

ORIGINAL

November 19, 2004

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852

Re: Docket Number 2004P-0324 (Citizen Petition) - Submission of Comments by IVAX Pharmaceuticals, Inc.

Dear Sir or Madam:

These comments are submitted on behalf of IVAX Pharmaceuticals, Inc., (IVAX) in response to the Citizen Petition filed by Dey, L.P., (Dey) on July 15, 2004 (Dey Petition or Petition). The petition requests that the Commissioner determine in writing that ANDA No. 76-724 submitted by IVAX should be subject to a 30-month stay of approval under section 505(j)(5)(B)(iii) of the Food, Drug, and Cosmetic Act (FDCA) and under 21 C.F.R. 314.95(a)(3).¹

As set forth below, the petition must be denied because:

1. Section 505(j)(5)(B)(iii) imposes a 30-month stay only with regard to a patent for which information was submitted for listing in the Orange Book prior to the submission of the relevant ANDA;
2. Dey submitted no patent information prior to IVAX's submission of ANDA No. 76-724; and
3. The regulation to which Dey refers, 21 C.F.R. 314.95(a)(3), no longer contains the provisions relied upon by Dey in support of its petition.

¹ Subsequent to the filing of the Petition, Dey filed an Amendment to Citizen Petition on August 30, 2004. Docket Number 2004P-0324-AMD1 (Dey Amendment). In the amendment, Dey states its belief that Eon Labs, Inc., rather than IVAX, was the first ANDA applicant for purposes of determining 180-day exclusivity. Dey argues in the amendment that it is entitled to a 30-month stay with regard to Eon's ANDA for the reasons set forth in the original Dey Petition, and for additional reasons that are peculiar to the timing and receipt of Eon's ANDA submissions. IVAX's comments are directed to the relief requested in the original Dey Petition with regard to IVAX's ANDA. (IVAX maintains that it was the first ANDA applicant for purposes of 180-day exclusivity, and is filing a petition on this date seeking FDA's acknowledgment of this status.) Some of IVAX's comments herein are also responsive to legal arguments that Dey restates in the amendment (see Dey Amendment at 3, n.**).

2004P-0324

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DISCUSSION

A. Dey Seeks to Overturn FDA's March 10, 2004, Rulemaking

In its petition, Dey challenges amendments to the 30-month stay provisions of the FDCA enacted by Congress in the Medicare Prescription Drug, Improvement, and Modernization Act (MMA).² Prior to the MMA, section 505(j)(5)(B) provided a 30-month stay in the approval of an ANDA containing a paragraph IV certification without regard to when the patent information was submitted to the agency. The pre-MMA statute provided as follows:

If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. . . .³

In the MMA, Congress added an important restriction to this language, as follows:

If the applicant made a certification described 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 . . .*⁴

Dey argues that this amendment to the statute was not intended to impose a new statutory restriction on 30-month stays, but rather to codify FDA's regulation promulgated in June 2003, which interpreted the pre-MMA provisions of the FDCA. In this regulation, the agency determined that, although the pre-MMA statute provided 30-month stays for patents listed either before or after the submission of an ANDA, the notice provisions of the pre-MMA statute required ANDA applicants to submit only one notice of submission of a paragraph IV certification to the NDA holder, resulting in only one 30-month stay.⁵

² Pub. L. No. 108-173, 117 Stat. 2066 (Dec. 8, 2003)

³ Former FDCA § 505(j)(5)(B)(iii).

⁴ Current FDCA § 505(j)(5)(B)(iii)(I) (emphasis added).

⁵ 68 Fed. Reg. 36,676, 36,688-90 (2003). This interpretation was based on the statutory mandate in FDCA § 505(j)(2)(B)(iii) that the notice be provided when an ANDA is amended to "include" a paragraph IV certification. 67 Fed. Reg. 65, 448, 65,455 (2002). In the MMA, Congress amended the notice provisions regarding paragraph IV certifications to require expressly that notice be provided for any new paragraph certification, regardless whether notice had previously been provided for a prior paragraph IV certification:

Following enactment of the MMA, the agency determined that its June 2003 regulation was no longer supported by the wording of the statute and, on March 10, 2004, revoked 21 C.F.R. 314.95(a)(3), which had permitted 30-month stays for patents listed after the submission of the ANDA and required notice only with regard to the first paragraph IV certification in the ANDA.⁶ The agency explained as follows:

In the Federal Register of June 18, 2003 (68 FR 36676), we (FDA) issued a final rule that amended our patent submission and listing requirements. . . . The final rule stated that there was only one opportunity for a 30-month stay of the approval date of each ANDA and 505(b)(2) application. . . .

On December 8, 2003, the [MMA] was signed into law. . . . *The new statutory provisions address the applicability of 30-month stays in approval of certain ANDAs and 505(b)(2) applications in a different manner than our final rule, which was issued under statutory language now superseded.*

Therefore, certain regulations issued in the final rule published on June 18, 2003 (68 FR 36676) are superseded by the new statutory provisions. The affected sections of the regulation are 21 CFR 314.52(a)(3) and 21 CFR 314.95(a)(3) that stay the effective date of approval for certain ANDAs and 505(b)(2) applications for 30 months in certain situations.⁷

Dey seeks to overturn this rulemaking by having the agency adopt an interpretation that the agency specifically rejected in the rulemaking and expunged from its regulations.

B. FDA Correctly Determined that the Statute Limits 30-Month Stays to Patents Listed Prior to the Submission of the ANDA.

1. Dey's Interpretation Is Contrary to the Plain Meaning of the Statute.

Under *Chevron U.S.A. Inc. v. Natural Resources Defense Council*, 467 U.S. 837 (1984), the plain meaning of the statute must govern its interpretation. Here the statute provides for a 30-month stay only where “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*

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

...

(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.*

Current FDCA § 505(j)(2)(B)(ii) (emphasis added).

⁶ 69 Fed. Reg. 11,309 (2004) (emphasis added).

⁷ *Id.* at 11,309-10 (emphasis added).

(excluding an amendment or supplement to the application), which the Secretary later determines to be substantially complete, was submitted.”⁸ Dey argues that this provision “does not expressly prohibit a 30-month stay when . . . the listing and challenge happen to occur after the relevant ANDA is submitted.” Dey Petition at 5. Dey ignores the fact that the requirement that the patent information be submitted prior to submission of the ANDA is an *express limitation*. By providing for a 30-month stay with an express limitation, and providing no other statutory basis for a 30-month stay, Congress did, in fact, expressly prohibit a 30-month stay that does not satisfy the requirement of the express limitation.

2. Dey’s Interpretation Is Contrary to the Legislative History

Even if the statute were ambiguous – which it is not – the legislative history clearly establishes Congress’ intent that 30-month stays be limited to patents listed prior to the submission of the ANDA. At a hearing on the proposed MMA legislation in August 2003,⁹ Senator Hatch made clear his understanding that the proposed legislation eliminated 30-month stays for patents filed after the submission of the ANDA:

And I’m pleased that the sponsors of this legislation have adopted a version of the 30-month stay provision that I first suggested last May and argued for on the floor last July. The one and only 30-month stay *for all patents filed when the NDA is submitted* was also a centerpiece of the Federal Trade Commission report released last summer.¹⁰

The FTC report to which the Senator referred examined generic drug market entry under the FDCA and specifically recommended that there be only one 30-month stay per drug and that it be limited to “disputes over *patents listed in the Orange Book prior to the filing date of the generic applicant’s ANDA.*”¹¹

Senator Hatch’s understanding of the proposed legislation was reiterated at the hearing by the FDA Chief Counsel, who stated in his prepared testimony that S. 1225

⁸ Current FDCA § 505(j)(5)(B)(iii)(I) (emphasis added).

⁹ The pending House bill, H.R. 1, contained the precise language on 30-month stays enacted in the MMA. The accompanying Senate bill, S.1225, the language limiting 30-month stays to patents listed prior to the submission of an ANDA was somewhat different. S.1225 would have added a new section 505(j)(5)(C) to provide as follows:

AVAILABILITY OF 30-MONTH PERIOD.—

(i) IN GENERAL.—The 30-month period provided under subparagraph (B)(iii) shall be available only with respect to a patent published by the Secretary under subsection (b)(1) or (c)(2) at least 1 day before the date on which the application is filed.

Greater Access to Affordable Pharmaceuticals Act, S. 1225, 108th Cong. § 2(a)(2)(C) (2003) (Tab 1).

¹⁰ *Hearing Before the Senate Judiciary Comm. on the Senate and House Versions of the "Greater Access to Affordable Pharmaceuticals Act,"* 108th Cong. (2003) (emphasis added).

¹¹ *Generic Drug Entry Prior to Patent Expiration: An FTC Study*, at ii (2002)(FTC Report) (emphasis added) (Tab 2).

"limits the patents eligible for the 30-month stay to those submitted to the Agency *prior to submission of the ANDA*, disallowing later-submitted patents from triggering additional 30-month stays. . . ." ¹² In his oral testimony, the FDA Chief Counsel further explained that the Senate bill would amend the pre-MMA statutory 30-month stay by "limit[ing] the patents eligible for the 30-month stay to those that are submitted to the agency *before submission of the ANDA*." ¹³

Dey suggests, based on a statement by Senator Hatch in the congressional Record of November 22, 2003, that the Senator understood the legislation to codify FDA's 2003 regulation on 30-month stays in all respects. ¹⁴ Although the Senator did state that proposed legislation included a "codification" of the new FDA rule, it is clear from the broader text of the Senator's remarks that the Senator was generally referring to a codification of the policy the Senator had initially proposed to limit 30-month stays, rather than to the mechanics of the FDA regulation, which the Senator acknowledged in his colloquy with the FDA Chief Counsel to be different from those of the proposed legislation. ¹⁵ Had Dey's included in its quotation the next two sentences of the Senator's remarks, Dey's petition would have reported that the Senator stated: "Last July, the Federal Trade Commission issued a report that recommended the policy I advocated and became a central feature of the FDA rule and the legislation contained in the conference report." As noted above, the FTC report recommended that the goal of a single 30-month stay be accomplished by limiting the stay disputes on patents filed before the submission of the ANDA. ¹⁶

Dey attempts to find support in the FTC Report by arguing that the report did not address a scenario in which there were no patent listings prior to the submission of the ANDA. ¹⁷ Dey notes that in this scenario the NDA holder is precluded from even a single 30-month stay, and argues that the FTC report assumed that there would be at least one 30-month stay, even if it were based on a patent listed subsequent to the submission of the ANDA. The clear wording of the FTC recommendation makes clear, however, that this is not the case. The report explains that the limitation of one 30-month stay per drug

¹² *Prepared Testimony of Dan Troy, Chief Counsel, FDA: Hearing Before the Senate Judiciary Comm. on the Senate and House Versions of the "Greater Access to Affordable Pharmaceuticals Act,"* 108th Cong. (2003) (emphasis added).

¹³ *Hearing Before the Senate Judiciary Comm. on the Senate and House Versions of the "Greater Access to Affordable Pharmaceuticals Act,"* 108th Cong. (2003) (emphasis added).

¹⁴ Dey Petition at 6, *citing* 149 Cong. Rec. S15566-67 (daily ed. Nov. 22, 2003) (statement of Sen. Hatch).

¹⁵ Dey also suggests that remarks by Senator Kennedy support Dey's position. Dey Petition at 6, *citing* 149 Cong. Rec. S15566-67 at S15884 (statement of Sen. Kennedy). A cursory examination of the Senator's remarks quoted in Dey's Petition demonstrates, however, that Senator Kennedy noted that the new legislation would limit 30-month stays, without addressing the mechanics of the new legislation.

¹⁶ FTC Report at ii (Tab 2).

¹⁷ Dey Petition at 7-8.

product “would be applied *only* to resolve disputes over patents listed in the Orange Book prior to the filing date of the generic applicant’s ANDA.”¹⁸

The FTC Report further explains that the proposed limitation of 30-month stays to patents listed prior to submission of the ANDA was based not on concerns related to the *number* of stays that may be entered but rather on *timing* of stays that may delay ANDA approvals significantly beyond the normal review period. The report explains:

One 30-month period historically has approximated the time necessary for FDA review and approval of the generic’s ANDA. Thus, it does not appear that the 30-month stay provision, as applied once to each ANDA for patents listed in the Orange Book prior to the ANDA’s filing date, has a significant potential to delay generic entry beyond the time already necessary for FDA approval of the generic’s ANDA.¹⁹

Dey also attempts to find support in the retroactive effect of the 30-month stay provisions of the MMA, which apply to patents listed on or after the effective date of FDA’s June 2003 regulation.²⁰ Dey argues that this provision suggests that “Congress intended the new provision to be consistent with . . . the regulation.”²¹ Because Congress does not explain the choice of this retroactive effect date, its intent is unclear. To the extent that speculation is warranted, however, it would be most reasonable to assume that Congress intended to replace the system instituted in FDA’s regulation regarding notice for paragraph IV certifications and 30-month stays because it was *inconsistent* with the statute. Had Congress not made the MMA notice and 30-month stay provisions retroactive to the promulgation date of the August 2003 regulation, FDA and the industry would have been left with three sets of standards to apply (standards for (1) ANDAs submitted prior to August 18, 2003, (2) ANDAs submitted between August 18 and December 8, 2003, and (3) ANDAs submitted after December 8, 2003) rather than the somewhat less complex application of pre-MMA standards and post-MMA standards.²²

3. FDA Has Already Rejected Dey’s Interpretation.

As discussed above, FDA has already rejected Dey’s proposed interpretation of the statute. Consistent with the congressional testimony of the FDA Chief Counsel regarding the proposed provisions of the MMA, the agency determined after enactment that the MMA provided a different approach to 30-month stays than that provided in the June 2003 regulation, and revoked the inconsistent provisions of the regulation that Dey

¹⁸ FTC Report at v, n.6 (emphasis added).

¹⁹ *Id.* at iv.

²⁰ Dey Petition at 9-10, *citing* MMA § 1101(c)(3).

²¹ *Id.*

²² The effective date may also reflect Congress’ view that the legislation is broadly consistent with the purpose of the regulation to limit 30-month stays (as noted by Senator Hatch and the FDA Chief Counsel) even though inconsistent with regard to the mechanics of advancing that purpose.

now attempts to rely on. The agency stated in the preamble to the rulemaking revoking the provisions of the 2003 regulation: “The new statutory provisions address the applicability of 30-month stays in approval of certain ANDAs and 505(b)(2) applications *in a different manner than our final rule*, which was issued under statutory language now superseded.”²³

The agency’s interpretation of the statute expressed in this preamble to the regulation revocation of the prior regulation constitutes a binding advisory opinion under the agency’s regulations.²⁴

FDA has recently reaffirmed its interpretation of the statute in a guidance document on the MMA, in which the agency states:

[T]he MMA provides that a 30-month stay may be available for litigation related to [the] patent only if the patent was submitted to FDA before the date that the ANDA or 505(b)(2) application (excluding an amendment or supplement) was submitted. In other words, the MMA precludes 30-month stays for *later listed* patents, that is, those patents submitted to FDA on or after the date the ANDA or 505(b)(2) application was submitted.²⁵

C. Equitable Considerations to Not Favor Dey’s Position.

Dey argues that equitable considerations favor its proposed interpretation of the statute. Dey attempts to support its position by suggesting that the primary rationale for revising the Hatch-Waxman Act was to stop gaming tactics through the elimination of multiple 30-month stays and inappropriate Orange Book patent listings.²⁶ It is clear from the legislative history cited above, however, that Congress was more specifically interested in concerns expressed in FTC Report related to patent listings following the submission of an ANDA that might delay generic competition significantly beyond the normal review period of the ANDA and that appear to raise more questions than do earlier-listed patents. The Report states:

[I]t does not appear that the 30-month stay provision, as applied once to each ANDA for patents listed in the Orange Book prior to the ANDA’s filing date, has a significant potential to delay generic entry beyond the time already necessary for FDA approval of the generic’s ANDA. . . . The history thus far of

²³ 69 Fed. Reg. at 11,309-10 (emphasis added).

²⁴ 21 C.F.R. 10.85.

²⁵ *Guidance for Industry: Listed Drugs, 30-Month Stays, and Approval of ANDAs and 505(b)(2) Applications Under the Hatch-Waxman, as Amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003* (Oct. 2004) (citation omitted; emphasis in original).

²⁶ Dey Petition at 7.

multiple 30-month stays caused by the filing of later-issued patents appears problematic. . . .²⁷

In addition, Dey's right to judicial protection of its patent is not extinguished by a straightforward reading of the statute. As the FTC report noted:

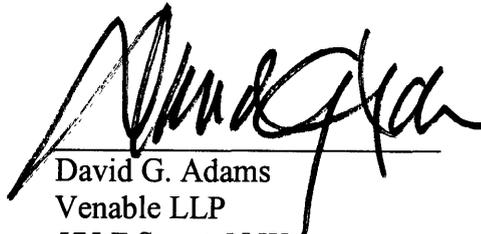
[L]ater-listed patents still receive the usual protections of patent infringement litigation. The brand-name company may sue for patent infringement . . . and may seek a preliminary injunction.²⁸

In sum, for patents listed after the submission of an ANDA, which pose the possibility of significant delays in generic competition beyond the completion of the FDA's review, Congress chose to avoid automatic stays in approval based on patent challenges and to instead place the burden on the patent owner to demonstrate the preliminary relief is warranted under general principles of patent law. This policy choice is reasonable and does not pose an inequity for companies such as Dey, that are unable to demonstrate an entitlement to preliminary relief with regard to a questionable patent issued well after the approval of an NDA and late in the review of a competitor's ANDA

CONCLUSION

Dey seeks to protect itself from generic competition by having FDA disregard a clear statutory mandate that 30-month stays be limited to patents listed prior to the submission of the ANDA. The plain meaning of the statute is compelling, the legislative history fully supports the plain meaning, and FDA has already adopted the plain meaning as its interpretation of the statute.

Respectfully submitted,



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²⁷ *Id.* at iv.

²⁸ *Id.* at iv-v.