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CHANGES TO HATCH-WAXMAN UNDER THE MEDICARE PRESCRIPTION DRUG, IMPROVEMENT, AND MODERNIZATION ACT OF 2003

This advisory is part of a series explaining the epic Medicare legislation passed by Congress and signed into law by President Bush in December and discussing its impact on the health care and life sciences industries. Notably, this advisory reflects invaluable input from two new members of our health care and legislative practices: Thomas A. Scully and Colin Roskey. Prior to joining Alston & Bird, Mr. Scully was the Administrator of the Centers for Medicare and Medicaid Services and a key player in developing this historic legislation for the Bush administration. Until recently, Mr. Roskey was Counsel and Health Policy Advisor to the Senate Finance Committee, reporting to Chairman Charles E. Grassley (R-IA), and was also instrumental in passage of the Medicare bill. They were joined in the preparation of this advisory by W. Murray Spruill, Partner and Chairman of the Biotechnology and Pharmaceutical Patent Group, and Edward R. Ergenzinger, Associate in the Biotechnology and Pharmaceutical Patent Group.

On December 8, 2003, President George Bush signed landmark health care legislation into law that adds a voluntary outpatient prescription drug benefit to Medicare and makes other significant reforms to the 35-year old federal health insurance program for the elderly and disabled. While much of the focus on this law has understandably been directed toward provisions affecting sweeping Medicare reforms, other provisions significantly change procedures associated with the entry of generic drugs into the marketplace.

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This advisory addresses key statutory changes to the Hatch-Waxman Act[1] included under Title XI of the Medicare Prescription Drug, Improvement and Modernization Act of 2003 (the Act).[2] Specifically, the discussion below will provide a very general overview of Hatch-Waxman with specific emphasis on sections of relevance to the Act, identify those changes to Hatch-Waxman as a result of the Act, and spotlight some of the implications of these changes for both generic and brand name drug companies.

[1] The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585(codified as amended at 21 U.S.C. § 355; 28 U.S.C. § 2201; 35 U.S.C. §§ 156, 271, 282) (commonly known as the Hatch-Waxman Act).

[2] Pub. L. No. 108-173, 117 Stat. 2066 (the Act) (unless otherwise noted, references to section numbers refer to sections of the Act).

HATCH-WAXMAN: OVERVIEW AND GOALS

The Hatch-Waxman Act represented an attempt at balancing the interests of the health care system in making lower cost generic drugs more widely available, and the interests of the patent system in providing incentives to develop new drugs. [3]

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In order to encourage competitors to bring cheaper, generic copies of drugs to the market, Hatch-Waxman established processes to: 1) expedite the approval of generic copies of pioneer drugs; 2) resolve patent challenges prior to generic entry; 3) provide a period of marketing exclusivity to generic manufacturers who challenge patents under certain circumstances; and 4) provide a "safe harbor" whereby use of patented drugs and drug products by generic companies is not an act of infringement if conducted for reasons reasonably related to submission of information to the FDA or other federal regulatory agency.

By contrast, in order to preserve market incentives to innovate, Hatch-Waxman allowed for the restoration of patent term arising from pre-market testing and approval procedures required by the FDA[4], and provided additional non-patent market exclusivity for certain drug innovations.

For the purpose of this advisory, a few of these provisions are of particular interest and are described in more detail below.

Abbreviated New Drug Applications

Hatch-Waxman established an expedited process for the approval of generic copies of pioneer drugs through the creation of an Abbreviated New Drug Application (ANDA). ANDAs allow generic manufacturers to avoid costly development of data required by the Food and Drug Administration (FDA) on the safety and efficacy of their products if they can show that their products are both the same as and "bioequivalent" to the brand name drug. By "same" is meant that the active ingredient, route of administration, dosage form, strength, and labeling are the same as that of the name brand drug or drug product.[5] "Bioequivalency" is achieved if the rate and extent of absorption of the generic drug's active ingredient are shown not to bear significant differences from the name brand's drug.[6]

Patent Challenges Prior to Generic Entry

Under Hatch-Waxman, patent disputes can be resolved before generic entry through a complex system predicated on requirements for brand name and generic companies to provide certain information about their drugs and drug

[3] For a more detailed description of provisions of Hatch-Waxman, see Elizabeth Stotland Weiswasser & Scott D. Danzis, The Hatch-Waxman Act: History, Structure, and Legacy, 71 Antitrust L.J. 585-608 (2003).

[4] 35 U.S.C. § 156(c).

[5] 21 U.S.C. § 355(j)(2)(A); 21 C.F.R. § 314.94(a)(5).

[6] 21 U.S.C. § 355(j)(8)(B).

products to the FDA. Brand name drug companies are required to submit patent information to the FDA on any drug or method of using a drug; information that is then listed in the *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book). Any ANDA applicants seeking to market a drug must make one of the following certifications:

I. that there are no patents listed in the Orange Book for the drug (a "Paragraph I" certification);

II. that the relevant patent has expired (a "Paragraph II" certification);

III. that the generic manufacturer will not seek approval of the ANDA until after the relevant patent expires (a "Paragraph III" certification); or

IV. that the relevant patent is invalid or will not be infringed by the manufacture, use, or sale of the new generic drug (a "Paragraph IV" certification).[7]

Although Paragraph I – III certifications are usually fairly straightforward, a Paragraph IV certification triggers additional provisions of the act that can result in litigation between the brand name and generic drug companies. ANDA applicants filing Paragraph IV certifications are required to provide notice to the patent holder, who then has 45 days to file a patent infringement suit. During that 45-day period, Hatch-Waxman precluded the filing of a declaratory judgment action by the ANDA applicant.[8] If a lawsuit is filed, the FDA must stay final approval of the ANDA until either a court decision, the patent expires, or 30 months from the patent holder's receipt of notice of the Paragraph IV certification.

Marketing Exclusivity for Generic Manufacturers

Hatch-Waxman provides a 180-day period of marketing exclusivity to the first generic manufacturer to file an ANDA with a Paragraph IV certification.[9] The original goal of this provision was to encourage challenges of patents by ensuring that a second generic manufacturer would not get a "free ride" by enjoying the benefits of the litigation efforts of the first. Under Hatch-Waxman, this period of marketing exclusivity is later triggered by either the "first commercial marketing" of the generic drug or a "court decision" holding the relevant patent covering the brand name drug invalid or not infringed.

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CHANGES TO HATCH-WAXMAN UNDER THE ACT

Title XI of the Act, entitled "Access to Affordable Pharmaceuticals," includes substantive changes to a number of the provisions in Hatch-Waxman described above. These changes include: 1) the definition of bioequivalence; 2) provisions governing 30-month stays; 3) provisions dealing with 180-day exclusivity; 4) the ability of generic companies to seek declaratory

[7] 21 U.S.C. § 355(j)(2)(A)(vii).

[8] 21 U.S.C. § 355(j)(5)(B)(iii).

[9] 21 U.S.C. § 355(j)(5)(B)(iv).

judgments concerning listed patents; and 5) the ability of an ANDA applicant to counterclaim to remove a patent from the Orange Book.

Bioequivalence

Because Hatch-Waxman defined bioequivalence as the lack of a significant difference between the proposed drug and the listed drug in the rate and extent of absorption, bioequivalence determinations for drugs not intended to be absorbed into the bloodstream were not encompassed. The Act codified regulations the FDA had promulgated to address this shortcoming by providing that the FDA 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."

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Thirty-Month Stays

In some cases, a brand name drug company will obtain additional patents around a drug or drug product after the filing of an ANDA, usually to improved formulations, dosage ranges, or drug delivery. For years, if the brand name drug company submitted information on an additional patent to the FDA, within 30 days of having the patent issued by the patent office, the holder of an ANDA was required to file a certification on the later-listed patent. If the certification is under Paragraph IV, the FDA's traditional view was to allow the notified parties to file suit with each new certification and receive a non-concurrent 30-month stay. On August 18, 2003, the FDA promulgated a regulation that limited brand name drug companies to a single 30-month stay per ANDA.[10]

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The Act codifies the FDA regulation limiting brand name companies to a single 30-month stay per ANDA and will apply to any patent information submitted on or after the date the FDA promulgated its regulation in August 2003. The Act also codified a practice by the FDA of approving an ANDA if a U.S. District Court found the relevant patent invalid or not infringed prior to the expiration of the stay, or if the district court found the patent valid and infringed and that decision was overturned by a court of appeals prior to the expiration of the stay.

Finally, under the Act, an ANDA applicant may not amend or supplement an application to change the drug originally identified in the application unless seeking approval of a different strength of the drug.

One Hundred Eighty-Day Exclusivity

The Act stipulates that the 180-day marketing exclusivity awarded to the first generic manufacturer to file an ANDA with a Paragraph IV certification may only be triggered on the first commercial marketing of the generic drug, and not by a court decision. This exclusivity is applied on the basis of a

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[10] Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676 (June 18, 2003) (final rule).

given product, not on individual patents around a given product. However, an ANDA applicant will forfeit its eligibility for exclusivity if any of the following occur:

- The applicant fails to market the drug within 75 days of approval or within 30 months after submission of the ANDA;
- The applicant fails to market the drug within 75 days after any final U.S. Court of Appeals decision on each of the patents that earned the applicant eligibility for the exclusivity;
- The applicant withdraws the ANDA or amends each of the paragraph IV certifications;
- The applicant fails to obtain a tentative approval within 30 months;
- The applicant enters into an agreement found to be in violation of the antitrust laws;
- All the patents that earned the applicant eligibility for the exclusivity expire.

Finally, the legislation provides that for ANDAs, in which Paragraph IV certifications were made before the date of enactment of the Act, and for which the 180-day exclusivity has not yet been triggered, a "court decision" for purposes of the current exclusivity trigger means a U.S. Court of Appeals.

The FDA originally interpreted "court decision" under Hatch-Waxman to mean a final judgment from which no appeal can be taken; an interpretation that was subsequently rejected by the D.C. District Court.[11] The FDA then published a Guidance Document in 2000 that adopted a definition of "court decision" to mean "the first court that renders a decision finding the patent at issue invalid, unenforceable, or not infringed."[12] Therefore, this provision in the Act clarifies confusion on the meaning of "court decision" for those cases that carry over from before enactment of the Act.

The Act permits generic applicants to file declaratory judgment actions if the brand name drug companies have not filed infringement suits within the 45-day period.

Declaratory Judgments

Under Hatch-Waxman, if the brand name drug company does not sue after receiving notice that a Paragraph IV certification has been filed, the ANDA applicant can receive approval after the FDA completes its review of the application. At that time, the brand name drug company can file an infringement action. This has been argued to create uncertainty about the marketability of the drug or drug product. To avoid creating this uncertainty, the Act permits generic applicants to file declaratory judgment actions if the brand name drug companies have not filed infringement suits within the 45-day period.

[11] *Mylan Pharms., Inc. v. Shalala*, 81 F. Supp. 2d 30, 38-43 (D.D.C. 2000).

[12] *See* Food & Drug Admin., Center For Drug Evaluation & Research, *Guidance For Industry: Court Decisions, ANDA Approvals, And 180-Day Exclusivity Under The Hatch-Waxman Amendments To The Federal Food, Drug, And Cosmetic Act (2000), available at* http://www.fda.gov/cder/guidance/3659fnl.htm

Counterclaims to Remove Patents From the Orange Book

The Act also allows an ANDA applicant, that has been sued for patent infringement, to assert a counterclaim seeking an order requiring the original New Drug Applicant to correct or delete patents listed in the Orange Book when the listed patent does not claim the drug for which the application was approved, or does not claim an approved method of using the drug. No damages are available under such a counterclaim and this section of the Act does not provide an independent cause of action.

IMPACT ON GENERIC AND BRAND NAME DRUG COMPANIES

Generic manufacturers in particular have lauded the Act as a significant victory that will provide timely and affordable access to pharmaceuticals for all Americans.[13] Although several of the provisions relating to Hatch-Waxman merely provide statutory authority for regulations promulgated by the FDA (e.g., limiting brand name drug companies to a single 30-month stay or defining bioequivalence for non-systemic drugs and drug products), other provisions dealing with 180-day exclusivity periods, declaratory judgments, and counterclaims by ANDA applicants present more significant changes.

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By contrast, although brand name drug and biotechnology companies have been quick to praise provisions of the Act that provide a Medicare prescription drug benefit and expansion of access to biotechnology products, their comments on Hatch-Waxman reform provisions have been more subdued.[14] Some areas where these companies are likely to be concerned are: 1) the abandonment of the "court decision" trigger for the180-day exclusivity period in favor of forfeiture provisions; and 2) ANDA applicant counterclaims.

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Abandonment of the "Court Decision" Trigger

Before the Act, there was a disincentive for generics to bring challenges to the patents around a given drug early in their terms because many brand name companies hold multiple patents around a given drug (e.g., the compound itself, methods of using the compound, manufacturing processes, formulations, etc.), and chances were good that at least one of the patents would survive the challenge (usually the original patent around the compound itself). If any of those patents survived, then the 180 day exclusivity period, triggered by the other findings of invalidity or non-infringement, would run out while there was time remaining in the surviving patent's term and the generic company would be unable to take advantage of their exclusivity period.

[13] Press Release, Generic Pharmaceutical Association, Consumers Score Landmark Victory with Medicare Passage (Nov. 25, 2003), *available at* http://www.prnewswire.com/micro/gpha.

[14] Statement by Alan F. Holmer, President and CEO, Pharmaceutical Research and Manufacturers Association (PhRMA), Signing of the Medicare Prescription Drug Benefit into Law (Dec. 8, 2003), *available at* http://www.phrma.org/mediaroom/press/releases/08.12.2003.877.cfm; Fact sheet of the Biotechnology Industry Organization (BIO), Hatch-Waxman Reform Provisions (Dec. 3, 2003), *available at* http://www.bio.org/medicare/factsheets/HatchWaxman_120303.pdf.

Under the Act, the trigger due to a court decision is replaced by a set of forfeiture provisions that can defeat the 180-day exclusivity period and that can be held until the challenged patent expires. This allows generic companies to "bank" their 180-day exclusivity period and pull it out at the end of the patent term. With no disincentive for generic companies to challenge patents early in their terms, some pharmaceutical executives have maintained that generic companies would be encouraged to pursue early and speculative challenges of patents, and that brand name drug companies would be faced with greater up-front costs associated with drug development.[15]

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Whether these effects will materialize remains to be seen.

ANDA Applicant Counterclaims

For some time, ANDA filers have sought to escape the 30-month stay by attacking the Orange Book listing for the patent at issue. In every case, the Federal Circuit held that there was no jurisdiction under the Patent Act to entertain an attack on an Orange Book listing, and that the FDA acted lawfully in deciding not to spend scarce agency resources to decide whether a particular patent should have been listed in the Orange Book. Brand name drug companies can therefore expect additional challenges as details of how courts will deal with this provision are worked out, such as allowing the delisting counterclaim to be litigated before the merits of the infringement claim; conducting discovery simultaneously; or deferring resolution of the infringement claim until after the delisting claim is resolved.

Until then, brand name drug companies will have to deal with uncertainty when faced with litigation arising from a Paragraph IV certification from an ANDA applicant.

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The Silver Lining

Brand name drug companies should take solace, however, in the fact that a provision in an early Senate version of the Medicare bill would have authorized a court, in awarding a remedy for patent infringement, to refuse to award treble damages if it determined that the patent holder did not meet statutory requirements for filing patent information. The proposal was aimed at punishing the patentee for not listing necessary patents in the Orange Book, but appeared to go beyond merely denying the benefits accrued by listing patents in the Orange Book (e.g., patent certifications by generic applicants and the ability to obtain a 30-month stay).

Luckily, for brand name drug companies, the Act did not incorporate this provision in its final form.

[15] Hearings on S. 1 Before the Senate Committee on the Judiciary, 108th Cong. (2003)(statement of Robert Armitage, Vice President and General Counsel, Eli Lilly & Co.).

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