

April 21, 2000

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
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Re: Comments To Proposed Rule, *Marketing Exclusivity And Patent Provisions For Certain Antibiotic Drugs*;
Docket Number 99N-3088

Dear Sir or Madam:

This letter provides the comments of Alcon Laboratories, Inc. ("Alcon") on the Food and Drug Administration's proposed rule entitled, *Marketing Exclusivity And Patent Provisions For Certain Antibiotic Drugs* ("Proposed Rule"). This Proposed Rule was published in the Federal Register on January 24, 2000 (65 Fed. Reg. 3623) and assigned Docket Number 99N-3088.

While Alcon is generally supportive of the Agency's efforts to implement Section 125 of the Food and Drug Administration Modernization Act ("FDAMA"), we believe the current proposal is incomplete. Although it exempts "pre-repeal antibiotics" from the marketing exclusivity and patent provisions in Section 505 of the Federal Food, Drug, and Cosmetic Act ("FD&C Act"), it fails to recognize that pre-repeal antibiotics are now eligible for the enhanced patent protections afforded under 35 U.S.C. §271(e)(2). That section permits patent owners to file infringement lawsuits earlier than would otherwise be allowed, i.e., at the time an Abbreviated New Drug Application ("ANDA") or 505(b)(2) application is submitted rather than when the allegedly infringing drug product is first commercially marketed.

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FDA's proposed regulatory framework, however, would significantly impair the ability of pre-repeal antibiotic patent holders to take advantage of this new patent remedy created by Congress. This is because: (1) ANDA and 505(b)(2) applicants for pre-repeal antibiotics are not required under the current proposal to notify the New Drug Application ("NDA") holder (or patent owner) of their submissions, and (2) FDA will not disclose the existence of a pending submission under its existing Freedom of Information ("FOI") regulations. 21 C.F.R. §314.430(b) (1999). FDA's proposed regulatory framework thus would restrict access to the very information needed to utilize the new patent remedy for pre-repeal antibiotics, i.e., information about the filing of ANDAs and 505(b)(2) applications for potentially infringing products

We believe it is highly unlikely that Congress intended to grant a remedy that, as a practical matter, can never be used. Accordingly, in tandem with exempting pre-repeal antibiotics from the patent listing and certification provisions of Section 505, FDA should implement alternative regulatory procedures by which pioneer manufacturers and patent owners of pre-repeal antibiotic drug products can be advised of the filing of an ANDA or 505(b)(2) application and, if warranted, take advantage of the Section 271(e)(2) remedy provided by Congress.

A. The Patent Remedy Set Forth At 35 U.S.C. §271(e)(2) Now Applies To Pre-Repeal Antibiotics

Prior to the enactment of FDAMA in 1997, antibiotic drug products were required to be marketed in accordance with Section 507 of the FD&C Act, 21 U.S.C. §357. As a result, they were not eligible for the exclusivity and patent protections afforded to non-antibiotic drug products under Section 505 of the Act, including three- and five-year non-

patent exclusivity and the patent listing, certification and 30-month stay procedures. 21 U.S.C. §§355(c)(3), (j)(5)(B), (D). Nor were antibiotic drug products eligible for the patent remedy set forth at 35 U.S.C. §271(e)(2), which applies only to human drug products that can be approved via an ANDA or 505(b)(2) application, both of which were unavailable to antibiotics prior to 1997.

In 1997, Congress repealed Section 507 and subjected antibiotic drug approvals to Section 505 of the FD&C Act. Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, §125(b)(1), 111 Stat. 2296, 2325 (1997). This revision made antibiotics eligible for the first time for Section 505's patent and non-patent exclusivity provisions.

It also brought antibiotics within the scope of the patent remedy set forth at 35 U.S.C. §271(e)(2). That section makes it an act of infringement to submit an ANDA or 505(b)(2) application for a drug or drug use claimed in a patent if the purpose of such submission is to gain FDA approval to commercially manufacture, use or sell the potentially infringing drug prior to expiration of the patent. 35 U.S.C. §271(e)(2). This is a "technical infringement" which provides a basis for the patent holder to file an infringement suit earlier than would otherwise be possible, i.e., while the ANDA or 505(b)(2) application is being reviewed by FDA and before the drug product can be commercially marketed. Glaxo, Inc. v. Novopharm, Ltd., 110 F.3d 1562, 1569 (Fed. Cir. 1997).¹ Since FDAMA for the first time subjected generic antibiotic products to approval

¹ This artificial act of infringement is necessary because most pre-approval uses of drugs and other medical products, including manufacture and clinical testing, are exempt from the infringement provisions under 35 U.S.C. §271(e)(1).

via ANDAs and 505(b)(2) applications, it concomitantly permitted owners of patents covering antibiotic drug products to take advantage of the patent remedy provided by 35 U.S.C. §271(e)(2).

The FDAMA provision affecting antibiotic drug products – Section 125 – also contains a transition provision affecting certain “old” antibiotics, i.e., antibiotics for which a marketing application had been submitted to FDA prior to the repeal of Section 507 (these are referred to as “pre-repeal antibiotics” in the Proposed Rule). The transition provision exempts pre-repeal antibiotics from the exclusivity and patent protections otherwise available under Section 505. Pub. L. No. 105-115, §125(d)(2), 111 Stat. 2296, 2325. In particular, Congress directed that the following statutory requirements would not apply to pre-repeal antibiotics:

1. Three- and five year non-patent exclusivity (21 U.S.C. §§355(c)(3), (j)(5)(D));
2. Patent listing (*Id.* §§355(b)(1), (c)(2));
3. Patent certification (*Id.* §§355(b)(2), (j)(2)(A)(vii), (j)(2)(A)(viii));
4. Notice to the NDA holder and patent owner of the filing of an ANDA or 505(b)(2) application containing a “Paragraph IV” certification (*Id.* §§355(b)(3), (j)(2)(B)); and
5. Thirty-month stay of approval of ANDAs and 505(b)(2) applications containing a Paragraph IV certification if a patent infringement suit is filed within 45 days of notice (*Id.* §§355(c)(3), (j)(5)(B)).

Pub. L. No. 105-115, §125(d)(2), 111 Stat. 2296, 2325.

Significantly, Congress did not exempt pre-repeal antibiotics from the enhanced

patent protections afforded under 35 U.S.C. §271(e)(2). Although the transition provision carefully lists the statutory provisions that do not apply to pre-repeal antibiotics, it is silent with respect to 35 U.S.C. §271(e)(2). *See* Pub. L. No. 105-115, §125(d)(2), 111 Stat. 2296, 2325. This silence should not be confused with ignorance of the issue. Congress was well aware of the interaction between the FD&C Act and the Patent Code and even amended portions of the Patent Code to reflect the repeal of Section 507. Pub. L. No. 105-115, §125(b)(2)(P), 111 Stat. 2296, 2325. Congress' refusal to exempt pre-repeal antibiotics from 35 U.S.C. §271(e)(2) thus must be considered deliberate.

Consequently, the patent remedy afforded by 35 U.S.C. §271(e)(2) now applies to all antibiotic drug products, both new antibiotics containing novel active moieties and pre-repeal antibiotics that are the subject of the Proposed Rule.

B. FDA's Proposed Rule Should Reflect The Fact That 35 U.S.C. §271(e)(2) Now Applies To Pre-Repeal Antibiotics

The Proposed Rule seeks to implement the transitional provision of Section 125 of FDAMA by exempting pre-repeal antibiotics from the regulatory requirements governing patent listing and certification and non-patent exclusivity, both of which affect the timing of approval of ANDAs and 505(b)(2) applications. Alcon is generally supportive of this aspect of the Proposed Rule and has no objection in that regard to the Agency's implementation of the transitional provision.

Alcon, however, believes that the Proposed Rule is incomplete and fails to reflect the fact that pre-repeal antibiotics are now covered by 35 U.S.C. §271(e)(2). If the regulation were to be finalized as proposed, it would operate – in conjunction with

existing FDA regulations – to essentially block pre-repeal antibiotic holders from taking advantage of the new patent remedy created by Congress by restricting access to the very information needed to use that remedy, i.e., information about the filing of ANDAs and 505(b)(2) applications for potentially infringing products.

Alcon does not believe it is reasonable to interpret Section 125 of FDAMA as granting a patent remedy that, for procedural reasons, cannot be used. Such an interpretation would effectively render a critical provision of Section 125 inoperative. *See Edison Elec. Inst. v. E.P.A.*, 996 F.2d 326, 335 (D.C. Cir. 1993) (a statute should not be interpreted so as to render one part inoperative). Yet this is precisely the interpretation that the Proposed Rule, in its current form, appears to adopt.

In order to remedy this situation, FDA should, in conjunction with exempting pre-repeal antibiotics from the patent listing and certification provisions of Section 505, implement alternative regulatory procedures by which pioneer manufacturers and patent owners of pre-repeal antibiotic drug products can be advised of the filing of an ANDA or 505(b)(2) application and, if necessary, take advantage of the Section 271(e)(2) remedy provided by Congress.

This can be accomplished in several ways. First, FDA could promulgate a regulation requiring that ANDA and 505(b)(2) applicants who intend to market a pre-repeal antibiotic prior to the expiration of an applicable patent provide notice to the NDA holder and patentee at the time the application is accepted for filing. Second, FDA could amend its existing FOI regulations at 21 C.F.R. §314.430(b) to permit public disclosure of the filing of an ANDA or 505(b)(2) application for a pre-repeal antibiotic. These alternatives are discussed further below.

1. **Required Notice By ANDA Or 505(b)(2) Applicant**

One regulatory option for fully implementing Section 125 of FDAMA is to require ANDA and 505(b)(2) applicants for pre-repeal antibiotics to notify the NDA holder and patentee of the filing of its application where the applicant intends to commercially market the drug product prior to expiration of any applicable patents. Although FDAMA exempts such ANDAs and 505(b)(2) applications from the patent certification and notification provisions of Section 505 of the FD&C Act, it does so only because those provisions have a significant effect upon the approval times of ANDAs and 505(b)(2) applications.

The legislative history indicates that Congress's sole purpose in enacting the transitional provision in Section 125 was to limit the availability of "market exclusivities," including patent certification exclusivity (e.g., 30-month stay), to "new" antibiotics. *See* H.R. Rep. No. 105-310, 105th Cong., 1st Sess., at 77 (granting of market exclusivities is limited to new antibiotic drugs). There is no indication that Congress intended to prohibit NDA holders and patentees from learning about the filing of an ANDA or 505(b)(2) application of a potentially infringing pre-repeal antibiotic in a manner that does not implicate any "market exclusivity." Accordingly, FDA is not precluded by Section 125 of FDAMA from implementing a "patent certification" and notice requirement provided such requirement has no effect upon the timing of FDA approval of the relevant ANDA and 505(b)(2) applications.

Since the purpose of the certification and notice requirement would be to implement the patent remedy set forth at 35 U.S.C. §271(e)(2) with respect to pre-repeal antibiotics, it should be limited to situations in which the ANDA or 505(b)(2) applicant

intends to commercially market its antibiotic prior to expiration of any applicable patent. In other words, it should be restricted to situations in which a "Paragraph IV" certification otherwise would be required. This limitation reflects the fact that, under 35 U.S.C. §271(e)(2), it is an act of infringement to submit an ANDA or 505(b)(2) application for a drug covered by a patent, but only if the purpose of the application is to obtain FDA approval to commercially market, use or sell the drug product before the expiration of the patent.

To discourage ANDA and 505(b)(2) applicants from manipulating the system by failing to give the required notice even though they intend to commercially market their drug product prior to expiration of an applicable patent, FDA should require ANDA and 505(b)(2) applicants for pre-repeal antibiotics to make one of two certifications:

1. that the applicant does not intend to market its antibiotic product until after a relevant patent or patents have expired; or
2. that the applicant intends to market its antibiotic product prior to expiration of a relevant patent or patents and that it will provide notice to the NDA holder and patentee of the reference listed drug when its application is accepted for filing.

If an ANDA or 505(b)(2) applicant provides a false certification (i.e., certifies that it does not intend to market until after a relevant patent has expired but, upon receiving FDA approval, immediately commences marketing the product), FDA should take all appropriate enforcement action, including withdrawing approval of the application and, in appropriate circumstances, criminal prosecution. *See* 18 U.S.C. §1001 (false statements); 21 U.S.C. §355(e)(5) (withdrawal).

The certification and notice requirement should apply to all patents that cover the pioneer product (i.e., drug substance, formulation, or and method of use)² which the ANDA or 505(b)(2) applicant is aware of or reasonably should be aware of. To facilitate the certification process, FDA should permit NDA holders of pre-repeal antibiotics to submit relevant patent information for inclusion in the Orange Book. Although FDAMA exempts such NDA holders from the *requirement* to submit patent information, FDAMA does not prohibit FDA from accepting patent information that is provided voluntarily. See Pub. L. No. 105-115, §125(d)(2), 111 Stat. 2296, 2325. Patent information that is published in the Orange Book, as well as patent information included in the labeling of a pioneer pre-repeal antibiotic, should presumptively be subject to the patent certification and notice requirement, since an ANDA or 505(b)(2) applicant should reasonably be aware of such patent information.

Alcon believes that a patent certification and notice process applicable to pre-repeal antibiotics can be implemented, consistent with the general principles discussed above, in several different ways. First, FDA could retain the existing patent certification and notice provisions set forth in its regulations (e.g., 21 C.F.R. §§314.50(i), 314.52, 314.94(a)(12), 314.95), but clarify that, for pre-repeal antibiotics, such certifications will not affect the timing of approval of the ANDA or 505(b)(2) application. This distinction should not create administrative difficulties since FDA has already decided to distinguish between pre-repeal antibiotics and other drugs through its application numbering system.

² Section 271(e)(2) of the Patent Code applies to patents which claim a “drug” or a drug “use.” FDA previously has interpreted these terms to include drug substance (ingredient) patents, drug product (formulation and composition) patents, and method of use patents, but not process patents. 21 C.F.R. §314.53(b). Alcon sees no reason to depart from this interpretation.

See Guidance for Industry and Reviewers – Repeal of Section 507 of the Federal Food, Drug, and Cosmetic Act at 2-3 (May 1998). Accordingly, new applications assigned a pre-repeal antibiotic number (i.e., 50,000 or 60,000 series) would have to contain a certification like other applications, but this certification would not affect when they could be approved.

Second, FDA could create a separate certification and notification procedure specifically for pre-repeal antibiotics. These regulations could be added to the current proposal for 21 C.F.R. §314.109.

In sum, FDA clearly has broad discretion to fashion an appropriate patent certification and notification procedure that fully implements Section 125. Any such procedure that FDA adopts, however, should be consistent with the general principles discussed above.

2. Public Disclosure By FDA

As an alternative to requiring ANDA and 505(b)(2) applicants to provide notification to NDA holders and patentees, FDA could implement Section 125 of FDAMA by amending its FOI regulations to permit public disclosure of such information by FDA.

FDA's current regulations provide that "FDA will not publicly disclose the existence of an application or abbreviated application before an approvable letter is sent . . ." 21 C.F.R. §314.430(b). The purported basis for this regulation is that the mere existence of a pending ANDA or 505(b)(2) application constitutes "confidential commercial information" that is not required to be publicly disclosed by FDA under the Freedom of Information Act ("FOIA"). *See* 39 Fed. Reg. 44602, 44634 (Dec. 24, 1974);

see also 5 U.S.C. §552(b)(4) (FOIA exemption for trade secrets and confidential commercial information).

Even assuming that the existence of a pending ANDA or 505(b)(2) application constitutes confidential commercial information – a position FDA has seriously questioned in the past³ – FDA nevertheless retains authority to publicly disclose such information if, as here, there are strong policy reasons to do so. Indeed, the FOIA is not a prohibitive statute and does not enjoin federal agencies such as FDA from disclosing confidential commercial information. It merely provides that a federal agency may not be forced to disclose confidential commercial information under FOIA if it chooses not to. Chrysler Corp. v. Brown, 441 U.S. 281, 290-95 (1979). Accordingly, neither FOIA nor any other statute would restrict FDA from amending its existing regulations to permit the public disclosure of the existence of a pending ANDA or 505(b)(2) application for a

³ As originally proposed, FDA's regulations provided that a list of pending new drug applications would be available for public inspection. 37 Fed. Reg. 9128, 9131 (May 5, 1972). FDA reversed itself when it finalized the regulations in 1974. Four years later, FDA proposed to amend the regulations to permit public disclosure of the existence and status of applications on the basis that, upon reconsideration, FDA did not consider this information to be "confidential commercial information." 43 Fed. Reg. 12869, 12870 (March 28, 1978). This proposal was never acted on by FDA and was subsequently withdrawn in 1991. 56 Fed. Reg. 67446 (Dec. 30, 1991). Congress has recognized that public policy concerns sometimes outweigh a company's interest in confidential commercial information. For instance, in 1997 Congress required the Department of Health and Human Services to publicly release information about ongoing clinical trials for serious or life-threatening diseases. 42 U.S.C. 282(j) (added by Section 113 of FDAMA, Pub. L. No. 105-115, 111 Stat. 2310-12). This clinical trial information, like the existence of pending ANDAs and 505(b)(2) applications, traditionally has been considered to be confidential commercial information by FDA. See 21 C.F.R. 312.130(a).

pre-repeal antibiotic.⁴

In this case, there are strong public policy reasons to amend the existing regulations to permit such disclosure. First, such disclosure would promote the objectives of FDAMA, particularly Section 125, by providing NDA holders and patentees with the critical information they need to take advantage of the enhanced patent remedy provided by Congress. As discussed above, FDA's failure to make this information available to affected NDA holders and patentees would frustrate Congressional intent by making important provisions of Section 125 of FDAMA inoperative.

Second, public disclosure of the existence of ANDAs and 505(b)(2) applications for pre-repeal antibiotics would permit patent infringement cases to be filed – and resolved – earlier than otherwise possible, thereby facilitating the orderly market entry of generic antibiotics. It also would ease the burden on courts and litigants by providing several months advance notice of potentially infringing acts, thereby obviating the need for burdensome and potentially unnecessary interim injunctive relief (e.g., temporary restraining order). Both of these outcomes are in the public interest.

Moreover, all of these policy reasons, particularly the need to fully implement Section 125 in accordance with Congressional intent, outweigh any potential interest an ANDA or 505(b)(2) applicant for a pre-repeal antibiotic might have in maintaining the

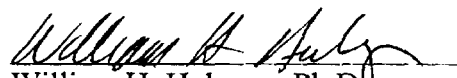
⁴ The Trade Secrets Act, 18 U.S.C. §1905, would not be violated because the disclosure would be “authorized by law,” i.e., by FDA's regulations. Chrysler Corp. v. Brown, 441 U.S. 281 (1979). Since the regulations permitting disclosure would be intended to implement Section 125 of FDAMA, if promulgated according to 5 U.S.C. §553, they should satisfy the necessary requirements for having the “force and effect of law.” See Parkridge Hospital, Inc. v. Califano, 625 F.2d 719, 722-25 (6th Cir. 1980).

confidentiality of the existence of its submission.⁵ Although such an applicant for a pre-repeal antibiotic might be sued for patent infringement sooner than if the information about its pending ANDA or 505(b)(2) application were not publicly disclosed, this is exactly the outcome Congress intended when it enacted Section 125 of FDAMA and brought pre-repeal antibiotics within the scope of 35 U.S.C. §271(e)(2).

C. Conclusion

FDA's Proposed Rule is a good start in implementing Section 125 of FDAMA, but it does not go far enough. FDA should implement the specific exemptions that are applicable to pre-repeal antibiotics as a consequence of Section 125, but also should recognize that pre-repeal antibiotics were not exempted from the patent remedy set forth at 35 U.S.C. §271(e)(2) and implement procedures to facilitate use of that remedy by NDA holders and patentees of pre-repeal antibiotics.

Respectfully submitted,


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⁵ Alcon notes that it is not suggesting that the *content* of the submissions (as opposed to their existence) should be publicly disclosed. Nor is Alcon suggesting that the existence of pending marketing applications for products other than pre-repeal antibiotics should be publicly disclosed, since the same public policy concerns are not implicated.