on the merits, (2) irreparable damage, (3) hardship on the plaintiff, and (4) public interest in granting the injunction.⁹² To strengthen the protection, the Hatch-Waxman Act goes above and

85. *Larami Corp. v. Amron*, 1993 WL 69581, *1, *3 (E.D. Pa. 1993) (stating that a finding of infringement requires the consideration of the “elements” or “limitations” of the claims (quoting *Key Mfg. Group, Inc. v. Microdot, Inc.*, 925 F.2d 1444, 1449 (Fed. Cir. 1991))).

86. Proposed Rules, *supra* note 18, at 65,454 (noting that the proposed declaration statement would “emphasize identification of the relevant patent claims by number”).

87. 21 C.F.R. § 314.53(c)(2)(i) (2002).

88. Applicants are asked to first give the patent number, and then give the claim number of the drug or method of using the drug in which they believe that infringement could reasonably be asserted. Proposed Rules, *supra* note 18, at 65,464.

89. See 21 U.S.C. § 355(b)(1) (2000).

90. *PhRMA Critical of FDA Generic Drug Proposal*, WASH. DRUG LETTER (Dec. 16, 2002) [hereinafter *PhRMA*] (reporting that the senior vice president of the industry trade group Pharmaceutical Research and Manufacturers of America, PhRMA, exerted concerns about generic drugs being approved “without a fair opportunity for litigation of patent infringement issues”).

91. F.T.C. REPORT, *supra* note 24, at 4.

92. *Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1451 (Fed. Cir. 1988) (listing the four factors that a court should consider and balance in granting a preliminary injunction under the Patent Act).

beyond the Patent Act, mandating a thirty-month preliminary injunction each time a plaintiff files an infringement suit after receiving notice from the defendant.⁹³ The plaintiff has no burden of proof in obtaining a preliminary injunction.⁹⁴ However, the Proposed Rules restrict the number of thirty-month stays on an ANDA to only one.⁹⁵ A preliminary injunction beyond the first thirty-month stay is no longer mandatory.⁹⁶ The FDA argued that a patent owner and the NDA holder could still seek judicial remedy through patent infringement litigation, including injunction under the Patent Act,⁹⁷ without the grant of multiple thirty-month stays.⁹⁸ However, the proposed amendment pushes the parties to seek relief outside the reign of the Hatch-Waxman Act for a cause of action that is brought under the very same act.

C. Impact on the Pharmaceutical Industry and Consumers

Understandably, the pioneer drug companies have the most at stake and are therefore scrutinizing the Proposed Rules. For years, the pioneer drug companies have been enjoying multiple thirty-month stays,⁹⁹ and have lacked oversight when listing more patents, even though the “new” patents are only tangentially related to the drug described in the NDA.¹⁰⁰ The Proposed Rules attempt to close these loopholes.¹⁰¹ Bruce Kuhlik, senior vice president of the trade group Pharmaceutical Research and Manufacturers of America, commented that the Proposed Rules hit hard on the innovator industry.¹⁰² It is estimated that over \$800 million and fifteen years of research are invested before an innovative drug gets into the market.¹⁰³ It is understandable that the innovator will want as long and as

93. See 21 U.S.C. § 355(j)(5)(B)(iii) (2000).

94. *Id.*

95. See *infra* Part II.C.

96. Proposed Rules, *supra* note 18, at 65,455.

97. 35 U.S.C. § 283 (2000) (allowing a court with jurisdiction to hear patent infringement cases and grant injunction as a form of equitable relief).

98. Proposed Rules, *supra* note 18, at 65,455 (suggesting that the parties could continue with patent litigation without the benefit of multiple thirty-month stays).

99. See *supra* note 46.

100. Alfred B. Engelberg, *Special Patent Provisions for Pharmaceuticals: Have They Outlived Their Usefulness? A Political, Legislative and Legal History of U.S. Law and Observations for the Future*, 39 J.L. & TECH. 389, 415 (1999) (commenting that many of the approved drug products listed in the Orange Book contain patents that claim “unapproved uses, special crystalline forms of the active ingredient, specific formulations, tablet shape or other subject matter which can easily be circumvented while still producing an equivalent generic version of an approved drug”).

101. See Proposed Rules, *supra* note 18, at 65,460.

102. PhRMA, *supra* note 90.

103. Styli Engel & Kimberly Sentek, *First Develop the Best Drug: There's No Surviving*

broad a monopoly as possible on his product in order to recoup his investment.¹⁰⁴ This same monopoly also attracts pharmaceutical companies into investing in drug research.¹⁰⁵ If the pioneer drug companies' monopoly rights are trimmed as the Proposed Rules suggest, investors may reconsider putting money into research and development. This extra precaution will likely translate into a delay in new treatment inventions, potentially jeopardizing health care in the long run.

Generic drug companies, on the other hand, welcome the Proposed Rules.¹⁰⁶ With the FDA's guaranteed equivalence between a brand name drug and its generic version,¹⁰⁷ and the significantly lower prices of generic drugs,¹⁰⁸ many consumers have no objection to switching to generic drugs.¹⁰⁹ Therefore, generic drugs often take the market by storm and bring large profits to the manufacturers.¹¹⁰ By adopting the Proposed Rules, generic drug companies will have a great financial incentive to bring more generic drugs into the market,¹¹¹ thereby realizing one of the purposes behind the Hatch-Waxman Act and benefiting the consumers in return.

D. Effectiveness of the Proposed Rules

The FDA promulgated the Proposed Rules with the goal of balancing the competing interests of increased introduction of generic drugs, and the

Without a Broad and Deep Pipeline, MED AD NEWS, July 1, 2002, at 4.

104. See also Giles, *supra* note 15, at 364 (stating that the "stakes are very high for a pioneer drug company when its patent . . . is set to expire.").

105. James T. O'Reilly, *Prescription Pricing & Monopoly Extension: Elderly Drug Users Lose the Shell Game of Post-Patent Exclusivity*, 29 N. KY. L.REV. 413, 415 (2002) (suggesting that future financial investment in pharmaceutical research relies, at least partly, on the possibility of innovators being able to recoup their investment at a profit).

106. *Bush's Proposed Patent Move Gets Mixed Industry Reaction*, FOOD & DRUG LETTER (Dec. 6, 2002) (reporting that the "generic industry . . . greeted the Bush proposal as a good start").

107. An ANDA has to show that the generic version of the drug is bioequivalent to the pioneer drug. 21 U.S.C. § 355(j)(2)(iv) (2000). See also *supra* note 8.

108. Gary Martin, *Proposal Boosts Generic Drugs; Patent Lawsuits Would Be Blocked*, SAN ANTONIO EXPRESS-NEWS, Oct. 22, 2002, at 3A (reporting that the average cost of a pioneer drug is over \$72 per prescription while that of a generic drug is less than \$17).

109. Thom Calandra, *Generic Drug Makers to Clobber Big-Pharma, Survey Says*, CBS MARKETWATCH, Nov. 4, 2002 (reporting that 54% of consumers would choose generic drugs if they are available).

110. Barr Laboratories, Inc. gained the 180-day exclusive period to market the generic version of Prozac, a popular antidepressant. During the period, the company made \$350 million in sales. Charles Boersig, *Patent Woes for Big Pharma: Generic Manufacturers Are Becoming Increasingly Aggressive in Their Efforts to Invalidate Drug Patents*, MED AD NEWS, Nov. 1, 2002, at 1.

111. "With huge sales revenue on the line, generic drug makers are working harder than ever to copy top-selling drugs." *Id.*

protection of the patent rights of pioneer drug manufacturers.¹¹² However, the proposal has been criticized for not doing enough to prevent the pioneer drug companies from gaming the system.¹¹³ Even though the FDA has proposed to allow only certain types of patents to be listed in the Orange Book, there is no punishment for submitting the “wrong” type of patent information.¹¹⁴ The pioneer drug company could continue to submit to the FDA whatever types of patent information it sees fit.¹¹⁵ This patent information will likely lead to a listing in the Orange Book, because the FDA will not question the information, due to its lack of expertise in patent law.¹¹⁶ Of course, a generic drug maker could eventually challenge the validity of these patents. But even if the generic drug company wins in court, the pioneer drug company would have gained months or even years in stalling the approval of the ANDA, effectively preventing the entry of generic drugs into the market.

The lack of comment on the 180-day exclusivity period is perhaps the biggest criticism that the Proposed Rules are getting.¹¹⁷ Under the current regulations, the first ANDA applicant who successfully challenges a NDA with a Paragraph IV Certification will have 180 days to market its product exclusively.¹¹⁸ During that time, the FDA may not approve other ANDAs on the same drug.¹¹⁹ This arrangement has lured the pioneer drug and generic drug companies to come to a mutual agreement not to market the generic version, even when the FDA has approved an ANDA.¹²⁰ If the ANDA

112. Proposed Rules, *supra* note 18, at 65,456 (indicating that limiting the number of thirty-month stays to one “would preserve the balance between encouraging ANDA . . . approvals and encouraging innovation”).

113. See Seidenberg, *supra* note 75 (reporting that the proposed regulation was criticized for not going far enough).

114. *Drugs and the Orange Book*, 170 N.J. L.J. 754 (Dec. 2, 2002) (criticizing that the Proposed Rules do not penalize for a patent that is listed in the Orange Book incorrectly).

115. *Id.*

116. See *supra* note 19.

117. *Generic Drug Backers Look to Congress for Patent Law Reform*, 19 GENERIC LINE No. 21, Nov. 8, 2002 (criticizing that the *Proposed Rules* do not alter the 180-day exclusivity provision).

118. 21 U.S.C. § 355(j)(5)(B)(iv) (2000).

119. *Id.*

120. When Andrx Corporation, an ANDA applicant for the generic version of Cardizem CD, a popular heart medicine, received preliminary approval from the FDA in 1995, Andrx and Hoechst Marion Roussel, Inc., maker of Cardizem CD, agreed to use Andrx's right to the 180-day exclusivity period to block other generic companies from selling the generic versions of Cardizem CD. Under the agreement, Hoechst Marion Roussel would pay Andrx \$10 million per quarter for not selling any generic Cardizem CD. The agreement was terminated in 1999 when FTC initiated an investigation on the arrangement. By then, Hoechst Marion Roussel had paid over \$80 million to Andrx. Andrx started selling the generic version of Cardizem CD in June 1999. David E. Swarts, *Still on the Hook: Why the*

applicant does not start marketing its generic drug, the 180-day exclusive period never runs, and other generic companies may never get their ANDAs approved.¹²¹ Unless the FDA starts to address this issue, it is unlikely that the Proposed Rules could have any significant impact on the introduction of generic drugs.

IV. CONCLUSION

With the goal of making generic drugs more available while retaining the incentive in pharmaceutical research and development, the FDA proposes to tighten the patent listing requirements, revise the patent declaration statements submitted by the NDA applicant, and restrict the number of thirty-month stays on an ANDA to only one in response to patent infringement litigation. These changes do have the potential to lower the threshold of overcoming the patent rights of NDA holders and, hence, ease the introduction of generic drugs into the market. However, it is questionable if the FDA has the legal authority to make all the changes. More importantly, the FDA has neglected to address the issue of the 180-day exclusivity period granted to the first ANDA applicant who successfully challenges the patent of the pioneer drug. Without a revision of the 180-day exclusivity policy, it is uncertain whether the FDA can achieve the goal of making generic drugs more available.

The Proposed Rules completed its mandatory sixty-day comment period on December 23, 2002. After reviewing the comments,¹²² the FDA will decide whether to enact the rules.

Hatch-Waxman Act Does Not Provide Drug Companies Immunization from the Antitrust Laws, 54 RUTGERS L. REV. 563, 570-72 (2002).

121. See *supra* text accompanying notes 16-17.

122. A list of comments that the FDA has received can be found on its website at <http://www.fda.gov/ohrms/dockets/dockets/02n0417/02n0417.htm>.