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December 20, 2002

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

Re: Comments on Draft Regulations Concerning
Stays of ANDA Approvals and Patent Listing
Requirements;
FDA Docket No. 02N-0417

Dear Sir or Madam:

Greenblum & Bernstein is a general patent law firm having substantial experience with issues surrounding approval of generic drugs. While we count a number of generic and branded drug companies among our clients, the enclosed comments were prepared in the public interest, and not with any particular client in mind. That is, these comments were not requested or paid for by any client, and should not be taken as espousing the views or furthering interests of any particular company.

Because the comment period is scheduled to expire on December 23, 2002, these comments are timely submitted. The undersigned respectfully asks FDA to consider these comments when preparing the final regulations.

*FDA Should Reconsider the Basis for FDA's New Interpretation
Eliminating Multiple Stays of Approval:*

In the draft regulations, FDA reverses its longstanding, publicly stated, and judicially endorsed position that the possibility of multiple 30-month stays is a natural outcome, and reasonable interpretation, of the Hatch-Waxman amendments. In contrast, the draft regulations now state that limitation to only a single 30-month stay is a natural outcome and reasonable interpretation of the statute. These are mutually contradictory interpretations of the statute – “exactly one stay” simply cannot be reconciled with “multiple stays.” Nevertheless, according to the Federal Register

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announcement of the proposed rule, it is FDA's position that these two irreconcilable interpretations are merely alternate reasonable interpretations of the statute.

It is true that agencies are generally given wide latitude when interpreting their own statutes, and any reasonable interpretation will generally be upheld in court. *Chevron, U.S.A., Inc. v. Natural Resources Defense Counsel*, 467 U.S. 837 (1984). In this case, however, FDA has made a complete about-face when re-interpreting the statute. FDA refuses to recognize that both interpretations cannot simultaneously be reasonable interpretations but instead maintains that both interpretations are reasonable.¹ This in itself is not reasonable, and may seriously jeopardize the regulations when (as is virtually certain to happen) the regulations are challenged in court.

Thus, if FDA truly wants the new regulation to pass judicial review, then FDA must admit that the earlier interpretation was incorrect. This may be difficult to do in view of FDA's long history of espousing and enforcing the older interpretation, but it is necessary. Otherwise, FDA's denial of this fact will likely compromise FDA's position in court, and may even lead to nullification of the new regulation. An unfavorable court decision on this basis may call into question FDA's motives and competence, and may undermine FDA's credibility.

FDA's basis for the new interpretation is that an amendment to an ANDA already containing a paragraph IV certification does not amend the ANDA to "include" a paragraph IV certification, and as such, does not trigger the notice requirement, thus averting an additional 30-month stay. It is respectfully submitted that there is firmer support in the relevant statutes for the proposition that multiple stays were never intended.

This is perhaps most easily seen through an examination of 35 U.S.C. § 271(e)(1).² This section states that it shall be an act of infringement to submit an ANDA (or a 505 (b)(2) application). It is this provision that confers standing upon the NDA holder and patentee to bring the patent infringement suit. See *Eli Lilly and Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990). In *Medtronic*, the Court discusses at length the certification requirement in ANDAs and the litigation that may result from a Paragraph IV certification. *Id.* at 676-79. The Court then notes:

This scheme will not work, of course, if the holder of the patent pertaining to the pioneer drug is disabled from establishing in court that there has been an act of infringement. * * * Thus, an act of infringement had to be created for these ANDA

¹ Indeed, if two contradictory interpretations were both reasonable, this would raise serious questions regarding the statute itself.

² This is a patent statute, but as part of the Hatch-Waxman amendments, this section of the U.S. Code links FDA law with patent law. Accordingly, it should also be considered part of FDA law.

and paper NDA proceedings. That is what is achieved by § 271 (e)(2) – the creation of a highly artificial act of infringement that consists of submitting an ANDA or a paper NDA containing the fourth type of certification

Id. at 678 (emphases added). Thus, without this “highly artificial act of infringement that consists of submitting an ANDA,” there is no standing for the NDA holder or patentee to bring suit. *Id.*

Note that, according to the statutory interpretation in this Supreme Court decision, the technical act of infringement that confers standing is the *submission* of an ANDA. Merely having an ANDA on file is not defined as an act of infringement, neither is sending FDA correspondence in an as yet unapproved ANDA an act of infringement. The only act of infringement defined in the statute is the initial act of sending FDA a new ANDA, one that is not yet on file. The technical act of infringement occurs, if ever, only when the ANDA is first submitted, and not at any time thereafter. Accordingly, it follows that if a patent is late listed, then, by definition, there is no infringement of the patent merely by a company already having an ANDA on file.³ Put another way, the NDA holder cannot “force infringement” upon the ANDA applicant by listing a patent — it is only the ANDA applicant’s act of submitting the ANDA that is defined as infringement, *not* the NDA holder’s act of listing a patent.

This idea – that only an originally-submitted paragraph IV certification can result in a stay – also has support in the FDCA. In particular, attention is drawn to FDCA § 505 (j)(5)(B), which codifies the imposition and effect of the 30-month stay. In relevant part, the statute states:

The approval of an application *submitted* under paragraph (2) shall be made effective on the last applicable date determined under the following:

* * *

(iii) If the applicant made a certification [under paragraph (IV)] the approval shall be made effective immediately unless an action is brought for infringement of a patent

FDCA § 505 (j)(5)(B) (emphasis added). Thus, the statute clearly refers to the application as submitted, and provides that paragraph IV certifications in the originally submitted application shall be subject to the 30-month stay. Accordingly, a reasonable interpretation of the statute is that only paragraph IV certifications in originally submitted ANDAs can lead to a 30-month stay of approval.

³ It is noted that should litigation be filed, this position may also be argued in court as a basis for dismissing a lawsuit on a late-listed patent. This additional aspect of the statute is apart from, and independent of, FDA’s interpretation of the statute as it relates to the certification and notice requirements.

Thus, contrary to FDA's previous position, there does not appear to be statutory basis at all for imposing a 30-month stay of approval as a result of a late-listed patent. Accordingly, in order to maximize the new provisions' (and FDA's) chances of surviving judicial review unscathed, the notice of final rule-making should make clear that FDA's previous interpretation leading to multiple stays was *not* a reasonable interpretation of the statute. On the other hand, based on the reasoning in the Proposed Rule, in the present letter, and any other arguments that FDA may develop, limitation to but a single stay *is* a reasonable interpretation of the relevant statutes.

FDA Should Use the Newly-Required "Patent Declaration" to Limit Stays of Approval

Under the draft regulations, the NDA applicant/holder must submit a "Patent Declaration" addressing whether specific claims of the submitted patent cover the approved drug (active ingredient or product) or an approved method of use. The patent declaration is a major conceptual improvement to the existing regulatory scheme because it finally recognizes the importance of the individual claims of a patent, and does not treat patents as monolithic objects. FDA deserves ample praise for recognizing this important point despite FDA's professed reluctance to address substantive issues of patent law.

As the draft regulation is written, however, there are no implications or consequences associated with the Patent Declaration. The only patent declarations FDA will receive are those in which the NDA holder determined, on its own, that submission is proper. As to how the Patent Declaration will actually be used, the draft regulations are completely silent.

At the very least, FDA should incorporate into the regulations that where the only claims being asserted in a listed patent are claims that the NDA holder has not represented to cover the approved product (drug substance or composition), or an approved method of use, then such a suit should not be basis for a thirty-month stay of approval.⁴ Such an interpretation is reasonable, because the FDCA does not reasonably contemplate lawsuits or stays of approval based on patents or claims that do not cover the approved product or an approved method of use.

Perhaps the simplest way to implement such a rule would be for FDA to assume that a stay is proper unless informed otherwise by either part to the lawsuit. To document that a stay is improper, FDA should require a copy of the relevant complaint or other official court document to establish that the only claims being litigated are claims that the NDA holder did not assert to cover the approved product or an approved method of use.

⁴ Whether or not such a suit can even be sustained is a matter for an Article III court to decide. FDA need not address this issue, but need only address whether a 30-month stay of approval is proper.

FDA Should Not Exempt Approved NDAs from the Patent Declaration Requirement

The proposed regulations would only apply the enhanced Patent Declaration requirement prospectively. Under this proposal, more emphasis is placed on NDA holders and NDA applicants to clearly identify the specific patent claims that cover the approved product and method of use. This intent is beneficial as far as it goes, but the proposal does not go far enough, because there are many questionable patents already listed in the Orange Book, and the draft regulations do not address these listings.

Accordingly, it is proposed that FDA include provisions in the regulations to address patents that are already listed. Such provisions could take several forms, some of which are proposed herein.

First, FDA should amend its rules regarding patent challenges under 314.94 (a)(12)(vii). Under current rules, if the propriety of a patent listing is questioned, the NDA holder need merely report to FDA that the listing is correct, without providing any substantiating statements. It is hereby suggested that the draft regulations also amend this provision, and require the NDA holder to reply to a patent challenge with the same Patent Declaration that the draft regulations propose to prospectively apply to applicants of new NDAs. It is also suggested that the reply include a brief factual explanation why each cited claim covers the approved product or method of use. If the NDA holder declines to respond within a predetermined amount of time (e.g., 30 days), then FDA should de-list the patent in question.

FDA likely has statutorily-grounded authority to de-list patents. This directly follows from FDCA §§ 505 (b)(1) and (c)(2), which authorize FDA to list only patents that cover the approved product or an approved method of use. Just as a reasonable interpretation of these sections supports the newly proposed enhanced Patent Declarations, so too do these sections support removal of patents that the NDA holder does not assert to cover the approved product or an approved method of use. Unless the NDA holder asserts that the patents in question cover the approved product or an approved method of use, then there is no statutory basis for listing the patent.

Second, FDA should timetable (e.g., two years) for all NDAs to have Patent Declarations submitted for listed patents. This is no undue burden on the NDA holders. After all, far more time, money, and effort is involved with obtaining the patents than would be required to fill out a short questionnaire. If the NDA holders and patentees have the resources and interest to obtain the patents in the first place, then they should also have the resources and ability submit this relatively small amount of information to FDA.

In the alternative, FDA should require the NDA holder to submit a Patent Declaration as to any patent subject to a certification under Paragraph IV (or Paragraph iv for applications under 505(b)(2)). If the Patent Declaration is not submitted within the 45-day time frame for filing suit, then the patent in question should be de-listed.

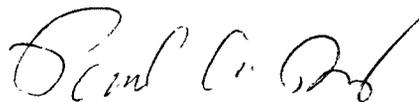
FDA Should Emphasize Again That Its Role in Listing Patents Remains Purely Ministerial

FDA must clarify that even with the enhanced Patent Declaration requirements associated with listing a patent, FDA's role nevertheless remains purely ministerial. That is, even under the new regulations, FDA does not review the declarations for legal or factual accuracy, but, as before, simply accepts the NDA holder's statements, and lists the submitted patents. Accordingly, FDA's acceptance of a Patent Declaration and patent submission should not be construed to imply FDA's review or endorsement of the contents of the Patent Declaration. Nor should an NDA holder's patent submission (or reply to a patent challenge) be construed as FDA's finding that the patent covers the approved product or an approved method of use.

In concluding these comments, we would like to state that problems with preventing entry of generic drugs into the market are broader than these proposed rules have endeavored to address, and do not have an adequate regulatory solution. For example, the 30-month stay no longer protects the generic industry (even assuming it ever did), but merely serves to delay generic approvals by encouraging frivolous lawsuits. Thus, the 30-month stay should be entirely eliminated. Further, there remains no method for generic companies to seek de-listing of inappropriate patents from the Orange Book. FDA, however, is bound by the Food, Drug, and Cosmetic statute, and so is unable to completely address these problems itself. It must be emphasized, therefore, that the current proposed regulations are by no means a cure to the problem, but instead should be considered a temporary stopgap measure. The true solution to permitting fair entry of generic drugs into the U.S. market is legislative, not regulatory.

Thank you for the opportunity to comment on the above-referenced draft regulations.

Sincerely,
GREENBLUM & BERNSTEIN, P.L.C.



Paul A. Braier, Ph.D., Esq.