AstraZeneca Pharmaceuticals LP v Food and Drug Administration, Et AL., No. 12-5227, 26 April 2013 (United States Court of Appeals, District of Columbia Circuit)

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Summary

The United States Court of Appeals affirmed the district court's decision, holding that AstraZeneca's labeling change of its antipsychotic medication Seroquel was not entitled to an additional period of market exclusivity.

The facts

The pharmaceutical manufacturer, AstraZeneca, has developed and marketed the drug "Seroquel", used primarily for the treatment of schizophrenia and bipolar disorders, since 1997. In 2008, AstraZeneca filed two supplemental new drug applications (hereinafter "sNDAs") with the U.S. Food and Drug Administration (hereinafter "FDA") for new pediatric indications of Seroquel. A year later, the FDA approved the sNDAs and granted a three-year exclusivity period with respect to the new pediatric uses of Seroquel supported by pediatric clinical trial results. In its response letter for the sNDAs, the FDA simultaneously approved labeling changes of Seroquel, including the addition of a table summarizing glucose data, referred to as "Table 2". This "Table 2" forms the basis of the dispute involving AstraZeneca and the FDA.

In 2011, the FDA denied two citizen petitions filed by AstraZeneca, requesting exclusivity for Table 2 pursuant to section 355(j)(5)(F)(iv) of the U.S. Federal Food, Drug, and Cosmetic Act (hereinafter "FDCA"). In response, AstraZeneca filed a lawsuit against the FDA in the district court, which denied motion for preliminary injunction and dismissed the case as unripe because the FDA had not yet decided whether to grant abbreviated new drug applications ("ANDAs") that included Table 2 in the labeling for generic versions of Seroquel.[1] Four days later, on March 27, 2012, the FDA approved eleven ANDAs for generic versions of Seroquel that included Table 2. On the same day, the FDA issued a letter to AstraZeneca explaining why Table 2 was not entitled to a period of exclusivity and pointed out three main reasons. First, "changes in labeling that involve the addition of warnings or other similar risk information are generally not entitled to 3-year exclusivity" and since Table 2 only contained "generally applicable safety information", the exclusivity period could not apply.[2] Second, Table 2 did not include the pediatric or any other indications for which Seroquel still had exclusivity. Finally, it was a mere coincidence that the FDA approved that the pediatric supplements and Table 2 at the same time and in the same letter. As the FDA stated, "there is no relationship between the exclusivity for pediatric indications ... and the data in Table 2".[3] Following the FDA's ANDA approvals, AstraZeneca filed a second suit in the district court, seeking to prevent the FDA from granting approvals of generic versions of Seroquel before the expiration of the claimed exclusivity period. The district court denied AstraZeneca's motion for a

[1] *AstraZeneca Pharm. LP v. FDA*, 850 F. Supp. 2d 230 (D.D.C. 2012).
[2] See Decision, p. 6.
[3] See Decision, p. 6.

temporary restraining order and granted summary judgment in favor of the FDA on July 5, 2012. The district court held *inter alia* that the FDA's interpretation of section 355(j)(5)(F)(iv) of the FDCA, i.e. "that a substantive relationship between new clinical studies and changes in the supplement, not the format of a submission, dictates what changes receive exclusivity" was reasonable.[4] AstraZeneca appealed to the U.S. Court of Appeals.

The relevant provision of the FDCA reads as follows:

> 21 U.S.C. § 355(j)(5)(F)(iv): "If a supplement to an application […] contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement […]".

The legal issues

The main question raised by the case is whether or not Table 2 was entitled to a period of exclusivity. To answer this question, the U.S. Court of Appeals examined the FDA's interpretation of section 355(j)(5)(F)(iv) of the FDCA by applying the two-step *Chevron* test.[5] At *Chevron* step one, the U.S. Court of Appeals must determine whether the intent of Congress is clearly stated in the statute in question. If not, the U.S. Court of Appeals can proceed to *Chevron* step two and examine whether the FDA's interpretation was reasonable or not.

AstraZeneca argued that the Court of Appeals should resolve the case at *Chevron* step one because section 355(j)(5)(F)(iv) of the FDCA clearly entitles Table 2 to exclusivity based on two grounds. First, AstraZeneca noted that Table 2 was "a change approved in" the pediatric supplements, and the supplements included "reports of new clinical investigations ... essential to the approval of the supplement[s]".[6] Second, AstraZeneca argued that Table 2 should be entitled to independent exclusivity as some of the clinical studies that provided the data for Table 2 were "new clinical investigations" "essential to the approval" of the labeling changes.[7]

On the contrary, the FDA maintained from the beginning of the case that Table 2 was not "a change approved" in any supplement, stating that only changes approved in a supplement are entitled to a statutory period of exclusivity.[8]

The U.S. Court of Appeals found the statutory language, in particular the term "supplement", ambiguous. It therefore applied *Chevron* step two.

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[4] *AstraZeneca Pharm. LP v. FDA*, 850 F. Supp. 2d 230 (D.D.C. 2012), p. 37.
[5] See *Chevron U.S.A. Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984).
[6] See Decision, p. 9.
[7] See Decision, p. 9.
[8] See Decision, p. 10.

In its analysis, the U.S. Court of Appeals noted *inter alia* that the supplements at issue dealt with new pediatric indications of Seroquel while Table 2 was contained in the "Adult" section of Seroquel's labeling, unrelated to data from pediatric studies. Referring to the district court's decision, the U.S. Court of Appeals underlined that "the administrative record shows that the pediatric supplements were approved on their own merits based upon clinical investigations unrelated to the Table 2 labeling change, which standing alone does not entitle AstraZeneca to exclusivity".[9]

The U.S. Court of Appeals therefore affirmed the district court's decision by finding the FDA's interpretation reasonable. As the U.S. Court of Appeals noted, section 355(j)(5)(F)(iv) of the FDCA only provides exclusivity for changes approved as part of a supplement. The FDA however considered Table 2 as independent of the pediatric supplements and thus not entitled to exclusivity.

Points of significance

- According to the FDA's interpretation of section 355(j)(5)(F)(iv) of the FDCA, confirmed by the district court and the U.S. Court of Appeals, "a substantive relationship between new clinical studies and changes in the supplement, not the format of a submission, dictates what changes receive exclusivity".[10]
- Both, the district court and the U.S. Court of Appeals affirmed the FDA's interpretation under *Chevron*'s step two, finding that section 355(j)(5)(F)(iv) of the FDCA was ambiguous.
- The TRIPS Agreement (Article 39.3) contains no obligation to provide for an exclusivity period for pharmaceutical test data. Developing country Members are free to protect test data through non-exclusive means, such as laws against unfair competition.

Key words: Data exclusivity, supplemental new drug application (sNDA), abbreviated new drug application (ANDA), additional period of exclusivity.

Available at:
http://www.cadc.uscourts.gov/internet/opinions.nsf/3708EBCAC4BE9BC885257B59004F8C17/$file/12-5227-1432745.pdf

[9] See Decision, p. 11.
[10] See *AstraZeneca Pharm. LP v. FDA*, 850 F. Supp. 2d 230 (D.D.C. 2012), p. 37.