

9165 '02 DEC 23 P5:04

December 23, 2002

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

Re: Docket No. 02N-0417

To Whom It May Concern:

We are writing to comment on FDA's proposed rule on patent listing requirements and 30 month stays.¹ See 67 Fed. Reg. 65,448 (Oct. 24, 2002). We believe that FDA's proposed rule fails to address some significant gaps in the agency's regulations with regard to patent listing and have a number of comments and suggestions. We also dispute FDA's most recent interpretation of the Hatch-Waxman 30 month stay provision and provide the following comments.

Patent Listing

FDA's abdication of its patent listing oversight duties under the Act is contrary to the plain meaning of the Federal Food, Drug, and Cosmetic Act, unlawful under the Administrative Procedure Act, and runs afoul of the holding in Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc.

FDA's current regulations, and as proposed, fail to assure that NDA holders list all patents eligible for listing. Currently, if a third party informs FDA that an NDA holder's patent listing is incomplete, under 21 CFR 314.53(f), FDA will merely inform the NDA holder of the third party's concern, explicitly stating that FDA will not change the patent information unless the NDA holder amends its patent information in response. 21 CFR 314.53(f). FDA's proposed "checklist" declaration focuses solely on assuring that NDA holders do not list inappropriate patents, and fails to assure that all properly-listable, or eligible, patents are listed. Essentially, the regulations leave unaddressed an NDA holder's failure to list eligible patents known to FDA. As

02N-0417

C23

¹ 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, 67 Fed. Reg. 65,448 (Oct. 24, 2002).

a result, the regulations permit persons who are similarly situated – for example, owners of patents eligible for listing – to be treated differently under the statute, depending on whether a separate private party – the NDA holder – elects to list an eligible patent or not. The regulations also leave parties with statutory remedies without a remedy to correct improper failures to list. Both of these deficiencies create fatal flaws in the FDA’s current and proposed regulations pertaining to patent listing in the Orange Book.

FDA takes the position that its role in administering patent listing under section 505(c)(2) of the Federal Food, Drug, and Cosmetic Act (the “Act”) is merely “ministerial.” *See* 67 Fed. Reg. at 65,453. Thus it has no affirmative role to play in patent listing decisions. Although a few courts have accepted that position, *aaiPharma* strongly disagrees. The statute places an affirmative duty on the agency to require NDA holders to submit omitted patent information for eligible patents to FDA. *See* § 505(e)(4) of the Act. If the NDA holder does not submit the omitted information, the agency “shall” withdraw the NDA after notice and opportunity for hearing. *See id.* (stating as grounds for NDA withdrawal the failure to file patent information within 30 days after notice from the Secretary “specifying the failure to file such information”).² *See also* § 505(d)(6) (requiring the agency to deny approval, after notice and opportunity for hearing, if an applicant fails to submit information on eligible patents).

FDA’s abdication of its duty to enforce proper patent listing for approved drugs under subsection 505(e)(4) of the statute results in the unlawful delegation of that duty to the NDA holder, a private party. That unlawful delegation leaves the owner of the non-listed patent without a means of enforcing its statutory right to listing because there is no private right of action under the Act and thus it has no grounds to sue the NDA holder to enforce the right. Therefore, under FDA’s current and proposed regulations, a third party patent owner is left without a remedy for its loss of its Hatch-Waxman rights of notice from ANDA applicants who would be required to submit paragraph IV certifications with respect to its patent, with the consequential loss of an automatic 30 month stay – even a single 30 month stay, as proposed by FDA’s new regulations – that would be otherwise available if the third party patent owner sought to sue for infringement within 45 days of receiving the notice. Importantly, the right of a third party patent owner to vindicate its patent against an infringement under a 30 month stay on the approval of an ANDA has been recognized by the Fourth Circuit, *see aaiPharma v. Thompson*, 296 F.3d 227, 236 (4th Cir. 2002).

We believe that FDA’s abdication of its patent listing oversight duties is not in accordance with the plain meaning of the Act and is thus unlawful under the Administrative Procedure Act (“APA”), *see* 5 USC § 706(2)(A). Specifically, the use of the word “shall” in subsection (e)(4) is unambiguous as to the mandatory nature of FDA’s enforcement responsibilities when holders of approved NDAs fail to list eligible patents. Moreover, FDA’s position results in similarly situated persons being treated differently under the statute, which is arbitrary and capricious and therefore also unlawful under section 706(2)(A) of the APA.

² *See also* H. Rep. No. 98-857, Part I at 31 (“An NDA may be revoked if the patent information available is advisable and is not filed within 30 days after receipt of a written notice by FDA specifying the failure to provide the patent information.”).

We disagree with the Fourth Circuit's analysis in *aaiPharma* because the court ran afoul of *Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984). Contrary to the plain language of the statute identifying Congress's intent to have FDA ensure that information for all eligible patents be submitted by NDA holders to the agency, the Court of Appeals found an ambiguity not argued by the government to progress to the second step of the *Chevron* analysis to eliminate the (e)(4) statutory remedy for an NDA holder's failure to submit information for eligible patents to FDA. Even assuming the correctness of the Fourth Circuit eliminating the remedy that would make *aaiPharma* whole, and then ruling against *aaiPharma* for having a right but not a remedy, FDA's ministerial role is still inappropriate because it is contrary to settled law.

First, a decision that acknowledges a statutory right and then concludes that the statute fails to provide a remedy to protect the right because of FDA's self-assigned ministerial role offends the fundamental legal principle that where there is a right, there must be a remedy, and it is one of the principal duties of government to assure such remedies exist. See *Marbury v. Madison*, 1 Cranch 137, 163 (1803); see also *Peck v. Jenness*, 48 U.S. 612, 623 (1849) ("A legal right without a remedy would be an anomaly in the law.").

Second, maintaining FDA's position that it has no responsibility under the Act to ensure the listing of eligible patents results in an unlawful delegation of authority to private persons. See *Sierra Club v. Sigler*, 695 F.2d 957, 962 n.3 (5th Cir. 1983) ("[A]n agency may not delegate its public duties to private entities, particularly private entities whose objectivity may be questioned"); see also *Perot v. Fed. Election Comm'n*, 97 F.3d 553, 559 ("We agree with the general proposition that when Congress has specifically vested an agency with the authority to administer a statute, it may not shift responsibility to a private actor"). These two shortcomings undermine any claim of deference for FDA's view that the statute limits its role to merely doing what NDA holders tell the agency to do.

In sum, we believe that the agency's interpretation that Hatch-Waxman patent listing relegates it to a ministerial role runs afoul of a clear reading of the Act, *Chevron*, and the APA. To ensure that patent information is submitted for all eligible patents, FDA must take steps to hold NDA holders accountable for fulfilling their obligation to submit patent information under the Act. Whether this is accomplished by amending section 314.53(f) or taking other steps to ensure that NDA holders submit patent information for all eligible patents, it is critical to third-party patent owners who are currently at the mercy of NDA holders. Owners of patents eligible for listing have a valuable right that FDA must recognize and protect for the Hatch-Waxman Act to work as Congress intended.

Whether NDA holders should be required to provide additional information regarding sameness?

In its proposal, FDA asks whether NDA applicants and holders that submit patent information on a patent that claims a drug that is different in form from the drug that is the subject of the NDA, *e.g.*, a polymorph or anhydrous or hydrated form of the drug substance, should be required to submit additional information regarding the basis for the assertion that the drug substances are the same for purposes of section 505(j)(2)(A)(ii) of the Act. We believe that submis-

sion of such information, when necessary to demonstrate sameness, would be beneficial to ensuring the appropriateness of patent listings only when there is a legitimate question about sameness. Under this circumstance, information similar to that required in an ANDA would be appropriate to demonstrate sameness.³ When different forms of an active ingredient are known to be the same, no additional information should be required to show sameness.

FDA's interpretation that only one 30 Month Stay is permissible is unsupported by the Act and impermissible under the APA.

FDA's new interpretation is an extremely strained construction of the Act and legislative history that ignores the plain meaning of the 30 month stay provisions.

The agency takes the position that it can reinterpret the Act to arrive at the opposite conclusion from its longstanding view that multiple stays were part of the compromise reached in the Act between innovators and generic firms. The agency held the view that multiple stays were authorized by the Act until the proposed rule, and argued that view forcefully a year and a half before the proposal. *See* 67 Fed. Reg. at 65,448 (discussing the agency's longstanding position in favor of multiple stays, and citing FDA's brief in *Andrx Pharmaceuticals, Inc. v. Biovail Corp.*, No. 01-6194-civ-Dimitrouleas/Johnson (S.D. Fla.) (filed April 30, 2001) as the most recent articulation of that position). In effect, FDA "reexamined" the Act to determine if there was another reasonable interpretation that would support a limitation on 30 month stays. The credibility of such an outcome-driven interpretation is obviously suspect and the strained manner in which FDA reached its new interpretation does not inspire confidence in the agency's proposed position.

FDA now seeks to interpret the Act to mean that if an ANDA holder amends the application to include an additional paragraph IV certification, *i.e.*, in response to a late listed patent, no new notice is required to the patent owner and NDA holder. That conclusion is based on imputing a new meaning to the word "include" in section 505(j)(2)(B)(iii) of the Act, which states that "[i]f an application is amended to include a [paragraph IV] certification, . . . notice [to the patent owner] . . . shall be given when the amended application is submitted." The agency reasons that for ANDAs that already contain a paragraph IV certification, an amendment containing another paragraph IV certification does not amend the ANDA to "include" a paragraph IV certification, and therefore, notice related to that certification is not required. Because no notice will be given, the predicate for a 30 month stay will be eliminated, thus eliminating the automatic stay if a lawsuit were filed alleging infringement. In other words, by eliminating the law's notice trigger to patent owners and NDA holders, the agency likewise eliminates the 30 month stay provision for late listed patents.

Clearly, the law requires the listing of all eligible patents, including those issued after the approval of an NDA. As a result, Hatch-Waxman obviously considered the potential for amendment of pending ANDAs whenever an eligible patent was listed. Therefore, whenever a

³ The Orange Book states, "Anhydrous and hydrated entities, as well as different polymorphs are considered pharmaceutical equivalents and must meet the same standards and, where necessary, as in the case of ampicillin/ampicillin trihydrate, their equivalence is supported by appropriate bioavailability/bioequivalence studies." FDA, CDER Approved Drug Products with Therapeutic Equivalence Evaluations, 22nd Ed., Preface at "A" Codes.

patent is listed during the pendency of an ANDA, a paragraph IV certification would be required or the new patent would block FDA approval for years. Unquestionably, the certification to the amended ANDA would be “included” in the application, thus requiring notice. Under any normal meaning of the word “include”, a paragraph IV certification must be “included” in an ANDA *with respect to each new patent to which the certification necessarily applies*.

“Inclusion” does not connote homogeneity or heterogeneity. It merely means that something is made a part of a larger grouping or whole. Indeed, the word “include” is defined by Random House Webster’s College Dictionary (2d ed. 1997) as “to contain or encompass as part of a whole” or “to place as part of a category.” The illogic of FDA’s new interpretation is demonstrated by section 505(j)(7)(A)(iii), pertaining to updating drug approvals and listings in the Orange Book every 30 days. There it states that the Secretary “shall, in [such] revisions . . . include such [patent] information for such drug.” § 505(j)(7)(A)(iii) of the Act. Obviously, “include” carries its normal meaning – there, adding new information to existing similar information. Contrary to FDA’s suggestion, whether items in a grouping are similar or different, the word “include” means one thing – here, each new paragraph IV certification to a listed patent is “included” in, and amends, an ANDA.

Indeed, FDA’s proposal would eviscerate a fundamental purpose of the Hatch-Waxman Act – *i.e.*, to ensure that the patent owner whose patent has been listed is aware of the ANDA and given the opportunity under the statute to bring a patent infringement litigation within the statute’s 45 day period and thereby obtain the benefits of the 30 month stay. This is yet another example of how the FDA’s current and proposed regulations fail to ensure that patent owners who are not also the NDA holders receive the rights provided to them by statute. The statutory compromise embodied in the Hatch-Waxman Act is clear:

- an NDA holder is required to list all properly-listable patents in the Orange Book for the ANDA applicant to have proper notice of them (including any post-approval, eligible new patents within 30 days of the patents’ issuance);
- the ANDA applicant through written notice is required to provide the appropriate certification with respect to such patents, to both the NDA holder and the patent owner; and
- the patent owner has a statutory right to bring an infringement action within a 45 day period and thereby obtain an automatic 30 month stay to litigate the relevant patent.

As proposed, however, an NDA holder could list a patent owner’s new patent in the Orange Book without the ANDA applicant being required to provide the patent owner – who is not necessarily the NDA holder – with any notice of a certification, thereby keeping the patent owner from becoming aware of this listing until after the 45 day Hatch-Waxman period has expired and the patent owner’s rights to obtain a 30 month stay have expired.

FDA further unconvincingly relies on Hatch-Waxman legislative history to support its view. The agency quotes the House Report, which states “an ANDA ‘is subsequently amended so as to bring it within this notice requirement.’” 67 Fed. Reg. at 65,456 (quoting H.Rep. 98-

857, Part 2, 98th Cong., 2d Sess. 14 (1984)). Again, FDA strains to find meaning and suggests that only an amendment that contains a first paragraph IV certification would “bring” an application “within” the notice requirement, as opposed to the more logical and normal meaning of such language, *i.e.*, any amendment of the ANDA to contain a paragraph IV certification would “bring” the application “within” the notice requirement *with respect to the listed Orange Book patent, thereby requiring notifications by ANDA applicants*. Certainly, an ANDA could be – and would logically need to be – brought within a notice requirement multiple times because the application would no longer be within the requirement after notice was served. In other words, there is nothing compelling about an isolated sentence that is neither more definitive nor clear than the language of the statute itself.

Indeed, only a year and a half before this proposal, in FDA’s brief in the Andrx case, the agency unequivocally stated:

“nothing in the legislative history [of the Hatch-Waxman Amendments] indicates that Congress intended the 30 month bar to apply only once To the contrary Congress’ decision to link the statutory stay to each individual patent claiming the approved drug, and not just the first such patent, is fully consistent with the balance it struck between encouraging competition and rewarding innovation. In any event, . . . the plain language of the statute makes clear that the 30 month stay provision of 21 U.S.C. § 355(j)(5)(B)(iii) is triggered whenever an infringement action is brought within 45 days of receipt of notice of a paragraph IV certification.”

Thus, clear legislative language and a devoid legislative history supported FDA’s view that is diametrically opposed to its proposed position on the availability of 30 month stays. FDA’s assertion that deference supports its new view is weak and untenable. In this respect, it is important to note that Congress has a number of bills pending, including Senate Bill 812 (the McCain/Shumer “Greater Access to Affordable Pharmaceuticals Act”),⁴ that legislatively address the 30 month stay issue.⁵ Clearly, Congress believes that changing the rules on 30 month stays is not a simple matter of reinterpretation, but requires new legislation.

The agency has failed to provide a legally acceptable explanation for its complete reversal in interpretation of the Act.

FDA bases its contemplated change in interpretation on a weak factual record. FDA’s explanation for its interpretive flip is based on the findings in the Federal Trade Commission’s (“FTC’s”) Report, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* (July 2002) (the “FTC Report”). The FTC found that since 1992, NDA holders have listed patents after an ANDA was filed eight times and six of the eight times occurred since 1998. The FTC Report

⁴ In addition to S.812, which passed the Senate last summer, three House bills and two Senate bills also address 30 month stays, either by limiting them to certain patents, or by not allowing any additional stays after the first.

⁵ S.812 would allow one 30 month stay and only for patents listed within 30 days of approval; it would eliminate 30 month stays for later listed patents. Of course, the fact that Congress has proposed legislation that would limit 30 month stays does not give the agency any authority to enact its own limit in regulations. In fact, as argued above, it supports the position that the Act must be amended by new statute – not by agency reinterpretation – in order to impose such a limit.

stated that for the eight products, the additional 30 month stays resulted in delays of FDA approval of between 4 and 40 months, representing significant additional profits for the drug companies. Notably, however, the eight products represented less than 8% of the 104 products in FTC's study. Further, as FTC's report shows, the year 2000 alone included 4 of the 8 drug products for which patents were listed after an ANDA was submitted and litigation ensued; in the other years, only 1996 had more than one drug (two) for which patents were listed late. In 1997 and 1998 there were none, and in 1999 and 2001 (through June 25, 2001), there was only one. The millennium year was anomalous and fails to represent a trend, let alone an adequate basis for a wholesale switch from a longstanding interpretation of the Act. Moreover, FDA clearly had knowledge of the data collected for the FTC Report at the time of its brief in the Andrx case, and with full knowledge of the data, nonetheless, fully supported multiple 30 month stays as the correct interpretation of the Act and legislative history. Simply put, the FTC Report cannot provide an adequate basis for the agency's dramatic change in position. Clearly, in light of the pending legislation, the agency's basis for the switch is a matter of political expediency and not rationally based on the Act or "new" information. Changes in law of such magnitude should be Congress's province, not FDA's.

Indeed, as discussed in the legislative history relied upon by FDA in the proposed rule, some members of Congress considering a 1983 version of the bill were concerned that NDA holders would obtain multiple patent term extensions, which like multiple 30 month stays would inhibit competition, and the bill was held up on a technicality despite strong support. Nonetheless, in 1984, despite the continuation of such concerns, the bill was enacted with not just the 18 month stay discussed in the legislative history, but with a 30 month stay, which represented the last compromise of the legislative negotiations.⁶ As FDA's brief in the Andrx case and court decisions emphasize,⁷ Hatch-Waxman was a compromise, a delicate balance between the availability of lower cost drugs and the protection of incentives for pharmaceutical innovators. The 30 month stay was a critical part of that compromise and a matter of great importance to innovators. Limiting 30 month stays therefore is a change in Congress's carefully crafted balance that can only be justified if the change meets Congress's intent. Here, FDA's new weighing of the interests of generic and pioneer drug manufacturers is without support in the Hatch-Waxman Amendments and represents a position of convenience for FDA without a rational connection to any facts or policy that would support the change.

While the agency is allowed reasonable modifications of its interpretation of the Act, for example, when new information is brought to its attention, or new circumstances such as resource constraints arise, such departures require a satisfactory explanation, including "a rational connection between the facts found and the choice made." See *Motor Vehicle Mfrs. Assn. v. State Farm Mut. Ins.*, 103 S. Ct. 2856, 2866 (1983) (quoting *Burlington Truck Lines v. U.S.*, 371 U.S. 156, 168 (1962)). Therefore, the sudden adoption of an opposite view without a reasonable explanation is clearly unacceptable under the APA, especially after the former view was consistently held by the agency over many years and argued by the agency in federal court as recently as Spring 2001. It is well understood that a

⁶ On the other side of the ledger, in the final bill patent term extensions were limited to one per approved product no matter how many patents were filed for that product. See 35 USC § 156(c)(4).

⁷ See, e.g., *Fisons plc v. Quigg*, 8 U.S.P.Q.2d 1491 (D.D.C. 1988), *aff'd*, 876 F.2d 99 (Fed. Cir. 1989).

“settled course of agency policy embodies the agency’s informed judgment that, by pursuing that course, it will carry out the policies committed to it by Congress. There is, then, at least a presumption that those policies will be carried out best if the settled rule is adhered to.”

Motor Vehicle Mfrs. Assn., 103 S. Ct. at 2866 (quoting *Atchison, T. & S.F.R. Co. v. Wichita Bd. of Trade*, 93 S.Ct. 2367, 2374-2375 (1973)).

The applicable parts of the Act and the policy issues related thereto are no different now from what they were when Hatch-Waxman was enacted in 1984 or during the Spring of 2001, when FDA filed motions and memorandums in federal court in the Andrx case against the generic company’s argument that only one 30 month stay is supported by the statute and legislative history. It is important to appreciate that most of the alleged abuses of the patent listing and 30 month stay provisions that supposedly support FDA’s change in position had already occurred and the agency was well aware of them at the time it argued in favor of an additional 30 month stay in the Andrx case.

Finally, if one presumes the effectiveness of FDA’s proposal to strengthen the patent listing certifications in order to remedy abuses in over-listing of patents, only legitimate patents would be listed, and all properly-listable patents should be entitled to the same 30 month stay protection that FDA has accorded other drugs over the years. If FDA’s proposed measure is not deemed strong enough to ensure that *only* properly-listable patents (and, indeed, *all* properly-listable patents) are so listed in the Orange Book, then it should be strengthened by agency action that more effectively polices the completeness and accuracy of the Orange Book patent listings, rather than using an artificial limit on 30 month stays to discourage illegitimate patent listings. Indeed, such a new and improper “reinterpretation” by FDA sweeps too broadly to be permissible: it eliminates the 30 month stay rights provided by statute for *properly-listable* patents (for which the 30 month stay is intended) instead of amending the regulations to avoid the listing of eligible patents. Achieving proper balance between the rights of generics and NDA holders by limiting 30 month stays unfairly injures third party patent owners, who are also entitled under the Act to 30 month stays in order to litigate the infringement of their patents.

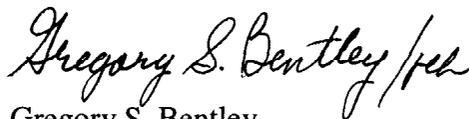
Conclusion

We are concerned that the rulemaking will become a lost opportunity for implementing FDA oversight of patent listing, consistent with the Act. We believe that active oversight by FDA is prescribed by the statute and would provide a solution to concerns regarding patent listing. Additionally, we are concerned that FDA is not reasonably following the Act’s clear language and its prior sound interpretation of the Act’s automatic stay provision. Instead, the proposal reveals an effort to distort the law to fit the current political climate, even where the distortion effectively eliminates rights granted under that law. The 30 month stay provision was central to Congress’s statutory compromise between generic and pioneer drug manufacturers, and if

changed, it should be changed by Congress and not by FDA legislating through the rulemaking process. Importantly, we continue to believe that the right of third-party patent owners to have their eligible patents listed remains unprotected by the proposed amendments to the regulations.

We appreciate FDA's consideration of our comments.

Sincerely,

Handwritten signature of Gregory S. Bentley in cursive script.

Gregory S. Bentley
Executive Vice President and
General Counsel
aaiPharma Inc.