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VIA HAND DELIVERY

Dockets Management Branch (HFA-305)

Food and Drug Administration

5630 Fishers Lane, rm. 1061

Rockville, MD 20852

RE: Docket No. 00D-1197 (Guidance for Industry on Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act)

Dear Sir/Madam:

Bristol-Myers Squibb Company ("BMS") submits these comments on FDA's Guidance for Industry on Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act ("Guidance").

I. THE GUIDANCE IS BASED ON A FLAWED INTERPRETATION OF THE STATUTE

FDA's Guidance is based on the Mylan and TorPharm¹ decisions from the United States District Court for the District of Columbia. Guidance at 1. However, those decisions, and consequently the Guidance, are based on a flawed interpretation of the governing statute.

¹ TorPharm was briefed, argued, and decided in a rapid two-week preliminary injunction proceeding, and FDA was appealing the decision when it later became moot. Its relevance is therefore questionable.

00D-1197

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A. The Guidance Ignores The “Last Applicable Date” Requirement of 21 U.S.C. § 355(j)(5)(B)

Mylan and TorPharm both held that a district court decision of patent invalidity or noninfringement is a “court decision” under subparagraph (I) of 21 U.S.C. § 355(j)(5)(B)(iii). Guidance at 2-3. Mylan used this holding to conclude that the 180-day period of a related provision, 21 U.S.C. § 355(j)(5)(B)(iv), can be triggered by a district court decision, while TorPharm used it to determine that the 30 month period provided for in the introductory part of 21 U.S.C. § 355(j)(5)(B)(iii) can be ended by a district court decision. Id. However, these cases ignored the unambiguous language of 21 U.S.C. § 355(j)(5)(B), which does not allow this result in the case of district court decisions for which the time for appeal has not yet run.

The language 21 U.S.C. § 355(j)(5)(B) is lengthy and complex. In relevant part, it provides that:

The approval of [an ANDA] shall be made effective on the last applicable date determined under the following:

(i) * * *

(ii) * * *

(iii) 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. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(I) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that—

(I) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision.

(II) if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of title 35, United States Code . . .

The cases and the Guidance ignore the “last applicable date” language at the beginning of this provision. Instead, they focus on only one of the potentially “applicable dates” in the provision, that found at 21 U.S.C. § 355(j)(5)(B)(iii)(I). They read the date described in this subparagraph (“subparagraph I”) to unambiguously allow an ANDA approval on the date of a district court decision of invalidity for which the time for appeal has not yet run.

The fatal flaw in this reasoning is that in many cases the date described in subparagraph I will not be the “last applicable date” under 21 U.S.C. § 355(j)(5)(B). As such, the subparagraph I date cannot be the date of ANDA approval, because an ANDA approval can only “be made effective on the last applicable date” under 21 U.S.C. § 355(j)(5)(B) (emphasis added).

An example illustrates the point. Consider the case of a district court ruling of patent invalidity which occurs in the tenth month of the 30-month litigation period. In month twenty-five, the court of appeals overturns the district court and rules that the patent has been infringed. In this scenario, the “last applicable date” under the statute is the date of the appellate court ruling. This is because although under subparagraph I there was an initial ruling of invalidity, on a later date, there was a ruling of infringement under subparagraph II. Both subparagraphs define relevant dates under 21 U.S.C. § 355(j)(5)(B), so the later appellate ruling is the “last applicable date” for purposes of determining when to grant ANDA approval.

Of course, in some circumstances the earlier district court ruling will become the “last applicable date” under 21 U.S.C. § 355(j)(5)(B). For example, if the district court ruling is not appealed and the time for appealing it has run, an appellate reversal is no longer possible, so the district court ruling, pursuant to subparagraph I, becomes the “last applicable date.”

Similarly, the underlying rule of 21 U.S.C. § 355(j)(5)(B)(iii) is that the ANDA is approved if the litigation continues for more than 30 months. Subparagraphs I and II are exceptions to that rule. 21 U.S.C. § 355(j)(5)(B)(iii). Thus, if the 30 month period runs without any of the exceptions coming into play, the ANDA will be approved upon expiration of the 30 months.

FDA’s regulation, 21 C.F.R. § 314.107(e), adequately implements this complex, but unambiguous statutory language.² Nonetheless, in ruling against the regulation, the Mylan and TorPharm courts did not take into account the “last applicable date” requirement. As a result, their holdings, and by extension the Guidance, are flawed because they do not allow FDA to accurately determine what the “last applicable date” is under 21 U.S.C. § 355(j)(5)(B). Instead, FDA is forced to approve the ANDA before it can know whether or not the district court ruling will be appealed, or, if it is appealed, what the appellate court’s ruling might be.

The scenario above again illustrates the point. When the district court rules in the tenth month that the patent is invalid, under the Guidance, FDA must approve the ANDA upon the date of that ruling. Guidance at 4. FDA’s approval, however, would not be authorized under

² 21 C.F.R. § 314.107(e) does not define Supreme Court rulings (certiorari denials or decisions on the merits) as relevant court decisions. To be completely faithful to the statutory language, that would be required. The change would probably have little real-world effect, however, as the 30-month period would be likely to run before a Supreme Court decision.

the plain terms of the statute, because the appeals court's subsequent reversal of the district court provides a later "applicable date." FDA would have approved the ANDA based not on the "last applicable date" as required by 21 U.S.C. § 355(j)(5)(B), but on an earlier date not authorized by the statute. The virtue of 21 C.F.R. § 314.107(e), by contrast, is that, in accordance with the statute, it requires FDA to wait until the "last applicable date" has been clearly determined by the course of proceedings in the infringement litigation.

FDA's Guidance fails to apply the "last applicable date" requirement of 21 U.S.C. § 355(j)(5)(B). As a result, it should be rescinded and FDA should return to applying its regulation, 21 C.F.R. § 314.107(e).

B. The Guidance Is Flawed For Other Reasons

In addition to ignoring the "last applicable date" provision, FDA's Guidance is flawed for a number of other reasons. FDA is already familiar with these reasons, because they have been used by the Agency and others as justification for 21 C.F.R. § 314.107(e), whether in rulemaking or litigation. Consequently, these reasons are merely summarized here.

The statute is ambiguous. When the term "court" is used in 21 U.S.C. § 355(j)(5)(B), whether it is referring to a district or appellate court is never specified. By contrast, other provisions of the statute do use the specific terms "district court" or "appellate court." See, e.g., 21 U.S.C. §§ 332, 334(a)(1) ("district court"); 21 U.S.C. §§ 335a(j)(1), 335b(c), 335c(d), 346a(h)(1), 348(g)(1), 355(h), 360g(a) ("appellate court"). Consequently, it is argued that the unqualified term "court" is ambiguous in 21 U.S.C. § 355(j)(5)(B). This is true as far as it goes. However, as explained above, in light of the "last applicable date" language of

21 U.S.C. § 355(j)(5)(B), the stronger argument seems to be that the statute unambiguously requires FDA to wait until a district court ruling of invalidity or noninfringement is either affirmed on appeal, or the time for its appeal has run.

Legislative History. The early Hatch-Waxman proposals discussed an 18 month, rather than 30 month period, and in some instances seemed to refer to the district court as the court making the relevant decision. See, e.g., Mylan, 81 F. Supp.2d at 40-41. However, once the period was expanded to 30 months, the references shifted to allowing the litigation to “conclude,” which, if the case is appealed, can only take place at the appellate level. Id. Consequently, the legislative history supports the interpretation that Congress meant appellate court decisions to be the relevant “court” decisions in cases which were appealed.

Congressional Intent. In 21 U.S.C. § 355(j)(5)(B)(iv), Congress intended to give a ANDA applicants a significant incentive to challenge pharmaceutical patents and thereby speed generic competition. Interpreting “court” to always mean district court, however, severely undermines this incentive, in some cases rendering it useless, or worse (e.g., if an ANDA applicant is bankrupted by an appellate judgment of infringement when it had marketed based on a district court ruling of invalidity). FDA’s original regulation, 21 C.F.R. § 314.107(e), maintained the value of the incentive, in particular for prudent ANDA applicants who wait for appellate affirmation of their district court victories before venturing into the market. It thereby preserved congressional intent. To avoid a radical rebuff to Congress’ intent, FDA’s original regulation should be preserved.

II. THE GUIDANCE IS PROCEDURALLY FLAWED

FDA's Guidance violates basic principles of procedural administrative law.

Moreover, any eventual regulation(s) based on the concept embodied in the Guidance would also be invalid unless promulgated through notice and comment rulemaking.

The Guidance provides that FDA will not apply the definition of "court" found at 21 C.F.R. §§ 314.107(e)(1) and (2)(i)-(iii). Guidance at 3. The cited regulations were adopted pursuant to notice and comment rulemaking. *Abbreviated New Drug Application Regulations; Proposed Rule*, 54 Fed. Reg. 28871, 28928-30 (July 10, 1989); *Abbreviated New Drug Applications Regulations; Patent and Exclusivity Provisions; Final Rule*, 59 Fed. Reg. 50337, 50367-68 (Oct. 3, 1994). FDA's decision to ignore its definition of "court" in 21 C.F.R. §§ 314.107(e)(1) and (2)(i)-(iii) violates the principle that regulations promulgated through notice and comment rulemaking can only be modified through notice and comment rulemaking. See, e.g., Shalala v. Guernsey Memorial Hosp., 514 U.S. 87, 100 (1995) (rulemaking required if agency adopts new position inconsistent with any of the agency's existing regulations); First National Bank of Chicago v. Standard Bank & Trust, 172 F.3d 472, 479 (7th Cir. 1999) ("once a regulation is adopted by notice-and-comment rulemaking . . . its text may only be changed in the same manner") (citing Homemakers North Shore Inc. v. Bowen, 832 F.2d 408, 413 (7th Cir. 1987)); Columbia Falls Aluminum Co. v. EPA, 139 F.3d 914, 919 (D.C. Cir. 1998) ("Once a rule is final, an agency can amend it only through a new rulemaking"). Because the Guidance is not a product of notice and comment rulemaking, it is invalid and of no effect.

FDA makes no attempt to reconcile its Guidance with this requirement of administrative law. Indeed, the Guidance reveals little of FDA's reasoning as to why it has decided to ignore its regulations. Although FDA cites two district court decisions (one vacated as moot) from the District of Columbia, the Agency does not claim that its action is mandated by court order. Rather, FDA casts its Guidance as a choice made in the process of "determining its response to the *TorPharm* and *Mylan* decisions." Guidance at 3. The Agency continues to believe that its old regulation was proper, but has decided, for reasons left vague, to ignore it: "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." *Id.* Thus, it would appear that FDA has chosen to overturn a regulation of national application, promulgated through a five-year notice and comment process, because two district court decisions from the District of Columbia caused it to rethink its regulatory approach.³ This lightly reasoned and barely explained reversal of meticulously promulgated regulations is arbitrary and capricious under the Administrative Procedure Act (APA). 5 U.S.C. § 706(A), (D).

It may be that FDA considers itself bound by the *Mylan* decision to abandon its regulation. This would be hard to fathom, given that the Fourth Circuit has held the regulation to be valid, *Granutec, Inc. v. Shalala*, 46 U.S.P.Q.2d (BNA) 1398 (4th Cir. 1998), and *Mylan* is a district court decision with no binding authority on any other court. Yet the Guidance fails to even mention the *Granutec* decision. Consequently, it neither contests the merits of *Granutec*'s

³ Indeed, until *Mylan*, FDA had ignored the vacated *TorPharm* decision for three years.

endorsement of FDA's regulation, nor describes on what legal basis the Agency feels it can ignore Granutec and simply apply the Mylan rule, whether in the Fourth Circuit, or anywhere else.

FDA, of course, could modify its regulation on a national scale if it did so through notice and comment rulemaking. This would alleviate the potential difficulties of a Circuit conflict. Unless FDA backs away from the Guidance or conducts a notice and comment rulemaking, however, these difficulties will persist.

Because the Guidance is procedurally flawed, it should be rescinded.

III. IF FDA STILL INTENDS TO FOLLOW MYLAN, THE DECISION TO ONLY APPLY MYLAN PROSPECTIVELY IS CORRECT

If, despite the analysis above, FDA insists on adopting Mylan, the Agency's decision to apply Mylan only prospectively is correct. The Mylan court's equitable determination that application of its ruling to the parties before it would upset their settled expectations, founded on the pre-existing regulation, was correct. Mylan, 81 F. Supp. 2d at 44. Similarly, until the date of the Guidance, regulated industry had no inkling that the Agency would abandon its long-established regulation. Thus, as the Guidance states, the same equitable considerations that motivated the Mylan court require that the Guidance only be applied prospectively. Guidance at 4-5.

**IV. IMPLEMENTATION OF THE GUIDANCE WOULD REQUIRE
REPROMULGATION OF THE PROPOSED 180-DAY EXCLUSIVITY RULE**

The Guidance states that FDA “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 [64 FR 42873, August 6, 1999].” Guidance at 3. FDA cannot take this action, however, because, as discussed in Section II above, the Agency must first engage in notice-and-comment rulemaking with respect to the changes proposed in the Guidance. FDA cannot make these changes as part of a final rule in another rulemaking, when they were not part of the proposed rule.

Moreover, the changes contemplated in the Guidance would significantly affect the substance of the proposed 180-day exclusivity rule itself. A pivotal assumption underlying that proposal was that a decision of a “court” would be an appellate decision or a district court decision for which the time for appeal had run. 64 Fed. Reg. at 42879-80. The Guidance proposes to turn that assumption on its head, which would affect not only the “court” definition, but the entire structure of the proposed 180-day exclusivity rule. Other parts of the proposed rule might need to be re-adjusted or re-thought to account for the changed definition. Those who submitted comments on the proposed rule might wish to modify or retract their comments in light of the new Guidance. In brief, the original proposed rule would have changed sufficiently to require its repromulgation.

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V. CONCLUSION

FDA's Guidance should be rescinded. It is contrary to the unambiguous requirements of the statute and its legislative history, undermines the statute's purpose, and is procedurally flawed. If not rescinded, the Guidance should only be applied prospectively, and as part of a re-promulgation of FDA's August 6, 1999, proposed rule on 180-day exclusivity.

BRISTOL-MYERS SQUIBB COMPANY

A handwritten signature in black ink that reads "Donald J. Barrack / MDP". The signature is written in a cursive style and is positioned above the typed name.

By: Donald J. Barrack