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February 14, 2003

BY HAND DELIVERY

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

Re: REQUEST FOR EXTENSION OF COMMENT PERIOD
Docket No. 02N-0417

Dear Dockets Management Branch:

The undersigned submits this petition under 21 C.F.R. §§ 10.35 and 10.40(b)(3) requesting that the Commissioner of Food and Drugs extend and reopen the comment period on FDA's proposed rule on "Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying that a Patent Claiming a Drug is Invalid or Will Not be Infringed" (Docket No. 02N-0417). The request is being made solely to extend and reopen the comment period for the limited purpose of accepting supplemental comments on the proposed rule from the Pharmaceutical Research and Manufacturers of America ("PhRMA"). The supplemental comments are attached to this petition.

The supplemental comments do not raise any new issues or respond to any points made in any other person's comments. Rather, they simply provide additional legal support for one point made in PhRMA's original comments. Acceptance of these supplemental comments will materially advance FDA's informed consideration of the matter, will not delay promulgation of a final rule, and will not prejudice any other person.

A. Decision Involved

On October 24, 2002, FDA published a proposed rule on "Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying that a Patent Claiming a Drug is Invalid or Will not be Infringed" (Docket No. 02N-0417). 67 Fed. Reg. 65448 (Oct. 24, 2002). FDA invited interested parties to submit written or electronic comments by December 23, 2002.

02N-0417 EXT 1

B. Action Requested

The undersigned requests that the Commissioner extend and reopen the comment period for the proposed rule to allow PhRMA to submit to Docket No. 02N-0417 the attached supplemental comments. PhRMA submitted comments on the proposed rule on December 23, 2002. These supplemental comments clarify and elaborate on an issue raised in PhRMA's prior submission.

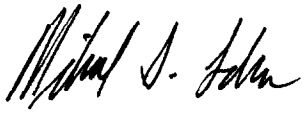
C. Statement of Grounds

FDA's proposed rule addresses a highly complex and important set of provisions of the law with substantial ramifications for the research-based pharmaceutical industry represented by PhRMA. As PhRMA explained in its December 23, 2002 comments, its members hold the overwhelming majority of the new drug applications filed with the agency. The ability of PhRMA's members to continue to invest in future drug research and development, depends in critical part on the intellectual property rights, specifically the patent rights, that protect their inventions. Accordingly, PhRMA and its members have a unique stake in the patent listing and stay provisions that are the subject of FDA's proposed rule.

PhRMA's supplemental comments are limited to addressing an issue raised in PhRMA's prior submission regarding the opportunity to obtain a 30-month stay, and provide additional legal support for PhRMA's previously stated position. Specifically, these supplemental comments provide further legal support for the rules that should govern notification of paragraph IV certifications when an abbreviated new drug application ("ANDA") or 505(b)(2) application is amended to change an existing paragraph III certification into a paragraph IV certification. This issue was not considered in FDA's proposed rule and should be addressed in any final rule. If FDA does not provide clarification on this issue, there will be a serious potential loophole in the regulatory regime for patent certifications, which ANDA and 505(b)(2) applicants could exploit to evade triggering *any* 30-month stay. As explained more fully in the attached supplemental comments, such a result cannot be reconciled with the statute or with Congress's intent.

The additional legal theory set forth in PhRMA's supplemental comments constitutes important new information for FDA's rulemaking proceeding. These comments do not raise any new issue or contain any response to comments filed by other parties. For these reasons, and in light of the importance of the 30-month stay issue, and the unique and substantial potential impact on PhRMA's members of FDA's proposed rule, there are sufficient grounds under 21 C.F.R. § 10.40(b)(3) to extend and reopen the comment period for the limited purpose of accepting PhRMA's supplemental comments.

Respectfully submitted,



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Supplemental Comments of the

Pharmaceutical Research and Manufacturers of America (PhRMA)

on

FDA's Proposed Rule:

"Applications for FDA Approval to Market a New Drug: Patent Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying that a Patent Claiming a Drug is Invalid or Will not be Infringed"

[Docket No. 02N-0417]

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February 14, 2003

Introduction

The Pharmaceutical Research and Manufacturers of America ("PhRMA") submits these supplemental comments in response to the proposed rule FDA published on October 24, 2002 regarding the agency's implementation of the patent listing and 30-month stay provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the "Hatch-Waxman Amendments").[1] PhRMA submitted comments on the proposed rule on December 23, 2002. These supplemental comments address an issue raised in PhRMA's prior submission regarding the opportunity to obtain a 30-month stay, and provide additional legal support for PhRMA's previously stated position.

In particular, these supplemental comments present further legal support for the rules that should govern notifications of paragraph IV certifications when an abbreviated new drug application ("ANDA") or 505(b)(2) application is amended to change an existing paragraph III certification into a paragraph IV certification. This issue was not considered in FDA's proposed rule, and should be addressed in any final rule. If FDA does not properly clarify this issue, there will be a serious loophole in the regulatory scheme for patent certifications, which ANDA and 505(b)(2) applicants could exploit to evade the triggering of *any* 30-month stay. Such a result cannot be squared with the statute or Congress's intent.

Summary

Under the proposed rule, an ANDA or 505(b)(2) applicant could avoid the possibility of a 30-month stay based on patents listed at the time the ANDA or 505(b)(2) application was submitted by making paragraph III certifications to those patents in the

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[1] 67 Fed. Reg. 65448 (October 24, 2002).

original ANDA or 505(b)(2) application and later changing the paragraph III certifications to paragraph IV certifications. So long as the ANDA or 505(b)(2) applicant previously made a paragraph IV certification to a single listed patent, under the proposed rule there would be no requirement to provide notice, and no opportunity for a 30-month stay, based on the new paragraph IV certifications.

This loophole in the proposed rule can be addressed within the new statutory interpretation framework FDA has set forth. FDA should provide that an ANDA applicant must give notice of a new paragraph IV certification to a previously listed patent because the change to the prior patent certification (a) relates back to, and substitutes for, the original patent certification, and/or (b) renders the applicant's section 505(j)(2)(B)(i) statement incomplete and invalid without the new notice. The same approach should apply to 505(b)(2) applications. This fix to the proposed rule is fully consistent with FDA's proposed approach to new paragraph IV certifications made to later listed patents. The fix is necessary to ensure that disputes concerning all of the patents listed at the time an ANDA or 505(b)(2) application is submitted are identified, and that new drug application ("NDA") and patent holders have an opportunity to resolve those disputes prior to generic drug approval in accordance with the basic Hatch-Waxman patent certification scheme.

Discussion

I. FDA's Proposed Rule Could be Manipulated by ANDA and 505(b)(2) Applicants.

FDA's proposed rule could be manipulated by ANDA and 505(b)(2) applicants to deprive NDA and patent holders from having a meaningful opportunity to obtain even a single 30-month stay. For example, ANDA applicants could cherry pick one

narrow listed patent for a paragraph IV certification, make paragraph III certifications to all other listed patents, and then later convert the paragraph III certifications to paragraph IV certifications. Under FDA's proposed rule, the ANDA applicant would not have to provide notice regarding the new paragraph IV certifications, and the affected NDA and patent holders would have no opportunity to obtain a 30-month stay with respect to those paragraph IV certifications.

If the ANDA applicant picks a narrow listed patent for its single paragraph IV certification, such that the NDA or patent holder could not bring an infringement action on that patent, the ANDA applicant would successfully avoid facing *any* 30-month stay.[2] This is a major loophole in the proposed rule and risks substantially undermining the entire Hatch-Waxman scheme if not fixed.

FDA's proposed rule does not address this circumstance. The proposed rule focuses only on amended patent certifications that arise due to later listed patents for an NDA. The proposed rule fails to consider the proper treatment of other amended patent certifications, which ANDA and 505(b)(2) applicants could make to game the new proposed rules.

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[2] The FTC considered 104 drugs in its study of the Hatch-Waxman Act and found that innovators did not file suit in response to a paragraph IV challenge for 29 drugs – approximately 28 percent of the time. Federal Trade Commission, "Generic Drug Entry Prior to Patent Expiration," July 2002 <http://www.ftc.gov/os/2002/07/genericdrugstudy .pdf> (August 1, 2002).

II. PhRMA's Previous Comments Offer One Way to Fix the Loophole in the Proposed Rule.

Under FDA's existing regulations, amendments to ANDA and 505(b)(2) applications that are made to change a patent certification that the applicant had already made should relate back to, and substitute for, the original patent certification. 21 C.F.R. § 314.94(a)(12)(viii). Under this approach, the amended patent certification must be treated as if it were made with the original ANDA or 505(b)(2) application. As such, the certification would trigger a notice obligation, because it would not be considered an additional paragraph IV certification to an application that already contains a prior paragraph IV certification. The NDA and patent holders would then have an opportunity to bring a patent infringement action and obtain a 30-month stay. Further explanation of this interpretation of the statute can be found in PhRMA's prior comments at pages 6 to 9.

III. FDA Can Fix the Loophole Under an Alternate Legal Theory.

A. FDA Must Consider Section 505(j)(3)(B)(i).

FDA's proposed rule focuses exclusively on the agency's interpretation of section 505(j)(2)(B)(iii) of the Federal Food, Drug, and Cosmetic Act ("FDCA" or the "Act"), which addresses the requirement for notice when an ANDA is "amended to include" a paragraph IV certification.[3] The agency's approach applies, for example, when an ANDA is amended to make a certification to a newly listed patent. Nowhere does FDA address section 505(j)(2)(B)(i) of the Act. This section is pivotal, however, and should be read to

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[3] The proposed rule also addresses the corollary provision for 505(b)(2) applications, section 505(b)(3)(C) of the FDCA. For convenience, the remaining portions of PhRMA's supplemental comments will only discuss ANDAs. The same analysis and points apply to 505(b)(2) applications.

require notice when an ANDA applicant revises a prior certification to make a new paragraph IV certification to a previously listed patent.

Section 505(j)(2)(A)(vii) of the Act provides that an ANDA must contain "a certification . . . with respect to each patent [in the Orange Book] which claims the listed drug . . . or which claims a use for such listed drug for which the applicant is seeking approval." Section 505(j)(2)(B)(i), in turn, requires that an ANDA contain

> a statement that the applicant will give the notice required by clause (ii) to (I) each owner of the patent which is the subject of the certification . . ., and (II) the holder of the approved application under subsection (b) for the drug which is claimed by the patent or a use of which is claimed by the patent . . . .

The notice required by clause (ii) is, of course, notice of paragraph IV certifications, and must include a detailed statement of the factual and legal basis for the applicant's opinion that the challenged patents are not valid or will not be infringed. FDCA § 505(j)(2)(B)(ii). These statutory provisions -- including section 505(j)(2)(B)(i) in particular -- require all ANDAs to contain a statement that the applicant will provide notifications to NDA and patent holders for *all* paragraph IV certifications to patents listed at the time the ANDA is submitted.[4] *See also* 21 C.F.R. § 314.95(a) (requiring notice "for each patent" for which an ANDA applicant submits a paragraph IV certification); *id.* at §§ 314.95(c)(5 & 6).

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[4] FDA underscored the operation of these provisions when it originally proposed regulations regarding the patent certification process:

> The [paragraph IV] certification must be accompanied by the statement required by section 505(j)(2)(B)(i) of the act that the applicant will give the notice required by section 505(j)(2)(B)(ii) of the act and proposed § 314.95(a) to the patent owner or its representative and the holder of the approved application for the listed drug and by a statement that

(continued...)

When an ANDA applicant makes a paragraph III certification in its original ANDA, and later changes that certification to a paragraph IV certification, the section 505(j)(2)(B)(i) statement in the ANDA becomes incomplete and invalid, unless the applicant provides notice for its newly made paragraph IV certification. That is, the ANDA specifically states -- as it must under section 505(j)(2)(B)(i) -- that the applicant will give notice to *all* NDA and patent holders for *each* paragraph IV certification in the ANDA. The prior notice is incomplete, however, because it did not address the patent challenged under the newly revised paragraph IV certification. The only way the notice can be made complete, and the terms of section 505(j)(2)(B)(i) met, is if a new or revised notice is given to the NDA and patent holders for the additional patent being placed at issue.

The need for an amended notice is underscored by the possibility that the newly challenged patent may be owned by a different entity than the other patents. This patent owner may have never received any notice of a paragraph IV certification and no prior opportunity to obtain a 30-month stay, even though the patent was listed at the time the ANDA was first filed.

The continuing accuracy of an ANDA applicant's representation to FDA that it has provided notice for each patent listed at the time of ANDA submission for which the ANDA applicant makes a paragraph IV certification has significance beyond the receipt of

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> the applicant will comply with the requirements under proposed § 314.95(c) with respect to the content of the notice. A certification in any other form will not be accepted by the agency as a paragraph IV certification.

54 Fed. Reg. 28872, 28885 (July 10, 1989).

notice by the NDA-holder and each patent owner of the ANDA applicant's contentions of non-infringement or invalidity. The statute provides that, for each such listed patent, the NDA-holder and patent owner shall have 45 days in which to evaluate those contentions and, if appropriate, vindicate those patent rights before ANDA approval. *See* 21 U.S.C. § 355(j)(5)(B)(iii). This statutory right attaches to each listed patent independently – an infringement action need not be brought on all patents in order to vindicate any particular listed patent under the Hatch-Waxman procedures. *Id.* (triggering 30-month stay if "an action is brought for infringement of **a patent** which is the subject of the [ANDA applicant's paragraph IV] certification" within 45 days) (emphasis added). A regulatory scheme that permits the ANDA applicant itself to determine which listed patents can be enforced under the 30-month stay procedures – and at times even which patent owners will have the opportunity to utilize such procedures – cannot be squared with the statutory scheme.

B. PhRMA's Proposed Reading of Section 505(j)(2)(B)(i) is Fully Consistent with FDA's Proposed Reading of Section 505(j)(2)(B)(iii).

The proposed reading of section 505(j)(2)(B)(i) offered here is fully consistent with FDA's proposed interpretation of section 505(j)(2)(B)(iii), and does not apply to patent certifications made in response to later listed patents. Under FDA's proposed interpretation of section 505(j)(2)(B)(iii), when an ANDA applicant makes a paragraph IV certification to a newly listed patent, it need only provide notice (and thereby trigger the possibility of a 30-month stay) if the ANDA contained no prior paragraph IV certification. Only in such circumstances would the ANDA be considered to be "amended to include" a paragraph IV certification. Even accepting FDA's interpretation of 505(j)(2)(B)(iii), notice should be

required under section 505(j)(2)(B)(i) when an ANDA applicant converts an *existing* paragraph III certification into a paragraph IV certification.

As explained above, the act of converting a paragraph III certification into a paragraph IV certification renders the section 505(j)(2)(B)(i) statement in the ANDA incorrect and thus deficient. The deficiency can be corrected only by providing a new or amended notice to the NDA and patent holders setting forth the basis for the converted paragraph IV certification.

By contrast, this same deficiency does not arise when an entirely new paragraph IV certification is made to a later listed patent. To be consistent with the statutory interpretation set forth by FDA in the proposal, the section 505(j)(2)(B)(i) statement applies to patents listed at the time the ANDA was submitted. That is, the section 505(j)(2)(B)(i) statement does not become incorrect (under FDA's interpretation) when a paragraph IV certification is added to an ANDA in response to a newly listed patent. For this reason, FDA's recognition in the final rule of the ANDA applicant's obligation to provide notice when it amends its ANDA to include a new paragraph IV notice to a previously listed patent would not provide the NDA-holder with the opportunity under the final rule to obtain additional 30-month stays in connection with subsequent patents listed after the ANDA was filed.

Moreover, the situation presented by ANDA applicants' amendments to existing patent certifications is logically distinct from that presented by later listed patents. Responsibility for changes in existing patent certifications -- unlike new patent certifications to later listed patents -- rests solely in the hands of the ANDA applicants themselves. They

therefore should not be heard to complain of a regime under which a voluntary change in certification gives rise to the opportunity for a 30-month stay.

Reading section 505(j)(2)(B)(i) in the manner articulated here fixes the loophole in the proposed rule by ensuring that ANDA applicants cannot evade the notice requirement under the Hatch-Waxman law by making a paragraph III certification when the ANDA is submitted and subsequently converting the certification to a paragraph IV certification. At the same time, FDA's proposed interpretation of section 505(j)(2)(B)(iii) would prevent NDA and patent holders from obtaining multiple 30-month stays by the listing of patents after ANDA submission. In essence, these later listed patents would be governed by section 505(j)(2)(B)(iii) and would be subject to the notice and stay rules set forth in the proposed rule, while changed patent certifications would be governed by section 505(j)(2)(B)(i) and would be subject to different notice and stay rules. This combined approach ensures that all pertinent provisions of the statute are given independent meaning and effect, and the result meets all of the policy objectives FDA articulated in the proposed rule.[5]

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[5] FDA could adopt the fix proposed here either through appropriate explanatory discussion in the preamble to a final rule or by modifying the agency's proposed regulatory language in 21 C.F.R. § 314.95(a)(3) as follows: "This paragraph does not apply to a use patent that claims no uses for which the applicant is seeking approval. This paragraph also does not apply if the applicant amends its application to add a certification under § 314.94(a)(12)(i)(A)(*4*) *for a patent as to which no certification under § 314.94(a)(12)(i)(A) previously was required* when the application already contained a certification under § 314.94(a)(12)(i)(A)(*4*) to another patent." A corresponding change could also be made to the agency's proposed regulatory language in 21 C.F.R. § 314.52(a)(3) for 505(b)(2) applications.

IV. The Legislative History Requires that NDA and Patent Holders Receive Notice of Paragraph IV Certifications with Respect to All Patents that are Listed When an ANDA is Filed.

The legislative history for the Hatch-Waxman law shows that Congress had an expectation that ANDA applicants would be required to provide notice of paragraph IV certifications for *all* patents listed at the time an ANDA is filed, and that NDA and patent holders would get an opportunity to litigate *all* such patents prior to generic market entry. By effectively permitting ANDA applicants to certify as to only one listed patent, and depriving NDA and patent holders of an opportunity to litigate other challenged patents during the pendency of a 30-month stay, FDA's proposed rule contravenes Congress's intent.

The legislative history of the Hatch Waxman Amendments makes plain that Congress anticipated that multiple patents would be listed in association with any particular drug, and that multiple patent certifications and notifications would be required to obtain approval of an ANDA. As explained in a House Committee Report, "[i]n most instances, an ANDA will contain multiple certifications." H. Rep. No. 98-857, pt. 1, at 28 (1984). "The Committee recognizes that in some instances an applicant will have to make multiple certifications with respect to product or controlling use patents" and intended "that the applicant make the appropriate certification for each" patent. *Id.* at 22. Moreover, "[w]hen an applicant certifies that any product or controlling use patent is invalid or will not be infringed,... it must give notice of such certification to either the owner of the patent or the representative of the patent owner" and to the holder of the NDA for the drug. *Id.* at 24.

Congress also specifically noted the potential for abuse and gamesmanship by ANDA applicants. The House Committee stated that it "does not intend that applicants be permitted to circumvent this notice requirement by filing sham ANDA's or ANDA's which

are substantially incomplete." *Id.* FDA's proposed rule does precisely that by inviting ANDA applicants to select one listed patent to challenge at the time the ANDA is submitted, and avoid notice for all other listed patents. This result is directly at odds with Congress's express intent.

FDA's proposed rule would provide for a nominal opportunity to obtain one 30-month stay as to the single patent selected for challenge in an ANDA. However, Congress recognized that certain patents are broader in application than others, and that the 30-month stay provisions will only operate as intended if they apply, at a minimum, to all patents listed at the time an ANDA is submitted, regardless of when in the ANDA process the applicant decides to challenge them. The House Committee expressly acknowledged that

> in certain instances, the patent owner may agree with the certification of the applicant. For example when the applicant certifies that patent No. 1 is invalid and patent No. 2 is not infringed, the patent owner may agree with the certification regarding patent No. 2. Then an action for patent infringement need only be brought with respect to patent No. 1.

Id. at 27 n.13.

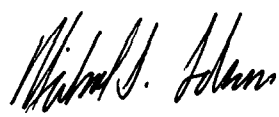
The loophole in FDA's proposed rule flows precisely from this scenario envisioned by Congress. In the example cited in the legislative history, the ANDA applicant would select patent No. 2 for a paragraph IV certification at the time it submitted its ANDA and would reserve making a paragraph IV challenge to patent No. 1 until some later date. The patent owner would agree with the certification regarding patent No. 2, and thus would not bring suit. However, the patent owner would be deprived of the opportunity for a 30-month stay with respect to patent No. 1 if the ANDA applicant later converted its paragraph III certification for it into a paragraph IV certification.

FDA's proposed rule can only be squared with Congress's intent as expressed in the legislative history if the agency fixes the existing loophole and requires notice when an ANDA applicant amends a prior patent certification to convert it from a paragraph III certification to a paragraph IV certification.

Conclusion

PhRMA appreciates FDA's consideration of these supplemental comments. For the reasons stated here and in PhRMA's prior submission, PhRMA urges FDA to fix the loophole that exists in the proposed rule concerning notifications of paragraph IV certifications.

Respectfully submitted,



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