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EXHIBIT C

Guidance for Industry

Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act

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*Office of Training and Communications
Division of Communications Management
Drug Information Branch, HFD-210
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, Rockville, MD 20857
(Phone 301-827-4573)*

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Guidance for Industry¹

Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act

I. WHY IS FDA ISSUING THIS GUIDANCE?

This guidance is being issued in response to recent litigation and is intended to provide guidance to the pharmaceutical industry regarding (1) the timing of approval of abbreviated new drug applications (ANDAs) following an unsuccessful patent infringement action by the patent owner or new drug application (NDA) holder and (2) the start of 180 days of generic drug exclusivity.

FDA's interpretation of two provisions of the Federal Food, Drug, and Cosmetic Act (the Act) have been affected by recent court decisions interpreting the phrase "decision of a court" or "court decision." Section 505(j)(5)(B)(iii) of the Act governs the approval of ANDAs when the patent owner or NDA holder has brought a timely patent infringement action in response to the ANDA applicant's notice of filing of a paragraph IV certification to a listed patent. Section 505(j)(5)(B)(iv) of the Act governs the eligibility for and timing of 180-day exclusivity. The regulations implementing these statutory provisions are found at 21 CFR 314.107. Certain aspects of these regulations have been successfully challenged in *TorPharm, Inc. v. Shalala* and *Mylan Pharmaceuticals, Inc. v. Shalala*.² This guidance describes the Agency's response to those court decisions.

¹This guidance has been prepared by the Office of Generic Drugs in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration. This guidance represents the Agency's current thinking on sections 505(j)(5)(B)(iii)(I) and (iv) of the Act. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

²*TorPharm, Inc. v. Shalala*, No. 97-1925, 1997 U.S. Dist. LEXIS 21983 (D.D.C. Sep. 15, 1997), *appeal withdrawn and remanded*, 1998 U.S. App. LEXIS 4681 (D.C. Cir. Feb. 5, 1998); *vacated* No. 97-1925 (D.D.C. Apr. 9, 1998); *Mylan Pharmaceuticals, Inc. v. Shalala*, No. 99-2995, slip op. (D.D.C. Jan. 4, 2000).

II. STATUTORY AND REGULATORY BACKGROUND

A. ANDA Approvals and Court Decision

The concept of a court decision is used in two important places in section 505(j) of the Act — in the provision governing the timing of ANDA approvals and in the 180-day exclusivity provision. There is a 30-month statutory bar to approval of an ANDA that is the subject of patent infringement litigation except if "before the expiration of such period the court decides that such patent is invalid or not infringed, the approval will be made effective on the date of the *court decision*" (section 505(j)(5)(B)(iii)(I) (emphasis added)). In implementing this provision, FDA interpreted *court* to mean "the court that enters final judgment from which no appeal can be or has been taken" (21 CFR 314.107(e)(1) (1999)). The Agency's reasons for adopting this interpretation are discussed in the preambles to the proposed and final rules implementing the 1984 Drug Price Competition and Patent Term Restoration Act.³

B. 180-Day Exclusivity and Decision of a Court

Certain court decisions are also important for 180-day generic drug exclusivity. FDA's interpretation of *court* in the court decision described in Section 505(j)(5)(B)(iii)(I) was influenced by the role such a decision plays in 180-day exclusivity. The 180-day period of exclusivity can begin on either (1) the date of first commercial marketing or (2) "the date of a *decision of a court* ... holding the patent which is the subject of the [paragraph IV] certification to be invalid, or not infringed, whichever is earlier" (section 505(j)(5)(B)(iv) (emphasis added)). As described in the preambles to the implementing regulations, FDA believed that for the 180-day exclusivity to have real meaning for the eligible ANDA applicant, the court decision triggering the exclusivity must be the one that finally resolves the patent infringement litigation related to the ANDA.⁴ Therefore, for purposes of section 505(j)(5)(B)(iv), FDA determined that *court* means "the court that enters final judgment from which no appeal can be or has been taken" (21 CFR 314.107(e)(1) (1999)).

III. LITIGATION, CURRENT ISSUES, AND AGENCY POSITION

FDA's interpretation of the term *court* has been successfully challenged in the context of both the timing of ANDA approvals and the commencement of 180-day exclusivity. In *TorPharm v. Shalala*, the D.C. District Court found the FDA's interpretation not supported by the statute and directed FDA to approve an ANDA upon a decision of the district court finding a patent invalid, unenforceable, or not infringed. When the case became moot, FDA's appeal of that decision was withdrawn, and the district

³ 54 FR 28872, 28893-95 (July 10, 1989); 59 FR 50338, 50352-54 (October 3, 1994).

⁴ 54 FR 28893-95 (July 10, 1989); 59 FR 50352-54 (October 3, 1994).

court opinion was vacated. In the period since the *TorPharm* decision, FDA has continued to apply the definition of *court* set out at 314.107(e).⁵

Recently, in *Mylan Pharmaceuticals, Inc. v. Shalala*, the D.C. District Court found FDA's interpretation of *court* as used in the 180-day exclusivity context inconsistent with the statute's plain meaning. However, the court also determined that the applicant who relied in good faith on FDA's interpretation of the 180-day exclusivity provision should not be punished by losing its exclusivity. The court therefore refused to order FDA to begin the running of 180-day exclusivity upon the decision of the district court in the patent litigation at issue.

These recent decisions add considerable uncertainty to FDA's implementation of the ANDA approval and 180-day generic drug exclusivity programs. These regulatory programs already have been disrupted by the changes in eligibility for 180-day exclusivity necessitated by *Mova Pharmaceutical Corp. v. Shalala* and *Granutec, Inc. v. Shalala*.⁶ Therefore, in determining its response to the *TorPharm* and *Mylan* decisions, a primary concern for the Agency has been to identify an approach that will minimize further disruption and provide the regulated industry with reasonable guidance for making future business decisions.

The government has decided not to appeal the *Mylan* decision and will follow that court's interpretation of the statute in approving ANDAs and calculating the commencement of 180 days of exclusivity. Although the Agency believes that the statutory provisions at issue may properly be interpreted as FDA sets out in § 314.107(e), the Agency nonetheless has determined that it is in the interest of the regulated industry and the Agency to accept the interpretation of the *TorPharm* and *Mylan* courts. Therefore, the Agency will not apply the definition of the *court* found at § 314.107(e) (1) and (2) (i)-(iii).⁷ The Agency intends to formally remove the relevant sections of § 314.107(e), and will incorporate the *TorPharm* and *Mylan* courts' interpretation of the statute into the final rule implementing the changes in 180-day exclusivity.⁸ As described in section IV, FDA will implement the new interpretation of the term "court" prospectively, in a manner consistent with the court's approach in *Mylan*.

⁵ Guidance for industry *180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*, June 1998, p. 2, n. 3.

⁶ *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060 (D.C.Cir. 1998); *Granutec, Inc. v. Shalala*, 46 U.S.P.Q.2d 1398 (4th Cir. 1998).

⁷ Applicants will still be required to submit a copy of the relevant order or judgment to the Office of Generic Drugs under § 314.107(e)(2)(iv).

⁸ 64 FR 42873 (August 6, 1999).

IV. EFFECT ON ANDA APPROVALS AND 180-DAY EXCLUSIVITY

A. New Definition of Court

FDA will interpret the term *court* as found in section 505(j)(5)(B)(iii)(I) and 505(j)(5)(B)(iv) to mean the first court that renders a decision finding the patent at issue invalid, unenforceable, or not infringed. When it is the district court that renders such a decision, FDA may approve the ANDA as of the date the district court enters its decision. For eligible applicants, 180-day exclusivity will also begin to run on that date, unless it has already begun with commercial marketing. If the district court finds the patent is infringed, but that decision is reversed on appeal, the Agency may approve the ANDA on the date the district court issues a judgment that the patent is invalid, unenforceable, or not infringed pursuant to a mandate issued by a court of appeals.⁹

Neither a stay nor a reversal of a district court decision finding the patent invalid, unenforceable, or not infringed will have an effect on the approval of the ANDA or on the beginning, or continued running, of exclusivity. Should the NDA holder or patent owner wish to prevent an applicant with an approved ANDA from marketing its product during the course of an appeal, it must obtain an injunction from the court. If there is an injunction barring marketing of an approved drug, the ANDA applicant and NDA holder are asked to notify FDA, and the Agency will move the drug to the discontinued section of *Approved Drug Products with Therapeutic Equivalence Evaluations* (the *Orange Book*), so as to minimize confusion in the marketplace. Once the injunction is lifted or expires and if the ANDA applicant notifies the Agency it has begun marketing its product, the drug will be moved back to the active section of the *Orange Book*. The 180-day exclusivity period will continue to run during the pendency of a stay or injunction.

B. Implementation of New Definition of Court

The new definition of *court* will apply to certain ANDAs submitted after the publication of this guidance. Specifically, the new definition will be used for approval and exclusivity determinations for ANDAs containing a paragraph IV certification where the ANDA cites a reference listed drug for which no other ANDA containing a paragraph IV certification has been submitted.

This new interpretation of the statute may substantially change the value of the 180-day exclusivity. As Judge Roberts recognizes in the *Mylan* opinion, applicants who have made certain business decisions in good faith reliance upon an FDA regulation should not be penalized for their actions. For example, the potential change in the value of exclusivity may have considerable effect upon an ANDA applicant's willingness to file a paragraph IV certification to a patent and to undertake the effort and expense of litigating a patent infringement suit. This may be particularly true for patent challenges that are seen as risky, but for which the possible award of a full exclusivity was an adequate incentive. Judge Roberts also noted that based upon FDA's interpretation of the statute, ANDA applicants have held products off the market even after a victory in the district court.

⁹ This is the same process as described in current § 314.107(e)(2)(iii).

The Agency believes that an implementation plan for the new definition of *court* that recognizes the industry's reliance on the previous definition and establishes a *bright line* for ANDAs affected by the new definition will minimize the disruption to the ANDA approval and 180-day exclusivity programs. Moreover, the Agency believes that this approach will lessen the likelihood that ANDA applicants will sue the Agency alleging that they, like Geneva in the *Mylan* case, relied in good faith on the Agency's regulation and would be irreparably injured by application of the new interpretation to pending ANDAs.

**AXINN,
VELTROP &
HARKRIDER LLP**

1801 K STREET, N.W., SUITE 411
WASHINGTON, D.C. 20006

TEL: (202) 912-4700
FAX: (202) 912-4701
www.axhlaw.com

1370 AVENUE OF THE AMERICAS
NEW YORK, NY 10019
TEL: (212) 728-2200
FAX: (212) 728-2201

30 STATE HOUSE SQUARE
HARTFORD, CONN 06103-2702
TEL: (860) 275-8100
FAX: (860) 275-8101

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Date: April 4, 2007

From: John Will Ongman

Tel. No.: (202) 721-5400

Addressee	Tel. No.	Fax No.
Gary J. Buehler, Director Office of Generic Drugs	(301) 827-5845	(301) 594-0183
Dockets Management Branch	(301) 827-6860	(301) 827-6870

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