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UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

WESTERN DIVISION

AMERICAN BIOSCIENCE, INC., Plaintiff, v. BRISTOL-MYERS SQUIBB COMPANY, and DOES 1- though 10, inclusive, Defendants.	Case No. CV-00-08577 WMB (AJWx) BRIEF OF FEDERAL TRADE COMMISSION AS AMICUS CURIAE

The United States Âé¶¹´«Ã½ Trade Commission ("FTC") files this brief as Amicus Curiae to alert the Court to the potential anti-competitive ramifications of court approval of the proposed settlement between American Bioscience, Inc. ("ABI") and Bristol-Myers Squibb Co. ("Bristol"). Because the Commission has just recently initiated an investigation of the conduct of ABI and Bristol, the Commission does not presently take a position with regard to the fact that ABI and Bristol have agreed to settle their dispute. However, the precise terms of the settlement that the parties ask this Court to approve do raise potential competitive issues. The parties seek court approval of a Final Order and Judgment which asks this Court to find that U.S. Patent No. 6,096,331 ("the '331 patent") must be listed in the Food and Drug Administration's ("FDA") "Orange Book" and to order Bristol to maintain that listing. The Commission is concerned that a judicial finding that the patent meets the statutory requirements for listing in the Orange Book will prejudice parties who may later challenge the listing.

I. INTEREST AND EXPERTISE OF THE FEDERAL TRADE COMMISSION

The FTC's mission is to protect consumers. It is an independent administrative agency charged with promoting the efficient functioning of the marketplace by taking law enforcement action against commercial practices injurious to consumers and against conduct that harms competition. The Commission enforces, *inter alia*, Section 5 of the Âé¶¹´«Ã½ Trade Commission Act, which prohibits "unfair methods of competition."[1]

[1] 15 U.S.C. § 45.

The Commission recently commenced an investigation of the conduct of Bristol and ABI involving Taxol to determine whether such conduct may restrict competition and harm consumers.

The Commission has significant expertise concerning competition in the pharmaceutical industry. In particular, the Commission has brought a number of antitrust enforcement activities affecting both the branded and generic drug industries.[2] The staff of the FTC's Bureau of Economics has recently released an in-depth report of competition issues in the pharmaceutical industry.[3] In addition, the Commission commented twice in the past year to the FDA[4] concerning its implementation of the Hatch-Waxman Act, which encourages the introduction of

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[2] *See, e.g.*, *Âé¶¹´«Ã½ Trade Commission v. Mylan Laboratories, Inc. et al.*, 1999-2 Trade Cas. (CCH) ¶72,573 (D.D.C. 1999); *Roche Holding Ltd.*, C-3809 (February 25, 1998) (consent order); *Ciba-Geigy, Ltd.*, 123 F.T.C. 842 (1997) (consent order); *Hoechst AG*, 120 F.T.C. 1010 (1995) (consent order). For a discussion of all FTC pharmaceutical enforcement actions, *see* FTC Antitrust Actions Involving Pharmaceutical Services and Products, <http://www.ftc.gov/bc/rxupdate>; *see also* David A. Balto & James Mongoven, Antitrust Âé¶¹´«Ã½ in Pharmaceutical Industry Mergers, 54 *Food & Drug Law Journal*, 255 (1999).

[3] Staff of the Âé¶¹´«Ã½ Trade Commission, "The Pharmaceutical Industry: A Discussion of Competitive and Antitrust Issues in an Environment of Change" (March 1999) <http://www.ftc.gov/reports/pharmaceutical/drugexsum.htm>.

[4] FTC Staff Comments to the Food and Drug Administration, Citizen Petitions (March 2, 2000); FTC Staff Comments to the Food and Drug Administration, 180-Day Exclusivity Period for Generic Drugs (November 4, 1999), <http://www.ftc.gov/be/advofile.htm>.

generic drugs while protecting the incentives of brand drug companies to invest in new drug development.[5]

In two recent cases, the Commission charged brand and generic drug companies with entering into anticompetitive settlement agreements that delayed or were intended to delay generic drug competition. In one of these matters, the administrative complaint charged that Hoechst Marion Roussel (now Aventis), the maker of Cardizem CD, a widely prescribed drug for treatment of hypertension and angina, paid Andrx Corporation over $80 million to refrain from bringing its competing generic drug, or any other non-infringing version, to market during patent infringement litigation.[6] The complaint further alleged that Andrx's agreement not to market its product was intended to delay the entry of other generic drug competitors, thereby denying consumers access to lower priced generic drugs. The effect of delaying other generic competitors flows from the fact that the Hatch-Waxman Act grants an exclusive 180-day marketing right to the first generic entrant, in this case Andrx.[7] This case is set for trial on December 5, 2000, before an administrative law judge.

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[5] *See* H.R.Rep. No.98-857(I), at 14-15 (1984), reprinted in 1984 U.S.C.C.A.N. 2647-48 (stating that the purposes of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as "the Hatch-Waxman Act," are “to make available more low cost generic drugs [and] to create a new incentive for increased expenditures for research and development of certain products which are subject to pre-market approval”).

[6] *Hoechst Marion Roussel, Inc.*, Docket 9293 (March 16, 2000) (complaint), <http://www.ftc.gov/os/2000/03>.

[7] 21 U.S.C. § 355(j)(5)(B)(iv).

The Commission's complaint against two other companies, Abbott Laboratories and Geneva Pharmaceuticals, Inc., involved allegations of similar conduct in connection with a proprietary drug (Hytrin) that Abbott manufactures and a generic version that Geneva prepared to introduce.[8] The complaint charged that Abbott paid Geneva approximately $4.5 million per month to keep Geneva's generic version of the drug off the U.S. market, potentially costing consumers hundreds of millions of dollars a year. This agreement also allegedly delayed the entry of other generic versions of Hytrin because of Geneva's 180-day exclusivity rights under the Hatch-Waxman Act. Both companies agreed to settle, and the Commission issued final orders in May.[9]

II. BACKGROUND

As with the Commission's recent cases involving Hoechst, Andrx, Abbott and Geneva, the potential anticompetitive effects of the proposed settlement between ABI and Bristol flow from the role that generic drugs play in the pharmaceutical marketplace and the statutory framework governing FDA approval of those generics.

A. Generic Drug Entry Into the Marketplace

Generic drugs, which contain active ingredients that are chemically identical to their branded counterparts, typically are sold at substantial discounts from the branded price. The first

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[8] *Abbott Laboratories, C-3945 (*May 26, 2000) (Analysis to Aid Public Comment), <http://www.ftc.gov/os/2000/03>.

[9] *Abbott Laboratories, C-3945 (*May 26, 2000) (consent order); *Geneva Pharmaceuticals, Inc.*, C-3946 (May 26, 2000) (consent order), <http://www.ftc.gov/os/2000/05>.

generic manufacturer to enter the market typically charges 70% to 80% of the brand manufacturer's price. As additional generic versions of the same drug enter the market, the price continues to drop, sometimes decreasing to a level of 50% or less of the brand price.[10] The benefits to consumers are dramatic. A Congressional Budget Office Report estimates that consumers saved $8 to $10 billion on prescription drugs at retail pharmacies in 1994 by purchasing generic drugs instead of brand name products.[11] Within the next 4 years, patents on 33 drugs, representing over $14 billion in sales, will expire.[12] The successful entry of generic versions of those drugs will affect dramatically the amount that consumers pay for those drugs.

Taxol, an anti-cancer drug sold by Defendant Bristol, had 1999 U.S. sales of one billion dollars.[13] The availability of a generic version of Taxol would significantly reduce its cost to consumers, potentially saving them hundreds of millions of dollars in the aggregate. Ivax Corp. announced August 29, 2000, that it received tentative approval from the FDA to market its

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[10] Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry* (July 1998) <http://www.cbo.gov>.

[11] *Id.* at xiii, 13.

[12] Amy Barrett, "Crunch Time in Pill Land," Business Week 52 (November 22, 1999).

[13] Scott Hensley, "Bristol-Myers Move May Slow Taxol Challengers," Wall Street Journal, B2 (August 16, 2000).

generic version of Taxol.[14] Only Brisol's listing of the '331 patent in the Orange Book prevents full FDA approval and Ivax's marketing of generic Taxol.[15] Several other applications to market generic Taxol are currently pending before the FDA[16]. ABI acknowledges that one or more of these "could be granted approval by that agency, literally any day."[17]

B. Hatch-Waxman Act

The Hatch-Waxman Act establishes the statutory framework for the FDA's approval of generic drugs, as well as procedures for considering patent claims that may cover those drugs. This Act complements and builds on the procedures for approving new branded drugs. The FDA approves a new branded drug through the filing of a New Drug Application (NDA).[18] In accordance with 21 U.S.C. § 355(b)(1), an NDA must list each patent which "claims the drug or a method of using the drug" and "with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in

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[14] Glenn Singer, "Miami-Based Firm May Face Delay in Marketing Cancer Drug," Knight Ridder/Tribune, (August 30, 2000), <http://www.ventius.com/library.nsf>.

[15] *Id.*

[16] *Bristol-Myers Squibb Co. v. Ben Venue Lab.*, 90 F. Supp.2d 522 (D.N.J. 2000).

[17] ABI Application for Temporary Restraining Order at 3 (August 10, 2000); ABI First Amended Complaint, ¶¶ 22-23; *see also* Scott Hensley, "Bristol-Myers Move May Slow Taxol Challengers," Wall Street Journal, B2 (August 16, 2000) (stating that FDA approval of a generic version of Taxol was expected this summer).

[18] 21 U.S.C. § 355(a).

the manufacture, use or sale of the drug."[19] Once the FDA approves the NDA, the patents submitted with the application are listed in the FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book."[20] The listing of patents in the Orange Book which issue after approval of the NDA is governed by 21 U.S.C. § 355(c)(2), which establishes the same criteria for patent listing as does section 355(b)(1), quoted above. Only the NDA holder may request that the FDA list patents in the Orange Book.[21]

As described below, the listing of a patent in the Orange Book has significant legal effects. However, "the FDA's listing should not create any presumption that [a] patent was correctly listed."[22] The FDA has stated that it lacks the resources and the expertise to review patents submitted with NDAs. The agency does not ensure that patent information is complete and relevant to an approved drug before publishing it in the Orange Book.[23]

The Hatch-Waxman Act promotes generic drug entry by streamlining the FDA's approval process for generic drugs. A generic drug manufacturer may seek expedited approval to market a

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[19] 21 U.S.C. § 355(b)(1). The pertinent FDA regulation, 21 C.F.R. § 314.53(b), essentially parrots the statute and elaborates upon it by giving examples of the type of patents which may be listed in the Orange Book.

[20] 21 U.S.C. § 355(j)(7)(A)(iii).

[21] 21 U.S.C. § 355(b)-(c).

[22] *Ben Venue Lab., Inc. v. Novartis Pharmaceutical Corp.*, 10 F. Supp. 2d 446, 456 (D.N.J. 1998).

[23] 59 Fed. Reg. 50338, 50343 (October 3, 1994).

generic version of an already-approved drug by submitting an Abbreviated New Drug Application (ANDA).[24] While performing development work necessary to seek such approval, a generic drug manufacturer is free from liability for patent infringement.[25] If a patent listed in the Orange Book has not expired, however, the generic drug manufacturer seeking approval of an ANDA must certify either that the generic drug will not enter the market before the patent's expiration date (a paragraph III certification), or that the patent is "invalid or will not be infringed by the manufacture, use, or sale of the drug for which the [ANDA] is submitted" (a paragraph IV certification).[26]

If the ANDA contains the paragraph IV certification of invalidity or non-infringement, the generic drug manufacturer must notify the patent owner and the NDA holder. If the patent owner disagrees with the certification and sues the ANDA applicant for patent infringement within forty-five days of notification, the Hatch-Waxman Act prohibits the FDA from approving the ANDA for 30 months.[27] (An NDA holder who is not also the patent owner may sue as co-plaintiff with the patent owner if it is the exclusive patent licensee.[28]) This automatic stay forestalls the sale of the generic drug for 30 months,

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[24] 21 U.S.C. § 355(j); 21 C.F.R. § 314.94.

[25] 35 U.S.C. § 271(e)(1).

[26] 21 U.S.C. § 355(j)(2)(A)(vii)(III-IV).

[27] 21 U.S.C. § 355(j)(4)(B)(iii).

[28] *Rite-Hite Corp. v. Kelley Co.*, 56 F.3d 1538 (Fed. Cir. 1995).

regardless of the merits of the suit, unless the suit is resolved earlier in the generic company's favor or the patent expires.[29] In contrast, for patents not listed in the Orange Book, the patent owner's recourse is to sue a generic company for patent infringement only after the company obtains FDA approval of its ANDA. To prevent sale of the generic product prior to conclusion of the suit, the patent owner must obtain a preliminary injunction, which requires that it demonstrate, *inter alia*, a likelihood of success on the merits.[30]

A generic company may cut short the automatic 30-month stay by successfully challenging the listing of a patent in the Orange Book on the grounds that it does not claim the drug or a method of using the drug. For instance, the generic company may bring a declaratory judgment action and seek a preliminary injunction requiring the NDA holder to delist the patent.[31] (A generic company may also challenge the appropriateness of an Orange Book listing as a counterclaim in a patent infringement suit.[32])

There is no effective way for a party to challenge an Orange Book listing through the FDA, however. The FDA has declined to enact any administrative procedures for resolving listing disputes. If a party disputes the accuracy of a listed patent,

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[29] *Id.*

[30] *See Purdue Pharma. L.P. v. Boehringer Ingelheim, GmbH*, 2000 Lexis 6563 (S.D.N.Y. 2000).

[31] *See Ben Venu Lab., Inc.*, 10 F. Supp. 2d at 450.

[32] *See Abbott Lab. v. Novopharm Ltd.*, 104 F.3d 1305 (Fed. Cir. 1997).

the FDA will request that the NDA holder confirm that the listed patent information is correct. But unless the NDA holder voluntarily withdraws or amends its listed information, the FDA will not change the patent information in the Orange Book. As long as the patent remains listed, ANDA applicants must still make a paragraph IV certification, potentially triggering the 30-month stay of FDA approval of generic drug applications.[33]

III. POTENTIAL COMPETITIVE IMPACT OF THE PROPOSED SETTLEMENT

The parties to this action ask this Court to enter a proposed settlement which requires the Court to make a specific factual finding and issue an order without any examination and testing of the evidence through discovery and the adversarial process. The Proposed Final Order and Judgment submitted by the parties states:

> WHEREFORE, this Court, BASED ON GOOD CAUSE SHOWN, including the representations made and evidence offered by plaintiff ("ABI") in its papers herein, hereby finds, determines, and concludes that:
>
> 1. ABI has established that, within the meaning and for the purposes of 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(b), (d) (the "Listing Statute and Regulations") United States Patent Number 6,096,331 (the '331 Patent) claims the drug or a method of using the drug that is the subject of the Taxol New Drug Application filed by defendant ("Bristol") and with respect to that product a claim of patent infringement could reasonably be asserted against Bristol;
>
> 2. Bristol is ordered to maintain the listing of the '331 Patent with the FDA in the Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book")[.]

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[33] 21 C.F.R. § 314.53(f); *Ben Venue Lab.*, 10 F. Supp. 2d at 456; *see also* Elizabeth Dickinson, "FDA's Role in Making Exclusivity Determinations," 54 *Food & Drug L.J.*, 195, 196 (1999).

Paragraph one would amount to a judicial conclusion that the '331 patent is properly listed in the Orange Book. As explained above, the "Listing Statute and Regulations" cited in paragraph one require Orange Book listing of a patent which "claims the drug or a method of using a drug" which is the subject of an approved new drug application, and "with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use or sale of the drug." A finding by this Court that the '331 patent satisfies these statutory and regulatory criteria is a judicial finding that the '331 patent must be listed by Bristol in the Orange Book. Paragraph two would result in a judicial order requiring Bristol to maintain the listing of the '331 patent in the Orange Book.

The Commission takes no position on whether the '331 patent meets the statutory criteria for listing in the Orange Book. However, this Court's imprimatur on the listing of the '331 patent in the Orange Book has several consequences for potential generic competitors that wish to introduce a generic Taxol product before expiration of the '331 patent in 2017.

Although no other valid patents currently prevent entry of generic Taxol, due to the listing of the '331 patent in the Orange Book, each potential generic competitor must certify to Bristol (the NDA holder) and ABI (the patent owner) that its generic product either does not infringe the '331 patent or that the patent is invalid. A patent infringement suit by ABI will trigger the Hatch-Waxman provision that prevents FDA approval of the company's generic product for 30 months. As a result,

consumers' access to a lower cost, therapeutically equivalent alternative to Taxol will be significantly delayed.

A generic company may wish to bring an action against Bristol alleging that the '331 patent has been improperly listed in the Orange Book, thereby removing the basis for the 30-month stay. A factual finding by this Court that the '331 patent satisfies the statutory and regulatory requirements for Orange Book listing may raise significant barriers to a generic company's challenge to that listing. Another court may well regard this Court's finding as persuasive, if not decisive, on the issue of whether the patent is properly listed.

Moreover, paragraph 2 of the Proposed Final Order, which requires Bristol to maintain the listing of the '331 Patent in the Orange Book, may also potentially block a generic company's later challenge to the listing. After the FDA lists the '331 patent in the Orange Book, a generic company wishing to challenge that listing must seek a court order requiring Bristol to delist the patent. If the generic company were successful, Bristol would face conflicting court orders, and resolving the conflicting court orders might further forestall generic entry.

Because the listing of the '331 patent may have serious ramifications for generic entry, the Commission urges the Court to consider whether it is necessary for settlement of this matter for the Court to make the factual finding that Orange Book listing is required; whether ABI and Bristol will be prejudiced by the court's failure to enter paragraphs 1 and 2 of the Proposed Final Order and Judgment; and whether such court approval may prejudice any party who later may seek to challenge

that listing. The Commission also urges the Court to consider the pendency of the Commission's investigation before entering the Order proposed by the parties.

IV. CONCLUSION

For these reasons, the Commission urges the Court to consider the ramifications for generic entry and the pendency of the Commission's investigation before entering the order proposed by the parties.

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