

INTELLECTUAL PROPERTY OWNERS ASSOCIATION

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**THE HATCH-WAXMAN AMENDMENTS IN TITLE XI
OF THE MEDICARE MODERNIZATION ACT OF 2003**

Brian P. Murphy
Vice-Chair, IPO Hatch-Waxman Committee
Morgan, Lewis & Bockius LLP
101 Park Avenue
New York, New York 10178-0060
(212) 309-6000
bmurphy@morganlewis.com

INTRODUCTION

The Medicare Modernization Act (“MMA”),¹ signed into law by President Bush on December 8, 2003, contains significant amendments to the Hatch-Waxman Act. These amendments alter everything from the Paragraph IV notification requirements for a patent challenger to the review of settlement agreements by the Federal Trade Commission (“FTC”) and, by and large, they attempt to ease the requirements for market entry of generic drugs. The intellectual property issues raised by these Hatch-Waxman amendments should be of interest to all practitioners and policy makers in the pharmaceutical industry.

The Hatch-Waxman legislation is very complex. I have chosen to use a format where I give a short identification of the subject, quote the relevant MMA-amended statutory language from 21 U.S.C. § 355(j) governing abbreviated new drug applications (“ANDAs”)², and then I provide explanatory comments to elucidate the changes and provide some helpful context. I have not included every technical amendment, but I have included all of the significant substantive ones. This statutory analysis is not for the faint-of-heart, but I hope it will help those with a willingness and need to understand this singular legislation.

¹ *Medicare Prescription Drug, Improvement, and Modernization Act of 2003*, Pub. L. 108-173, 117 Stat. 2006 (2003).

² Comparable provisions were enacted for applications under 21 U.S.C. § 355(b)(2) (“505(b)(2) applications”).

STATUTORY ANALYSIS

1. Paragraph IV³ Notification Requirements - 21 U.S.C. § 355(j)(2)(B)

If an ANDA applicant chooses to certify to the U.S. Food and Drug Administration (“FDA”) that a patent listed in the Orange Book⁴ is invalid or will not be infringed (a “Paragraph IV certification”), it must provide notice of the patent challenge to the patent owner and NDA holder within certain time limits:

(B) NOTICE OF OPINION THAT PATENT IS INVALID OR
WILL NOT BE INFRINGED.

* * *

(ii) TIMING OF NOTICE - An applicant that makes a certification described in subparagraph (A)(vii)(IV) shall give notice as required under this subparagraph-

(I) if the certification is in the application, not later than 20 days after the date of the postmark on the notice with which the Secretary informs the applicant that the application has been filed;
or

(II) if the certification is in an amendment or supplement to the application, at the time at which the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice with respect to another such certification contained in the application or in an amendment or supplement to the application.

Comments: Only the timing of the notice has been changed. If the Paragraph IV certification is contained in the originally-filed ANDA, the applicant must now notify the patent/NDA holder within 20 days after the FDA mails its notice confirming the

³ 21 U.S.C. § 355(j)(2)(A)(vii)(IV) permits an ANDA filer to certify, “in the opinion of the applicant and to the best of his knowledge,” that a patent listed by the holder of a New Drug Application (“NDA”) is invalid or will not be infringed by the manufacture, use, or sale of the proposed generic drug.

⁴ *Approved Drug Products with Therapeutic Equivalence Evaluations.*

filing of the ANDA. This sets a precise and rapid deadline for Paragraph IV notification, which triggers the 45-day statutory period for the patent/NDA holder to decide whether to bring an action for patent infringement under 35 U.S.C. § 271(e)(2). The previous provision required only that the ANDA applicant make a statement in the ANDA that it “will give” the required notice to the patent/NDA holder, without requiring any particular time period for providing such notice. While, in most instances, ANDA applicants have provided such notice early on in the FDA review process, this has not always been the case, particularly if the ANDA applicant was the first to file and could be assured of 180-day generic market exclusivity, or if preliminary FDA review revealed significant problems with the application. Any discretion as to the timing of the notice of a Paragraph IV certification is now removed.

Clause (II) was added to overrule that portion of FDA’s June 2003 “Final Rule” 68 Fed. Reg. 36676 (June 18, 2003), which permitted an applicant to avoid giving notice of a Paragraph IV certification contained in an ANDA amendment or supplement, if the applicant previously had given notice of another Paragraph IV certification in connection with the same ANDA. FDA’s Final Rule was an effort to eliminate the opportunity for multiple, overlapping 30-month stays of FDA approval triggered by the filing of patent infringement actions within 45 days of receiving notice of a patent challenge for more than one Orange Book listed patent. The MMA, as we shall see, has severely restricted the opportunities for more than one 30-month stay of FDA approval of an ANDA. FDA, in response to the passage of MMA, rescinded the referenced Paragraph IV notification

provision of the Final Rule. 69 Fed. Reg. 11309 (March 10, 2004). Notice of all Paragraph IV challenges must now be given to the patent/NDA holder either within 20 days of FDA confirmation of the ANDA filing or at the time an amendment or supplement is submitted to the FDA.

2. ANDA Amendments - 21 U.S.C. § 355(j)(2)(D)

There are certain limitations on the subject matter of ANDA amendments:

- (D) (i) An applicant may not amend or supplement an application to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary.
- (ii) With respect to the drug for which an application is submitted, nothing in this subsection prohibits an applicant from amending or supplementing the application to seek approval of a different strength.
- (iii) Within 60 days after the date of the enactment of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, the Secretary shall issue guidance defining the term “listed drug” for the purposes of this subparagraph.

Comments: This provision prevents an ANDA applicant from using the amendment process to seek approval of a generic drug by referring to a different reference listed drug (“RLD”) from the one identified in the original ANDA (also referred to as “switching the RLD”). Such an approach might otherwise avoid the patent certification and notice requirements of the statute. The ANDA applicant can, however, amend or supplement the ANDA to seek approval of a different strength or dosage from the listed drug product, but the FDA has not yet issued any guidance defining “listed drug.” This is a significant issue. For example, let’s say an ANDA applicant obtains FDA approval for a particular immediate release formulation of a drug product, but the applicant also wants approval of a sustained

release version of the product that is protected by a sustained release formulation patent. If a new ANDA is required by FDA for the new sustained release formulation, a 30-month stay of FDA approval is possible, but if an amendment to the original application will suffice, a 30-month stay may not be available to the patent/NDA holder. The patent/NDA holder may have to resort to preliminary injunction proceedings in such a circumstance. At this point we await the FDA's guidance on the definition of a "listed drug."

3. **The 30-Month Stay of FDA Approval - 21 U.S.C. § 355(j)(5)(B)(iii)**

If an ANDA applicant submits a Paragraph IV certification challenging a patent listed in the Orange Book, the patent/NDA holder has a 45-day statutory period to determine whether to sue for patent infringement and obtain the benefit of an automatic 30-month stay of FDA approval of the ANDA:

(B) The approval of an application submitted under paragraph (2) shall be made effective on the last applicable date determined by applying the following to each certification made under paragraph (2)(A)(vii):

. . . (iii) If the applicant made a certification describe in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in paragraph (2)(B) is received, an action is brought for infringement of the patent that is the subject of the certification **and for which information was submitted to the Secretary under subsection (b)(1) or (c)(2) before the date on which the application** (excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, **was submitted**. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the **thirty-month period beginning on the date of the receipt of the notice** provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to

the action failed to reasonably cooperate in expediting the action, . . .

Comments: This provision limits the availability of an automatic 30-month stay of FDA approval to patent infringement litigation filed in response to a Paragraph IV patent challenge only for patents submitted for listing in the Orange Book before the date on which an ANDA is submitted to the FDA. If a patent is submitted for Orange Book listing after an ANDA is submitted, a Paragraph IV certification and notice to the patent/NDA holder is still required, but the 30-month stay provision does not apply to that particular patent. If the patent/NDA holder wants to enforce a later-listed patent prior to FDA approval, a declaratory judgment action and application for a preliminary injunction would be required.

The bolded language in the first sentence of clause (B)(iii) above, -- “and for which information was submitted to the Secretary under subsection (b)(1)[patents for listing in the Orange Book]. . . before the date on which the application . . . was submitted”-- reflects Congress’ effort to implement the first recommendation contained in the FTC’s July 2002 generic drug study. The FTC identified several blockbuster pharmaceutical products where multiple Orange Book listed patents triggered multiple Paragraph IV certifications. This, in turn, led to multiple patent litigations and accumulative (although overlapping) 30-month stays of FDA approval. The FTC recommended that Congress “permit only one automatic 30-month stay per drug product per ANDA to resolve infringement disputes over patents listed in the Orange Book prior to the filing date of the generic applicant’s

ANDA.”⁵ The Medicare Conference Agreement in connection with MMA also notes that “[t]he single 30-month stay provisions are a centerpiece of this legislation, allowing lower-priced generic products to enter the market more quickly.”⁶ The statutory language accomplishes the goal of limiting a patent/NDA holder’s ability to obtain more than one automatic 30-month stay per ANDA.

It is still possible, however, for more than one automatic 30-month stay per ANDA to occur. For example, if two or more patents are listed in the Orange Book at the time of an ANDA submission, and the ANDA applicant submits a Paragraph IV certification for only one patent, the applicant may be sued for infringement of that patent within 45 days. A first 30-month stay of FDA approval would be triggered. If the ANDA applicant later amends the application from a Paragraph III (no patent challenge) to a Paragraph IV certification challenging another patent that was listed in the Orange Book at the time of the original ANDA submission, and the ANDA applicant is sued for infringement within 45 days, a second automatic 30-month stay would take effect. The ANDA applicant, therefore, controls whether a second 30-month stay is possible under such a scenario.

⁵ The Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* at ii (July 2002), at <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf>.

⁶ Medicare Conference Agreement (Nov. 21, 2003), at 387 available at <http://waysandmeans.house.gov/media/pdf/hr1/hr1;texplstate.pdf>.

4. 180-Day Generic Exclusivity and Forfeiture Provisions - 21 U.S.C. § 355(j)(5)(B)(iv) and § 355(j)(5)(D)

A. First Applicants and 180-Day Exclusivity - § 355(j)(5)(B)(iv)

When more than one applicant files an ANDA requesting FDA marketing approval for a generic version of the same listed drug product, the Hatch-Waxman Act provides a scheme for determining priority, such that a “first applicant” receives 180 days of generic marketing exclusivity:

(iv) 180 DAY EXCLUSIVITY PERIOD.

(I) EFFECTIVENESS OF APPLICATION. - Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is **180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.**

(II) DEFINITIONS.- In this paragraph:

(aa) 180-DAY EXCLUSIVITY PERIOD- The term ‘180-day exclusivity period’ means the 180-day period ending on the day before the date on which an application submitted by an applicant other than a first applicant could become effective under this clause.

(bb) FIRST APPLICANT- As used in this subsection, the term ‘first applicant’ means an applicant that, **on the first day** on which a substantially complete application containing a certification described in paragraph (2)(A)(vii)(IV) is submitted for approval of a drug, **submits a substantially complete application** that contains and **lawfully maintains a certification described in paragraph (2)(A)(vii)(IV)** for the drug.

(cc) SUBSTANTIALLY COMPLETE APPLICATION.- As used in this subsection, the term “substantially complete application” means an application under this subsection that on its face is sufficiently complete to permit a substantive review and contains all the information required by paragraph (2)(A). . .

Comments: This provision replaces the old scheme where, in theory, only one applicant could be the “first applicant” for a generic drug product. Under this new scheme, more than one applicant may qualify as a “first applicant” if such applicant files a substantially complete ANDA containing a Paragraph IV certification at any hour on the same “first” day and lawfully maintains a Paragraph IV certification. A substantially complete ANDA is one that, on its face, includes all of the information required by statute so as to permit substantive FDA review. This provision encourages ANDA applicants to file as soon as possible subject to the expiration of the FDA marketing exclusivity period for the patent/NDA holder’s RLD, so as to qualify to be “first” and benefit from 180-day generic marketing exclusivity.

The provision may have the effect of encouraging ANDA applicants to attack a basic compound patent protecting the active ingredient of the RLD, even in the face of long odds of success, just to preserve the 180-day generic marketing exclusivity period. This has been characterized as “parking” exclusivity in situations where a later-expiring patent (such as a formulation or use patent) is challenged at the same time as the compound patent. The issue is whether the ANDA applicant, by making an early but unsuccessful challenge to the compound patent, can “park” the 180-day exclusivity until the compound patent expires by preventing the 75-day forfeiture clock from starting to run under the “failure to market” provision, even if it successfully challenges the later-expiring patent before the compound patent expires . This rationale undoubtedly will be a factor in such filings, but whether it will spawn a demonstrable trend is too soon to tell.

The requirement to “lawfully maintain” a Paragraph IV certification is a continuing obligation until the time of commercial marketing of the generic drug product. Read in conjunction with the forfeiture provisions, discussed in the next section, the qualification of a first applicant entitled to 180-day generic marketing exclusivity may be extinguished in several circumstances. If a court enters a final, non-appealable judgment of patent infringement and no patent invalidity or unenforceability, the Paragraph IV certification must be changed to a Paragraph III certification requiring that approval of the ANDA await expiration of the patent. 21 C.F.R. § 314.94(a)(12)(viii)(A). Similarly, if a patent is delisted or expires, a Paragraph IV certification changes to a Paragraph I or II certification, respectively. 21 C.F.R. §314.94(a)(12)(viii)(B). These events are contrary to the statutory language requiring an ANDA applicant to “lawfully maintain” a Paragraph IV patent challenge. FDA has been asked to issue guidance clarifying that when an ANDA applicant has litigated and lost a patent infringement case, it must amend its paragraph IV certification to a paragraph III certification for that patent and will no longer qualify as a “first applicant” based on the paragraph III patent certification.

The new 180-day marketing exclusivity provisions were intended to encourage further generic competition and to eliminate lawsuits brought against FDA by generic applicants challenging the award of 180-day marketing exclusivity to generic competitors who may have been first to challenge different Orange Book listed patents for the same listed drug product. It also should have the salutary and practical effect of eliminating “campouts” in the FDA parking lot and the

subsequent dash to have an ANDA application clocked-in “first”. In addition, the new parenthetical language in subparagraph (I) - “(including the commercial marketing of the listed drug)” explicitly recognizes the right of a first applicant to market an “authorized generic” under license from the brand-name drug manufacturer. FDA recently recognized this right in a July 2, 2004 denial of citizens petitions filed by Mylan Pharmaceuticals Inc. and Teva Pharmaceuticals USA Inc. asking FDA to delay marketing approval of authorized generics until the 180-day generic exclusivity period ends.⁷

These provisions also eliminate the “court decision” trigger for starting the 180-day exclusivity period, leaving only a “commercial marketing” trigger that is subject, however, to the new forfeiture provisions (discussed immediately below). The commercial marketing of a generic drug by any first applicant triggers the 180-day generic exclusivity period for all first applicants, whether or not they have received FDA approval.

B. 180 Day Exclusivity Forfeiture Provisions - § 355(j)(5)(D)

A qualified first applicant may later forfeit the right to 180-day marketing exclusivity if a forfeiture event occurs:

(D) FORFEITURE OF 180-DAY EXCLUSIVITY PERIOD.

(i) DEFINITION OF FORFEITURE EVENT.- In this subparagraph, the term “forfeiture event,” with respect to an application under this subsection, means the occurrence of any of the following:

⁷ FDA Supports Broader Access to Lower Priced Drugs, FDA Talk Paper (July 2, 2004), available at <http://www.fda.gov/bbs/topics/answers/2004/ANS01296.html>.

(I) FAILURE TO MARKET- The first applicant fails to market the drug **by the later of -**

(aa) **the earlier of** the date that is -

(AA) **75 days after the date on which the approval of the application of the first applicant is made effective** under subparagraph (B)(iii); **or**

(BB) **30 months** after the date of submission of the application of the first applicant; **or**

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

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

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

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

(II) WITHDRAWAL OF APPLICATION.- The first applicant withdraws the application or the Secretary considers the application to have been withdrawn as a result of a determination by the Secretary that the application does not meet the requirements for approval under paragraph (4).

(III) AMENDMENT OF CERTIFICATION.- The first applicant amends or withdraws the certification for all of the patents with respect to which that applicant submitted a certification qualifying the applicant for the 180-day exclusivity period.

(IV) FAILURE TO OBTAIN TENTATIVE APPROVAL.- The first applicant fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(V) AGREEMENT WITH ANOTHER APPLICANT, THE LISTED DRUG APPLICATION HOLDER, OR A PATENT OWNER.- The first applicant enters into an agreement with another applicant under this subsection for the drug, the holder of the application for the listed drug, or an owner of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV), the Federal Trade Commission or the Attorney General files a complaint, and there is a final decision of the Federal Trade Commission or the court with regard to the complaint from which no appeal (other than a petition to the Supreme Court for a writ of certiorari) has been or can be taken that the agreement has violated the antitrust laws (as defined in section 1 of the Clayton Act (15 U.S.C. 12), except that the term includes section 5 of the Federal Trade Commission Act (15 U.S.C. 45) to the extent that the section applies to unfair methods of competition).

(VI) EXPIRATION OF ALL PATENTS.- All of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired.

(ii) FORFEITURE.- The 180-day exclusivity period described in subparagraph (B)(iv) shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant.

(iii) SUBSEQUENT APPLICANT.- If all first applicants forfeit the 180-day exclusivity period under clause (ii)-

(I) approval of any application containing a certification described in paragraph (2)(A)(vii)(IV) shall be made effective in accordance with subparagraph (B)(iii); and

(II) no applicant shall be eligible for a 180-day exclusivity period.

Comments: The statutory language eliminates the earlier proposed “rollover” feature of 180-day generic exclusivity and simply provides that if any one of the forfeiture events occurs, the first applicant loses 180-day generic exclusivity. In the event there was only one first applicant, then there will be no 180-day generic exclusivity for any applicant if exclusivity is forfeited. The forfeiture provisions, other than “(I) Failure to Market,” are straightforward and are based on the FTC’s July 2002 finding that these types of settlement agreement provisions caused unnecessary delays in generic market entry.

As for the “Failure to market” forfeiture event, it applies independently to each listed patent and boils down to the following:

- If there is no patent infringement litigation against a first applicant, then a first applicant must market its generic drug by the earlier of: 75 days after FDA approval is made effective or 30 months after submitting the ANDA, otherwise exclusivity is forfeited;
 - If there is patent infringement litigation against either a first applicant or any other applicant who has received tentative FDA approval, a first applicant must market its generic drug within 75 days after (i) entry of a final, non-appealable court decision finding patent invalidity or noninfringement, (ii) entry of a final judgment of invalidity or noninfringement embodied in a consent decree or settlement order, or (iii) the patent is delisted, otherwise exclusivity is forfeited.
- If the first applicant loses the patent litigation and a final, non-appealable court judgment of patent infringement and no patent invalidity or unenforceability is

entered, then the first applicant forfeits its “first applicant” status for failing to lawfully maintain a Paragraph IV certification.

5. New Provisions For Declaratory Judgment Actions - 21 U.S.C. § 355(j)(5)(C)(i)

If a patent/NDA holder does not sue for patent infringement within 45 days of receiving notice of a Paragraph IV patent challenge, then the ANDA applicant may bring an action for a declaratory judgment of noninfringement or invalidity under the following conditions:

(C) CIVIL ACTION TO OBTAIN PATENT CERTAINTY.

(i) DECLARATORY JUDGMENT ABSENT INFRINGEMENT ACTION.-

(I) IN GENERAL.- No action may be brought under Section 2201 of title 28, United States Code, by an applicant under paragraph (2) for a declaratory judgment with respect to a patent which is the subject of the certification referred to in subparagraph (B)(iii) unless-

(aa) the 45-day period referred to in such subparagraph has expired;

(bb) neither the owner of such patent nor the holder of the approved application under subsection (b) for the drug that is claimed by the patent brought a civil action against the applicant for infringement of the patent before the expiration of such period; and

(cc) in any case in which the notice provided under paragraph (2)(B) relates to non-infringement, the notice was accompanied by a document described in subclause (III).

(II) FILING OF CIVIL ACTION.- If the conditions described in items (aa), (bb), and as applicable, (cc) of subclause (I) have been met, the applicant referred to in such subclause may, in accordance with section 2201 of title 28, United States Code, bring a civil action under such section against the owner or holder referred to in such subclause (but not against any owner or holder that has brought such a civil action against the applicant, unless that civil action was dismissed without prejudice), for a declaratory judgment that the patent is invalid or will not be infringed by the drug for which the applicant seeks approval, except that such civil action may be brought for a declaratory judgment that the patent will not be infringed only in a case in which the condition described in subclause (I)(cc) is applicable. A civil action referred to in this subclause shall be

brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(III) OFFER OF CONFIDENTIAL ACCESS TO APPLICATION.-
For purposes of subclause (I)(cc), the document described in this subclause is a document providing **an offer of confidential access to the application that is in the custody of the applicant under paragraph (2) for the purpose of determining whether an action referred to in subparagraph (B)(iii) should be brought.** The document providing the offer of confidential access shall contain such restrictions as to persons entitled to access, and on the use and disposition of any information accessed, as would apply had a protective order been entered for the purpose of protecting trade secrets and other confidential business information. **A request for access to an application under an offer of confidential access shall be considered acceptance of the offer of confidential access with the restrictions as to persons entitled to access, and on the use and disposition of any information accessed, contained in the offer of confidential access, and those restrictions and other terms of the offer of confidential access shall be considered terms of an enforceable contract.** Any person provided an offer of confidential access shall review the application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the certification under paragraph (2)(A)(vii)(IV) and for no other purpose, and may not disclose information of no relevance to any issue of patent infringement to any person other than a person provided an offer of confidential access. Further, the application may be redacted by the applicant to remove any information of no relevance to any issue of patent infringement. . . .

Comments: This new section of the Hatch-Waxman Act is consistent with prior law in precluding any declaratory judgment action during the 45-day statutory period during which the patent/NDA holder may decide to sue for patent infringement. The new law clarifies that no such declaratory judgment action may be brought if the patent/NDA holder brings suit within 45 days. The provision also leaves unchanged the requirement that any declaratory judgment action be brought in a judicial district where the defendant maintains its principal place of business or a regular and established place of business.

These new provisions specifically authorize an ANDA applicant, who has filed a Paragraph IV certification and who has not been sued for patent infringement within the 45 day statutory period, to file a declaratory judgment action seeking a judgment of patent invalidity, noninfringement or both. The ANDA applicant must provide an offer of confidential access to its ANDA with its Paragraph IV certification notice sent to the patent/NDA holder in order to bring a declaratory judgment action for noninfringement of the patent being challenged. Failure to provide a timely offer of confidential access precludes a declaratory judgment action for noninfringement. The offer of confidential access is intended to allow the patent owners to make an informal decision about whether to sue for patent infringement during the 45-day statutory period while also providing ANDA applicants with “patent certainty.” If the patent owner requests access to the applicant’s ANDA, the request is considered an acceptance of the offer of confidential access, and the restrictions in the offer become terms of an enforceable contract.

The jurisdictional requirement of a “reasonable apprehension” of being sued was heavily debated in the House-Senate Conference. While acknowledging that the conferees do not intend for the courts to modify their application of “reasonable apprehension” subject matter jurisdiction, the conferees also explicitly stated that they expect the courts to apply the reasonable apprehension test in a manner that gives generic drug manufacturers “appropriate access” to declaratory judgment relief, citing the Federal Circuit decision in *Vanguard Research v. Peat, Inc.*, 304 F.3d 1249 (Fed. Cir. 2002). The case of *Teva Pharmaceuticals USA, Inc. v.*

Pfizer, Inc., No. 03-CV-10167, 2003 U.S. Dist. LEXIS 21940 (D. Mass. Dec. 8, 2003), decided on the same day that MMA was signed into law, was prescient in having granted Pfizer's motion to dismiss Teva's declaratory judgment action of non-infringement precisely because of a failure to meet the "reasonable apprehension" standard, even in the face of Pfizer's refusal to grant Teva a covenant not to sue. In two remarkably similar analyses, district courts in New Jersey and Delaware have refused to find declaratory judgment jurisdiction, even though patent/NDA holders had listed patents in the Orange Book, refused to grant a covenant not to sue and otherwise had generally exhibited "litigious tendencies" with respect to other Orange Book listed patents. See *Glaxo Group Ltd. v. Dr. Reddy's Laboratories Ltd.*, No. 01-4066, 2004 WL 1304053 (D.N.J. May 28, 2004) (unpublished opinion and order); *Torpharm Inc. v. Pfizer Inc.*, No. 03-990-SLR, 2004 WL 1465756 (D. Del. June 28, 2004).

6. New Provisions For A Counterclaim To Correct Or Delist A Patent Listed In The Orange Book - 21 U.S.C. § 355(j)(5)(C)(ii)

An ANDA applicant may now assert a counterclaim challenging the propriety of a patent/NDA holder's listing of a patent in the Orange Book:

(ii) COUNTERCLAIM TO INFRINGEMENT ACTION.

(I) IN GENERAL.- If an owner of the patent or the holder of the approved application under subsection (b) for the drug that is claimed by the patent or a use of which is claimed by the patent brings a patent infringement action against the applicant, the applicant may assert a counterclaim seeking an order requiring the holder to correct or delete the patent information submitted by the holder under subsection (b) or (c) on the ground that the patent does not claim either-

(aa) the drug for which the application was approved, or

(bb) an approved method of using the drug.

(II) NO INDEPENDENT CAUSE OF ACTION.- Subclause (I) does not authorize the assertion of a claim described in subclause (I) in any civil action or proceeding other than a counterclaim described in subclause (I).

(iii) NO DAMAGES- An applicant shall not be entitled to damages in a civil action under clause (i) or a counterclaim under clause (ii).

Comments: In order to list a patent in the Orange Book, the NDA holder must certify that the patent either claims the approved drug or an approved method of using the drug. In the past, when disputes arose between an ANDA applicant and the patent/NDA holder regarding the propriety of listing a patent, FDA required only that the patent/NDA holder explain and re-certify why the patent met the listing requirements, taking the view that FDA did not have the expertise or authority to make substantive judgments concerning patent claim scope. In one such dispute, Mylan Pharmaceuticals challenged the listing and asked for a preliminary injunction ordering Bristol Myers Squibb and FDA to delist a patent regarding Bristol Myers' BuSpar® (buspirone) anti-anxiety medicine. The Federal Circuit reversed the grant of the preliminary injunction for lack of subject matter jurisdiction. *Mylan Pharmaceuticals, Inc. v. Thompson*, 268 F.3d 1323 (Fed. Cir. 2001).

These new provisions are a response to the Mylan decision, but limit patent listing challenges exclusively to counterclaims in patent infringement actions. ANDA applicants do not have any independent cause of action to challenge a listed patent; only a right of counterclaim when sued for infringement of such patent. The statute provides for injunctive relief ordering the correction or deletion of the

patent information in the Orange Book. The ANDA applicant is not entitled to seek damages on the counterclaim.

7. **FTC and DOJ Review of Settlement Agreements**

All agreements resolving Paragraph IV patent challenges must now be filed with the FTC and Department of Justice Antitrust Division for possible review:

Section 1112 NOTIFICATION OF AGREEMENTS:

(a) AGREEMENT WITH BRAND NAME DRUG COMPANY-

(1) REQUIREMENT.- A generic drug applicant that has submitted an ANDA containing a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act and a brand name drug company that enter into an agreement described in paragraph (2) shall each file the agreement in accordance with subsection (c). The agreement shall be filed **prior to the date of the first commercial marketing of the generic drug that is the subject of the ANDA. . . .**

(b) AGREEMENT WITH ANOTHER GENERIC DRUG APPLICANT-

(1) REQUIREMENT.- A generic drug applicant that has submitted an ANDA containing a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act with respect to a listed drug and another generic drug applicant that has submitted an ANDA containing such a certification for the same listed drug shall each file the agreement in accordance with subsection (c). The agreement shall be filed **prior to the date of the first commercial marketing of either of the generic drugs for which such ANDAs were submitted. . . .**

(c) FILING.-

(1) AGREEMENT.- The parties that are required in subsection (a) or (b) to file an agreement in accordance with this subsection shall file with the Assistant Attorney General and the Commission the text of any such agreement, except that such parties are not required to file an agreement that solely concerns-

(A) purchase orders for raw material supplies;

- (B) equipment and facility contracts;
- (C) employment or consulting contracts; or
- (D) packaging and labeling contracts. . . .

Section 1113 FILING DEADLINES

Any filing required under section 1112 shall be filed with the Assistant Attorney General and the Commission **not later than 10 business days after the date the agreements are executed.** . . .

Section 1115 ENFORCEMENT:

(a) CIVIL PENALTY.- Any brand name drug company or generic drug applicant which fails to comply with any provision of this subtitle shall be liable for a civil penalty of not more than \$11,000, for each day during which such entity is in violation of this subtitle. Such penalty may be recovered in a civil action brought by the United States, or brought by the Commission in accordance with the procedures established in section 16(a)(1) of the Federal Trade Commission Act (15 U.S.C. 56(a)).

(b) COMPLIANCE AND EQUITABLE RELIEF.- If any brand name drug company or generic drug applicant fails to comply with any provision of this subtitle, the United States district court may order compliance and may grant such other equitable relief as the court in its discretion determines necessary or appropriate, upon application of the Assistant Attorney General or the Commission.

Comments: These new provisions embody the second major recommendation of the FTC's July 2002 generic drug study to allow the FTC to review settlement agreements resolving Hatch-Waxman patent litigation triggered by Paragraph IV certifications. The procedure allows the FTC and DOJ Antitrust Division to review such agreements before commercial marketing of a generic drug and to file an action for violation of the antitrust laws. Settlement agreements must be filed within 10 business days of execution and prior to the commercial marketing of the generic drug. An antitrust action brought by the FTC or Department of

Justice, Antitrust Division can lead to civil penalties, forfeiture of 180-day generic exclusivity (see §S 355(j)(5)(D)(i)(V), *supra* at pp. 12-13) and an injunction.

8. Bioavailability and Bioequivalence - 21 U.S.C. § 355(j)(8)

An ANDA applicant must provide FDA with information to show that the proposed generic drug is bioequivalent to the RLD:

(A) (i) The term “bioavailability” means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(ii) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may assess bioavailability by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or therapeutic ingredient becomes available at the site of drug action.

* * *

(C) For a drug that is not intended to be absorbed into the bloodstream, the Secretary may establish alternative, scientifically valid methods to show bioequivalence if the alternative methods are expected to detect a significant difference between the drug and the listed drug in safety and therapeutic effect.

Comments: These amendments codify existing FDA practice with regard to the assessment of bioavailability and bioequivalence. Subparagraph (A)(ii) adds a specific reference to drugs that are not intended to be absorbed into the bloodstream and permits flexibility for FDA to establish “scientifically valid measurements” to measure and assess bioavailability . The same flexibility is provided for the measurement and assessment of bioequivalence in subparagraph (C).

CONCLUSION

These are the MMA Hatch-Waxman amendments in brief. FDA has yet to weigh in with revised regulations and guidance on the definition of a “listed drug.” District Courts are already interpreting some of these provisions, and the Federal Circuit will be reviewing these decisions for years to come. This brief primer will be a handy reference for understanding the intellectual property issues raised by this significant legislation.