DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

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Re: Docket Nos. FDA-2009-P-0038
FDA-2009-P-0081
FDA-2009-P-0103
FDA-2009-P-0120

Dear Messrs. Labson, Henteleff, Bradshaw, Kracov, Allera, and Mss. Jungman and Davidson:

This letter responds to your respective citizen petitions dated (1) January 29, 2009, submitted on behalf of Mayne Pharma International Pty. Ltd. (Mayne) and Warner Chilcott (US), LLC, Warner Chilcott Laboratories Ireland Ltd., and Warner Chilcott Company, Inc. (collectively, Warner Chilcott) (hereafter referred to as the Warner Chilcott Petition); (2) February 13, 2009, submitted on behalf of Medicis Pharmaceutical Corporation (Medicis) (hereafter referred to as the Medicis Petition); (3) February 17, 2009, submitted on behalf of Hoffmann-La Roche Inc. and Roche Palo Alto LLC (collectively, Roche) (hereafter referred to as the Roche Petition), and (4) February 23, 2009, submitted on behalf of Stiefel Laboratories, Inc. (hereafter referred to as the Stiefel Petition).

Petitioners request that the U.S. Food and Drug Administration (FDA or the Agency) set out its position on the applicability of the 30-month stay provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA or Act) to abbreviated new drug applications (ANDAs) for certain "old" antibiotics in light of passage of the QI Program Supplemental Funding Act of 2008, Pub. L. No. 110-379, 122 Stat. 4075 (2008) (QI Act), section 4 of which is entitled "Incentives for the Development of, and Access to, Certain Antibiotics."[1] They specifically request that the Agency provide a 30-month stay of approval for specified ANDAs seeking approval for generic versions of old antibiotics for which Warner Chilcott, Medicis, Roche, and Stiefel, the new drug application (NDA) sponsors, have listed patents in accordance with the transition rules of the QI Act.

The petitioners request that FDA stay approval of specified pending ANDAs for 30 months from the date of the NDA holder's receipt of notice of paragraph IV certifications, or until an earlier resolution of the patent infringement action. Although different petitioners rely on somewhat varied arguments, the legal question raised in each petition is the same: Does the QI Act impose a 30-month stay of approval of an ANDA referencing an old antibiotic if that ANDA contains a certification described in section 505(j)(2)(A)(vii)(IV) of the FFDCA (paragraph IV certification) to a patent that was submitted by the NDA sponsor to FDA after the ANDA was submitted (a later-listed patent) and the NDA holder or patent owner sues the ANDA applicant for patent infringement as a result of notice of the paragraph IV certification.[2] Due to the similarity of issues involved in these four petitions and the requests for immediate action, FDA believes that a consolidated response is warranted and, indeed, is supported by the petitions themselves.[3]

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[1] As used in this response, the term "old antibiotics" refers to the group of antibiotic drugs that encompass petitioners' drugs. The old antibiotic drugs at issue in the petitions are subject to new section 505(v)(1)(B)(2) of the Act, enacted in section 4 of the QI Act. Each of petitioners' drugs is "an antibiotic drug that was the subject of an application approved by the Secretary under section 507 of this Act (as in effect before November 21, 1997)." The term "antibiotic drug" means any drug (except drugs for use in animals other than human) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin or any other drug intended for human use containing any quantity of any chemical substance which is produced by a micro-organism and which has the capacity to inhibit or destroy micro-organisms in dilute solution (including a chemically synthesized equivalent of any such substance) or any derivative thereof (see 21 U.S.C. 321(jj)).

[2] These petitions are subject to section 914 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), which amended section 505 of the FFDCA by adding new subsection (q). Section 505(q) applies to certain citizen petitions and petitions for stay of action that request FDA to take any form of action related to a pending application submitted under section 505(b)(2) or 505(j) of the Act, and governs the manner in which these petitions are treated.

[3] Medicis indicated it would not object to FDA consolidating its petition with the Warner Chilcott Petition (Medicis Petition at pg. 1). Roche noted the similarity of its petition to the earlier-filed Warner Chilcott Petition (Roche Petition at pg. 1). Stiefel both incorporated by reference the arguments set forth in both the Warner Chilcott and the Medicis Petitions, and noted that other sponsors of "old antibiotics" were similarly situated and would be affected by actions requested in Stiefel's Petition (Stiefel Petition at pgs. 4-5 and 22).

We have carefully considered the Petitions and the comments submitted to the public dockets[4] and have undertaken a thorough review of the FFDCA and the QI Act and its transitional rules. For the reasons described below, the Agency has determined that, under the QI Act, no 30-month stay of approval will apply to an ANDA referencing an old antibiotic based on the grounds that the ANDA contains a paragraph IV certification to a later-listed patent and the NDA holder or patent owner has sued the ANDA applicant for patent infringement as a result of notice of the paragraph IV certification. We note that, under current law, a 30-month stay will apply to an ANDA referencing an old antibiotic if that ANDA contains a paragraph IV certification to a patent submitted to the Agency *before* the ANDA was submitted, and the NDA holder or patent owner sues the ANDA applicant for patent infringement as a result of notice of the paragraph IV certification.

I. BACKGROUND

These petitions address the most recent chapter in the long and complex history of FDA regulation of antibiotic drug products. Among the more contentious aspects of this regulatory history have been questions about the applicability to antibiotic drugs of the patent listing, patent certification, and exclusivity provisions of sections 505(b), (c), and (j), which were added to the FFDCA by the Drug Price Competition and Patent Term Restoration Act of 1984.

The specific question raised by the petitions is whether FDA will impose a 30-month stay of approval on ANDAs that reference petitioners' antibiotic drug products, thus assuring a delay in market competition and permitting resolution of patent infringement litigation resulting from the ANDA applicants' patent challenges. The issue has arisen as a consequence of the addition of section 505(v)(4) to the FFDCA by the QI Act in October 2008. This section, together with specific transitional rules contained in the QI Act, describes the applicability to old antibiotic drug products of certain provisions of the FFDCA related to approval of generic drugs.

II. SUMMARY OF LEGAL AND REGULATORY FRAMEWORK

A. The Hatch-Waxman Amendments

The Drug Price Competition and Patent Term Restoration Act of 1984 amended the FFDCA and established a process for approving ANDAs for generic versions of innovator drug products that were approved under section 505. The statutory provisions enacted in 1984 are generally referred to as "the Hatch-Waxman Amendments."

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[4] See February 20, 2009, letter of Teva Pharmaceuticals USA (Teva) and February 18, 2009, and March 5, 2009, letters on behalf of Actavis Elizabeth LLC. In addition, the American Intellectual Property Law Association (AIPLA) submitted a January 30, 2009, letter to Docket FDA-2008-D-0609, a docket that was established with publication of FDA's draft guidance for industry on *Submission of Patent Information for Certain Old Antibiotics* (November 2008). The AIPLA letter identifies the complex interpretive issues raised in the QI Act, but does not take a position on the correct interpretation of the provisions.

As discussed in greater depth below, this same phrase is used to refer to these statutory provisions as they exist today (i.e., as enacted in 1984 and as subsequently amended). Under these provisions, the timing of ANDA approval will depend in part on patent protections for the approved innovator drug product, known as the "listed drug."[5] An innovator pharmaceutical company must submit to FDA as part of its NDA

> the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

Section 505(b)(1) and (c)(2). Upon approval of the NDA, FDA publishes this patent information in *Approved Drug Products with Therapeutic Evaluations* (the "Orange Book").

As part of an ANDA, the applicant must provide one of four certifications with respect to each of the patents listed in the Orange Book for the listed drug (section 505(j)(2)(A)(vii)). At issue in these petitions is a paragraph IV certification, whereby the applicant asserts that the listed patent is invalid or will not be infringed by the ANDA applicant's drug product. The ANDA applicant is required to provide the NDA holder and patent owner with notice of the paragraph IV certification (section 505(j)(2)(B)). In certain circumstances, if the NDA holder or patent owner sues the ANDA applicant for patent infringement within 45 days of receiving notice of the paragraph IV certification, FDA will not approve the ANDA for 30 months, unless a court orders otherwise (section 505(j)(5)(B)(iii)). As noted, the question raised by the petitions is whether this 30-month stay on approval is applicable to certain ANDAs that reference old antibiotic NDAs and contain paragraph IV certifications to patents listed after the ANDA submission, when notice of the paragraph IV certification has resulted in patent litigation. The answer depends generally upon whether 30-month stay provisions as enacted in 1984, or as amended in 2003, apply to the ANDAs at issue.

(1) 30-Month Stays Under the Pre-MMA Provisions of the Act

Until December 2003, section 505(j)(5)(B)(iii) of the Act permitted a 30-month stay regardless of when the patent at issue was submitted to FDA. This resulted in ANDAs being subjected to multiple overlapping 30-month stays, as NDA holders submitted new patents to FDA well after the ANDA had been submitted and after the initiation of an earlier 30-month stay (see Federal Trade Commission, *Generic Drug Entry Prior to*

[5] "Listed drug" means "a new drug product that has an effective approval under section 505(c) of the act for safety and effectiveness or under section 505(j) of the act, which has not been withdrawn or suspended under section 505(e)(1) through (e)(5) or (j)(5) of the act, and which has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness. Listed drug status is evidenced by the drug product's identification as a drug with an effective approval in the current edition of FDA's 'Approved Drug Products with Therapeutic Equivalence Evaluations' (the list) or any current supplement thereto, as a drug with an effective approval" (21 CFR 314.3(b)).

Patent Expiration: An FTC Study, at iv-v (July 2002), available at http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf). Concern over the significant delays in generic drug approvals resulting from multiple 30-month stays led to passage of the Medicare Prescription Drug, Improvement, and Modernization Act on December 8, 2003 (MMA) (Pub. L. No. 108-173), which included provisions modifying section 505(j) of the Act to reduce the availability of 30-month stays (149 Cong. Rec. S15882, S15884 (Nov. 25, 2003) (statement of Senator Kennedy that Hatch-Waxman provisions of MMA "will stop the multiple, successive 30-month stays that the Federal Trade Commission identified as having delayed approval of generic versions of several blockbuster drugs and cost consumers billions of dollars")).

(2) 30-Month Stays Under the MMA Provisions of the Act

When Congress passed the MMA in 2003, it amended section 505(j)(5)(B)(iii) of the Act to limit the availability of 30-month stays. Under the FFDCA as amended by the MMA, a 30-month stay is available only when the patent at issue in the paragraph IV-related litigation was submitted by the NDA holder to FDA before the ANDA was submitted (section 505(j)(2)(B)(iii)). No 30-month stay is available when the NDA holder or patent owner sues as a result of a paragraph IV certification to a patent listed following the submission of the ANDA (FDA guidance for industry on *Listed Drugs, 30-Month Stays, and Approval of ANDAs and 505(b)(2) Applications Under Hatch-Waxman, as Amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Questions and Answers,* at pg. 9 (Oct. 2004)). There is no guarantee that an ANDA applicant will be subject to even a single 30-month stay in the event that the only patents submitted to FDA for the listed drug are submitted to the Agency after the ANDA is submitted (*id.*). The MMA made additional changes to the provisions of the FFDCA governing generic drug approvals, as discussed below at page 12.

B. FDA Regulation of Antibiotics

(1) Antibiotics Prior to FDAMA

Until 1997, FDA reviewed and approved antibiotic drug products under section 507 of the FFDCA. FDA regulated most other drug products under section 505 of the Act.[6] When originally passed in 1984, the Hatch-Waxman Amendments amended the FFDCA to establish a new generic drug approval program, including patent listing, patent certification, and exclusivity protections. These changes to the FFDCA applied only to drugs approved under section 505 and thus did not apply to antibiotics[7] (see *Glaxo, Inc. v. Heckler*, 623 F.Supp. 69 (E.D.N.C. 1985)). Because the Hatch-Waxman Amendments did not apply to antibiotics when originally enacted in 1984, holders of NDAs for

[6] FDA regulated insulin under section 506 of the Act until 1997. Drugs that are biological products are regulated under section 351 of the Public Heath Service Act.

[7] The patent term extension provisions of the Hatch-Waxman Amendments did apply to antibiotics, thereby permitting the extension of the patent term for certain patents claiming antibiotic drugs (see 35 U.S.C. 156(f)(4)(B)(1984)(making antibiotics regulated under section 507 products eligible for patent term extension)).

antibiotic products were not eligible for certain marketing exclusivity and could not submit patents with their NDAs claiming the approved drug product or its use. In addition, abbreviated antibiotic applications referencing these antibiotic NDAs were not subject to the patent certification, notice, and 30-month stay provisions of section 505(j). FDA approved abbreviated antibiotic applications when they met the scientific and technical requirements, and any patent infringement claims arising from the approval and marketing of these generics drugs were resolved between the parties in private patent litigation.

(2) Antibiotics Under FDA Modernization Act

In November 1997, Congress enacted the Food and Drug Administration Modernization Act (FDAMA), Pub. L. No. 105-115, 111 Stat. 2296 (1997), which, among other things, repealed section 507 and required applications for antibiotic drugs to be submitted under section 505 (section 125(b) of FDAMA)). The transition provisions of FDAMA in section 125(d) provided that antibiotic applications that had been approved under section 507 would thereafter be considered to have been submitted and approved under section 505 (section 125(d)(1) of FDAMA)). FDAMA did not, however, apply the provisions of section 505 of the Act wholesale to these applications. Instead, Congress described exceptions that made certain provisions of section 505 as enacted in the Hatch-Waxman Amendments inapplicable not only to antibiotic drugs that had been approved before the date of enactment of FDAMA, but also to antibiotic drugs that were the subject of an application received by FDA before that date, whether approved or not (section 125(d)(2) of FDAMA; *Allergan, Inc. v. Crawford*, 398 F.Supp. 13, 16 (D.D.C. 2005)).[8] Among the enumerated provisions of section 505 that did not apply to old antibiotics are the Hatch-Waxman Amendment provisions governing patent listing, patent certifications, and 30-month stays.[9]

By exempting some antibiotics from certain Hatch-Waxman provisions, Congress maintained the status quo with respect to the expectations of those applicants who had submitted applications for these antibiotic drugs before passage of FDAMA; there were

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[8] This class of "old antibiotics" is broader than those at issue in this petition, as it includes antibiotic drugs for which applications were received by FDA before November 21, 1997, but not approved. As described at footnote 1, this response addresses only antibiotic drugs that were the subject of an application approved before November 21, 1997.

[9] Section 125(d)(2) of FDAMA provides:

> Exception.--The following subsections of section 505 (21 U.S.C. 355) shall not apply to any application for marketing in which the drug that is the subject of the application contains an antibiotic drug and the antibiotic drug was the subject of any application for marketing received by the Secretary of Health and Human Services under section 507 of such Act (21 U.S.C. 357) before the date of the enactment of this Act: (A)(i) Subsections (c)(2), (d)(6), (e)(4), (j)(2)(A)(vii), (j)(2)(A)(viii), (j)(2)(B), (j)(4)(B), and (j)(4)(D); and (ii) The third and fourth sentences of subsection (b)(1) (regarding the filing and publication of patent information); and (B) Subsections (b)(2)(A), (b)(2)(B), (b)(3), and (c)(3) if the investigations relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

no patent listings, patent certifications, or 30-month stays for these drugs before November 21, 1997, and there were none afterwards. That is, there were no patent listings, patent certifications, or 30-month stays until October 8, 2008, when Congress enacted the QI Act.

(3) Antibiotics under the QI Act

On October 8, 2008, Congress enacted the QI Act. This legislation, among other things, revises the applicability of certain provisions of section 505 of the FFDCA to old antibiotic drugs by amending section 505 to include 505(v). It provides incentives for the development of additional antibiotic drugs (see Statement of Senator Burr at 154 Cong. Rec. at S9638 ("Section 4 [of the QI Act], entitled 'Incentives for the Development of and Access to Certain Antibiotics,' is an important step forward to help spur research on new antibiotics and provide incentives for the creation of additional generic antibiotics")). The first two subsections of section 505(v) describe the applicability of the Hatch-Waxman Amendment provisions governing patent term extension and certain marketing exclusivity to old antibiotic drugs submitted after enactment of the QI Act (section 505(v)(1) and (2)). The third subsection sets out specific limitations on entitlement to exclusivity and patent term extension (section 505(v)(3)). The fourth subsection — the provision primarily at issue in these petitions — addresses the general applicability of the Hatch-Waxman Amendments to old antibiotic drugs. It states that, subject to certain limitations, "[n]otwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law ... the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to [old antibiotics]" (section 505(v)(4)).

Section 4(b) of the QI Act describes specific transition rules providing for patent listing, patent publication, patent certification deadlines, and 180-day exclusivity for certain old antibiotic drugs.[10] Petitioners, as holders of NDAs for old antibiotics, have complied with these provisions. They have submitted patent information for their old antibiotic drug products to FDA under the transition provision at (4)(b)(1). FDA has published that information as described in 4(b)(2).

Petitioners now assert that having complied with the patent listing provision, they are entitled under the QI Act to a 30-month stay of approval of ANDAs that reference the old antibiotics, when the ANDA applicant has submitted a paragraph IV certification to one or more of the patents listed by the NDA holder after the ANDA was submitted, and the NDA holder or patent owner has filed suit against the applicant for patent infringement in response to the notice of certification.[11]

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[10] As noted above at footnote 4, FDA has published draft guidance for industry on *Submission of Patent Information for Certain Old Antibiotics* (Nov. 2008).

[11] The FDA regulation at 21 CFR 314.430(b) provides that "FDA will not publicly disclose the existence of an application or an abbreviated application before an approvable letter is sent to the applicant under § 314.110, unless the existence of the application or abbreviated application has been previously publicly disclosed or acknowledged." In analyzing and responding to the petitions, the Agency has relied generally on the description of the facts provided in submissions to the dockets by petitioners and in comments.

III. THE OLD ANTIBIOTIC DRUGS AT ISSUE

Each petitioner asserts that it has an interest in FDA's resolution of this issue because (1) it is the sponsor of an NDA for an old antibiotic, (2) it has submitted at least one patent to FDA for listing under the patent listing provisions of section 4(b) of the QI Act, (3) it has received notice of a paragraph IV certification from at least one applicant that had submitted its ANDA before the patent was listed, and (4) it has sued at least one of these ANDA applicants for patent infringement within 45 days of receiving notice of the paragraph IV certification.

A. Doryx

Mayne holds NDA 50-795 for Doryx (doxycycline hyclate) delayed-release tablets. The Warner Chilcott Petition indicates that Mayne holds U.S. Patent 6,958,161 for Doryx (Doryx patent) and that Warner Chilcott markets Doryx under an exclusive license from Mayne. FDA considers Doryx an old antibiotic because it contains an antibiotic that was the subject of a marketing application approved by FDA under section 507 of the FFDCA prior to November 21, 1997.

Warner Chilcott submitted information on the Doryx patent to FDA that FDA listed in the Orange Book on December 5, 2008. Warner Chilcott states it has received notice that five ANDA applicants amended their respective ANDA applications to include a paragraph IV certification against the listed Doryx patent.). According to the Petition, Warner Chilcott has filed or will file patent infringement actions against each of these applicants within 45 days of receipt of notice of the paragraph IV certification.

B. Solodyn

Medicis holds the NDA for Solodyn (minocycline HC1) extended-release tablets. Like Doryx, Solodyn contains an antibiotic that was included in a product that was the subject of a marketing application approved by FDA prior to the enactment of FDAMA on November 21, 1997, and accordingly, Solodyn is classified as an old antibiotic.

Medicis submitted patent information to FDA on December 3, 2008, for listing in the Orange Book. Medicis states that on December 5, 2008, it received notice from an ANDA applicant that it had filed a paragraph IV certification against the listed Solodyn patent. The Medicis Petition indicates that Medicis received similar notices from two other generic drug manufacturers, indicating that they, too, had submitted paragraph IV certification amendments to their respective ANDA applications referencing Solodyn.

Existence of pending abbreviated new drug applications at issue in these petitions has been disclosed or acknowledged by virtue of notice by the ANDA applicants of paragraph IV certifications.

Medicis states that it filed suit against the ANDA applicants in the United States District Court for the District of Delaware claiming patent infringement.[12]

C. Cellcept

Roche holds NDAs 50-722 for Cellcept (mycophenolate mofetil) capsules and 50-723 for Cellcept tablets. Cellcept contains an old antibiotic that FDA first approved prior to FDAMA's effective date.

Roche states that it is the owner of U.S. Patent 4,753,935 covering Cellcept capsules and tablets, and it submitted patent information to FDA on December 1, 2008.[13] The Agency listed the patent information in the Orange Book on December 2, 2008. The Roche Petition indicates that Roche received notices of paragraph IV certifications from an ANDA applicant on January 29, 2009, related to pending ANDA applications for Cellcept capsules and Cellcept tablets.[14] Roche states that it filed a patent infringement suit against the ANDA applicant in the United States District Court for the District of New Jersey on February 13, 2009.

D. Evoclin

Stiefel holds NDA 50-801 for Evoclin (clindamycin phosphate). Evoclin contains an old antibiotic that was approved prior to the effective date of FDAMA. Steifel submitted two patents for Evoclin (U.S. Patents 7,141,237 and 7,374,747) to the Orange Book on December 3, 2008. FDA received a paragraph IV certification against these patents from an ANDA applicant on January 29, 2009. The ANDA applicant has informed the Agency that Stiefel filed a patent infringement suit against it on Friday, March 13, 2009, in the United States District Court for the District of Delaware.

Although each petitioner is interested in the application of a 30-month stay to ANDAs referencing a different listed drug, the fundamental legal issue in each case is essentially the same. Petitioners provide numerous and varied arguments for applying a 30-month stay in these circumstances. For the reasons described below, none of these arguments is persuasive.

IV. DISCUSSION

Petitioners describe three general grounds on which they believe they are entitled to a 30-month stay of approval of any ANDA that references an old antibiotic when the ANDA applicant has submitted a paragraph IV certification to one or more patents listed by

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[12] Medicis states that another ANDA applicant also notified Medicis that it had submitted a paragraph IV certification amendment to its ANDA application. However, this applicant and Medicis entered into a settlement and licensing arrangement and no infringement action was being filed against the ANDA applicant within 45 days of notice.

[13] According to the petition, Roche's patent expires on May 3, 2009.

[14] FDA had already approved ANDAs for mycophenolate mofetil capsules and tablets (referencing Cellcept) for two companies earlier in 2008, prior to Roche submitting Cellcept patent information to the Agency.

petitioners after the ANDA was submitted and petitioners have filed suit against the ANDA applicant for patent infringement in response to the notice of certification.[15] Petitioners assert variously that the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 as enacted — not as revised by subsequent legislation — apply to these applications. They also argue either that the patents at issue should be treated as having been submitted to FDA with the NDAs, or that the ANDAs at issue should be treated as having been submitted to FDA when the paragraph IV certification to the patent was submitted. Petitioners support each of these arguments with the claim that only by applying a 30-month stay to these ANDAs will the goals of the generic drug approval program be accomplished, and that any other outcome would be fundamentally unfair. The Agency has determined that petitioners' positions are not supported by either the plain language of the QI Act or by the regulatory framework for innovator and generic drug products of which the QI Act is a part.

A. The Drug Price Competition and Patent Term Restoration Act of 1984

Petitioners argue that the plain language of the QI Act directs FDA to apply the relevant statutory provisions of the Hatch-Waxman Amendments as they were enacted in 1984, not as subsequently amended by Congress. This argument is based solely on the reference in section 505(v)(4) of the QI Act to the statement that "the provisions of the Drug Price Competition and Patent Term Restoration Act *of 1984* shall apply to [old antibiotics]" (emphasis added). Under the original provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 (the original 1984 Act or 1984 law), petitioners assert they are entitled to a 30-month stay on approval of the ANDAs because the original 1984 Act required the application of a 30-month stay regardless of when the patent at issue was submitted by the NDA holder to the FDA.

Although petitioners are correct that the QI Act refers to "the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984," and that under the terms of the original 1984 Act, they would have been entitled to a 30-month stay of approval of the ANDAs,[16] the QI Act does not apply the original 1984 Act to these applications. Upon consideration of the reference in the QI Act to the original 1984 Act in light of additional statutory text, legislative history, and other regulatory considerations, it is apparent that neither this bare statutory reference, nor other statutory considerations require the Agency to apply the original 1984 Act to the ANDAs referencing petitioners' old antibiotics. Congress's reference to the 1984 Act did not impose a 30-month stay of applicants who had already submitted ANDAs when the QI Act was enacted, nor did it create a class of old antibiotic applications that will be subject to long-term differential treatment with respect to, among other things, the availability of multiple 30-month stays

[15] Each petition adopts a slightly different approach to the issues. This response addresses each of the general arguments made by any of the petitioners.

[16] FDA has required any pending ANDA that references an old antibiotic listed drug for which patent information was timely filed under section 4(b)(1) of the QI Act to submit an appropriate patent certification as described in section 505(j)(2)(A)(vii) of the Act. There seems to be no real dispute that such certification is required. For the transition provision at section 4(b)(3) of the QI Act regarding 180-day exclusivity to have any meaning, all ANDA applicants must be required to submit certifications to these newly listed old antibiotic patents.

and the terms of 180-day exclusivity. Rather, the reference to "Drug Price Competition and Patent Term Restoration Act of 1984" was a means to identify, as a general matter, the statutory provisions that would apply for the first time to old antibiotics (i.e., those provisions that comprise the generic drug approval program first enacted in 1984). The term "Drug Price Competition and Patent Term Restoration Act of 1984" is merely a more formal shorthand than the more common reference to "the Hatch-Waxman Amendments." Petitioners' reliance on other provisions of 505(v)(4) is similarly unavailing.

Section 505(v)(4) of the FFDCA, as added by the QI Act, states in relevant part that,

> Notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law, and subject to the limitations in [505(v)(1), (2), and (3)], the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 shall apply to any drug subject to paragraph (1) or any drug with respect to which an election is made under paragraph (2)(A).

Petitioners argue that by stating that "[n]otwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law," Congress intended not only that those provisions of section 125(d)(2) that exempted old antibiotics from certain enumerated provisions of section 505 would not apply, but that any changes to the Hatch-Waxman Amendments made since 1984 likewise would be inapplicable to their applications. Petitioners' argument goes too far.

As an initial matter, the Drug Price Competition and Patent Term Extension Act of 1984 amended several statutes, and therefore across-the-board application of the original 1984 Act in the manner suggested by petitioners would have effects far beyond the applicability of 30-month stays to certain ANDAs under the FFDCA. Title I of the 1984 Act generally amended Federal Food, Drug, and Cosmetic Act provisions governing drug approvals; Title II amended sections 156 and 271 of Title 35 of the U.S. Code governing patent term extensions and infringement of patents; and (in a relatively obscure and inapplicable provision) Title III amended the Textile Fiber Products Identification Act and the Wool Products Labeling Act of 1939. Although a thorough analysis of the subsequent changes to patent term extension and patent law is beyond the scope of this response, petitioners' argument that the QI Act requires wholesale application of the original 1984 Act suggests that the original 1984 version of the Patent Code provisions apply to old antibiotics as well, and any intervening amendments must be disregarded.[17]

[17] Indeed, the 1984 version of the patent extension provisions in section 156 of Title 35 of the U.S. Code includes numerous references to section 507 of the FFDCA, the provision governing regulation of antibiotics that, in 1997, was struck from the FFDCA in section 125(b) of FDAMA. If the 1984 version of the Drug Price Competition and Patent Term Extension Act of 1984 were to apply "notwithstanding section 125, or any other provision, of the Food and Drug Administration Modernization Act of 1997, or any other provision of law," this continuing reference in the original 1984 Act to section 507 with respect to old antibiotics would add additional ambiguity to antibiotic regulation.

Even if the scope of petitioners' argument were limited to the FFDCA provisions, the effect of applying the 1984 Act would go well beyond the application of a single 30-month stay to ANDAs referencing petitioners' old antibiotic drugs. Since 1984, Congress has revised the Hatch-Waxman provisions of the Act to, among other things, significantly alter the availability of multiple 30-month stays on ANDA approvals in section 505(j)(5)(B)(iii); change the eligibility for and triggering of 180-day exclusivity in section 505(j)(5)(B)(iv); revise the declaratory judgment provisions in section 505(j)(5)(C); establish forfeiture events for 180-day exclusivity in section 505(j)(5)(D), including forfeiture for entering into an agreement found to violate antitrust laws; and provide for an offer of confidential access to an ANDA to permit an NDA holder to assess whether to sue the ANDA applicant for patent infringement in section 505(j)(5)(C)(i)(III). Were petitioners' reasoning to prevail, none of these significant changes to the Act would apply to applications for old antibiotics such as petitioners'. There is no evidence that, by its solitary reference to the 1984 Act, Congress intended this far-reaching result.

In enacting the QI Act, Congress generally brought all antibiotic drugs within the scope of the Hatch-Waxman Amendments. It did so by stating that provisions of section 125 of FDAMA, which in 1997 expressly exempted certain old antibiotics from specifically enumerated Hatch-Waxman requirements, would no longer apply to those drugs. To eliminate potential conflicts with FDAMA and with any other statutes in accomplishing this outcome, section 505(v)(4) provides that the Hatch-Waxman provisions shall apply to old antibiotic drugs "notwithstanding section 125, or any other provision, of the [FDAMA]," and notwithstanding "any other provision of law." By so directing, Congress, however, did not require FDA to turn back the clock to 1984. Specific references in the QI Act to current law, the legislative history, and Congress's convention for referring to previous versions of the FFDCA elsewhere in the statute (and its failure to do so here) suggest, instead, that Congress intended to bring old antibiotics within the scope of the current statutory provisions of the Hatch-Waxman Amendments. In addition, policy considerations warrant, to the extent possible, a consistent approach to the scope and applicability of the Hatch-Waxman Amendments to all drug products regulated under the Act.

The text of the QI Act itself suggests that, notwithstanding reference to the original 1984 Act, current law should apply to old antibiotic drugs. All specific statutory references in the QI Act are to the current law, including a number of references to provisions that did not appear in the original 1984 Act. For example, the QI Act's transitional rules in section 4(b), to which the applications at issue are generally subject, rely upon the definitions of "first applicant" and "substantially complete application" set forth in section 505(j)(5)(B)(iv) of the Act. Both of these definitions were added to the FFDCA by the MMA, and were not present in any earlier version of the statute. In addition, the QI Act makes repeated reference to FFDCA sections 505(c)(3)(E) and 505(j)(5)(F) (see 505(v)(1)(A), (2)(A)(2)(i)), provisions that were not included in the original 1984 Act. These references in other parts of the QI Act to statutory provisions amended in 2003 by the MMA are fatal to petitioners' argument that Congress intended that the original 1984 Act apply to petitioners' drugs. Indeed, petitioners' argument that the original 1984 Act

should apply "notwithstanding any other provision of law" would render the specific references to the MMA in section 4(b) of the transitional rules superfluous, as it would the entire transition section of the QI Act, each provision of which describes a significant change from the corresponding provisions of the original 1984 Act.

As noted above, legislative history and past practice suggest that the reference to "the Drug Price Competition and Patent Term Restoration Act of 1984" is comparable to use of the term "Hatch-Waxman" to refer colloquially to those provisions of law governing certain innovator protections and generic drug approvals. Congress used this shorthand as early as 1997, when it enacted FDAMA, and throughout the legislative history of the QI Act, to refer to patent and marketing exclusivities (see, e.g., 154 Cong. Rec. at S9638 (Statement of Senator Burr that "Congress added language in FDAMA to ensure that antibiotics...would not be able to double dip on Hatch-Waxman benefits. . . . As a result, companies have no access to Hatch-Waxman incentives")). In addition, reference was made in this statement to the ability, under the QI Act, of certain antibiotics to receive "3 year and/or 5 year Hatch-Waxman exclusivity" (id.). Sections 505(v)(1)(A) and (v)(2)(A), added by the QI Act, which provide for such "3 year and/or five year Hatch-Waxman exclusivity," cite to the current statutory provisions governing market exclusivity at sections 505(c)(3)(E)(ii), (iii), and (iv) and 505(j)(5)(F)(ii), (iii), and (iv) of the Act. Similarly, the legislative history of FDAMA refers, for example, to "the granting of market exclusivity to all new [antibiotic] drugs under the so-called *Waxman-Hatch* provisions" (H. Rep. 105-310, at 77 (Oct. 7, 1997) (emphasis added), and the relevant section of FDAMA includes citations to the law as in effect at the time FDAMA was passed (see section 125(d) of FDAMA). It is far-fetched to argue that the shorthand references to "Hatch-Waxman" (or "Waxman-Hatch") in the legislative history of the QI Act and FDAMA are references to the original 1984 Act, when the corresponding statutory references in the laws are to the law that was in effect at the time each statute was passed. It is reasonable to assume that when Congress adopted comparable shorthand in the QI Act, it also was referring to the current version of the law rather than the original 1984 Act.

If Congress had intended to apply anything other than the current law to old antibiotics, it would have explicitly and unambiguously expressed its intent to do so. It is a settled principle that a statute referring specifically to another statute by title or section number incorporates the provisions referred to as they exist at the time of enactment of the latter statute. *Hassett v. Welch* 303 U.S. 303, 314 (1938); *Cf.* Singer & Singer, SUTHERLAND STATUTES & STATUTORY CONSTRUCTION § 51.08 (a statute referring specifically to another statute by title or section number "incorporates the provisions referred to from the statute *as of the time of adoption* without subsequent amendments, unless the legislature has expressly or by strong implication shown its intention to incorporate subsequent amendments with the statute" (emphasis added) and a statute "which generally refers to a subject adopts the law on the subject as of the time the law is enacted"). It is not necessary to decide at this juncture whether the reference to the Drug Price Competition and Patent Term Restoration Act of 1984 is a "specific" or "general" reference, as the outcome in the present matter would be the same in either case, that the QI Act adopts the current law governing generic drug approvals. If Congress had

intended to refer to a previous version of the FFDCA, it would have done so plainly. For example, in the definition of antibiotic drug set forth in sections 505(v)(1)(B)(ii) and (v)(2)(B)(ii), the QI Act references "section 507 of this Act (*as in effect before November 21, 1997*)" (emphasis added). If Congress intended to reject the legislative changes made to the Hatch-Waxman provisions over the course of two decades, and particularly those changes made by the MMA, it reasonably could have adopted the same convention as it did elsewhere in the law by referring to "the Hatch-Waxman Amendments of 1984 (as in effect on September 24, 1984)" or the Hatch-Waxman Amendments of 1984 (as in effect before December 8, 2003)."

It is particularly reasonable to look for a clear congressional intention to apply something other than the current law when current law embodies significant amendments made by Congress over the past two decades, including substantial changes to the requirements for 30-month stays and changes to the paradigm for 180-day exclusivity. Arguably, these changes represent important policy advancements over the 1984 law. There is no indication in the plain language of the QI Act or its legislative history that Congress intended that FDA reject the MMA 30-month stay and 180-day exclusivity amendments with respect to old antibiotics, and thus perpetuate a regulatory scheme that Congress was moved to significantly revise. Moreover, had Congress intended to make available a 30-month stay to old antibiotic NDA holders who sued applicants whose ANDAs were pending when the QI Act was enacted and who have subsequently challenged a listed patent, there were more effective, more explicit, and narrower ways to do so.[18]

The transition provisions in section 4(b) of the QI Act explicitly address situations in which current law will not apply to applications for old antibiotics. Section 4(b)(1) provides an alternative to the patent listing deadlines for NDA sponsors described in section 505(b)(1) and (c)(2) of the Act. Section 4(b)(2) provides a deadline for FDA publication of patent information for old antibiotics that differs from the publication requirements in current section 505(b)(1) and (c)(2) of the Act. Finally, section 4(b)(3) of the QI Act deems that certain ANDA applicants who would not otherwise meet the current definition of "first applicant" in section 505(j)(5)(B)(iv) will nonetheless be considered first applicants. In each of these transition provisions, Congress exempted applicants from current law that would otherwise apply. Had Congress intended to specifically exempt sponsors of already approved old antibiotic NDAs from the operation of the current provisions of the FFDCA that would make a 30-month stay unavailable

[18] The only element of the 1984 legislation that seems to be of any significant interest to petitioners is section 505(j)(5)(B)(iv), the provision that would permit a 30-month stay in the circumstances of petitioners' NDAs. No petitioner has identified any other provision of the original 1984 Act that specifically should apply to these applications. Moreover, should the original 1984 Act apply to old antibiotics, there will doubtless be litigation over which regulatory interpretation of section 505(j)(5)(B)(iv) of the original 1984 Act would control. The 1994 regulations at 21 CFR 314 which permitted multiple 30-month stays were amended in 2003, prior to passage of the MMA to effectively permit a 30-month stay only when the ANDA applicant had not previously submitted a paragraph IV certification (68 FR 36676 (June 18, 2003)). The later regulations, which went into effect on August 18, 2003, were superseded by the MMA, which on December 8, 2003, revised section 505(j)(5)(B)(iv) to adopt an alternative approach to 30-month stays, and which Congress made retroactive to the August 2003 effective date of FDA's amended regulations.

when a paragraph IV certification to a later-listed patent results in litigation, the transition provisions would have been an appropriate and effective place to do so. In the absence of persuasive evidence to the contrary, Congress's failure to add a specific provision to the transitional rules for old antibiotics exempting these products from the current law regarding 30-month stays should reasonably be read to signal that Congress did not intend for anything other than the current law on 30-month stays to apply to these applications.

Moreover, adoption of petitioners' argument that section 505(v)(4) applies the original 1984 Act to old antibiotics would perpetuate a different statutory scheme for certain antibiotic drugs, one that could delay approval of generic version of old antibiotics. This outcome is inconsistent with the purpose of the QI Act.[19] The Agency approved Petitioners' NDAs before passage of the QI Act, but the effect of petitioners' argument would be to extend 1984 law to NDAs for old antibiotics submitted and approved after passage of the QI Act as well. Application of the original 1984 Act to old antibiotics would permit sponsors of NDAs for old antibiotics submitted after enactment of the QI Act to obtain 30-month stays as the result of paragraph IV certifications to later-listed patents, as well as to any patents listed when the ANDA is submitted to FDA. This could result in multiple 30-month stays delaying approval of ANDAs for old antibiotics, precisely the outcome Congress corrected with the MMA. Because the NDA sponsors for old antibiotic drugs submitted for approval after passage of the QI Act would have had the opportunity to submit patent information prior to the submission of ANDAs (because the QI Act now permits patent information to be submitted for old antibiotics), this outcome would not establish equal treatment of old antibiotics and other drugs so much as perpetuate disparate treatment between these classes of drugs.

Even assuming that Congress's intention in the QI Act was ambiguous, it is reasonable, both as a matter of statutory construction and sound public policy, to interpret section 505(v)(4) to require the application of the current law to old antibiotics. As set forth above, there is a strong argument that Congress intended this result. The current law incorporates significant substantive amendments made by Congress to the regulatory scheme established by the Hatch-Waxman Amendments. In addition, implementation of the QI Act using the current statute and regulations scheme will generally permit the Agency to treat drug products consistently. It will obviate the need to determine which version of the FFDCA and regulations apply for each drug for purposes of 30-month

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[19] Senator Burr noted that the QI Act was intended to spur research on new antibiotics, and also expressed concern that the FDAMA provisions "had negatively impacted generic drug companies' ability to gain approval of and market generic equivalents of antibiotics approved under section 507" (154 Cong. Rec. at S9638). The negative impact referred to in this statement is likely to have been the failure of FDAMA to modify the "same labeling" requirement of section 505(j)(2)(A)(v) to permit an ANDA applicant for an antibiotic to omit from its labeling any uses of the antibiotic protected by patent, even when that patent has not been submitted to FDA. Because under the FFDCA, even as amended by FDAMA, the labeling for a generic antibiotic drug generally is required to be the same as the innovator labeling, an ANDA applicant might have been be required to obtain approval of a generic antibiotic with a labeled use that would infringe a patent, thus subjecting the ANDA applicant to the risk of patent infringement. Given the concern about negative effects of FDAMA on the approval of generic versions of antibiotics approved under section 507, it is unlikely that Congress would, with the QI Act, establish a regulatory scheme that would continue to disadvantage those seeking approval for generic versions of the same class of old antibiotics.

stays and 180-day exclusivity. Finally, applying the current statute to all drugs will provide predictability to regulated industry, and minimizes the administrative burden on the Agency.

B. Recalculation of ANDA Submission Date

Petitioners also argue that, even if the original 1984 Act does not apply to applications for old antibiotics, they are nonetheless entitled to a 30-month stay. Specifically, petitioners assert that as to any ANDA that was submitted to FDA before October 8, 2008 (the effective date of the QI Act) that contains a patent certification to a patent that was submitted to FDA after that date, the QI Act effectively "recalculates" the submission date of an ANDA from the date the ANDA was originally submitted to the date when the first possible application containing a paragraph IV certification could have been submitted (i.e., after the patent information was submitted). By "adjusting" the date on which the ANDA was submitted to a date after the patent was submitted, an NDA sponsor would be eligible under current law for 30-month stay on approval of the ANDA (section 505(j)(5)(B)(iii)).

Petitioners' analysis rests on the language in section 4(b)(3) of the QI Act, which states that each ANDA applicant that timely submits a paragraph IV certification in a substantially complete ANDA to a patent listed within 60 days of enactment "shall be deemed to be a first applicant (as defined in paragraph (5)(B)(iv) of such section 505(j))." Section 505(j)(5)(B)(iv) defines a "first applicant" as "an applicant that, on the first day on which a substantially complete application containing [a paragraph IV certification] is submitted for approval of a drug, submits a substantially complete application that contains and lawfully maintains a [paragraph IV certification] for the drug." In petitioners' view, in order to make ANDA applicants "first applicants" within the meaning of the MMA, their applications must be treated in a *nunc pro tunc* fashion as having been submitted only after the patents were listed (and on the same day), as that was the first point at which the ANDA could contain a paragraph IV certification. Petitioners' argument misinterprets the MMA definition of first applicant.

FDA does not interpret the MMA exclusivity provisions to grant 180-day exclusivity only when an ANDA contains a paragraph IV certification to a listed patent on the date the ANDA is originally submitted to FDA. An ANDA that is originally submitted containing no paragraph IV certification to a listed patent, but is then amended to contain a paragraph IV certification to a patent listed by the NDA holder after the ANDA was submitted, is also eligible for 180-day exclusivity.[20] The amendment containing the paragraph IV certification that is submitted to an otherwise substantially complete ANDA renders the application "a substantially complete application that contains a [paragraph IV certification]" as described in section 505(j)(5)(B)(iv)(II)(bb), and the date the amendment containing the paragraph IV certification is submitted becomes the date on

[20] For example, 180-day exclusivity for oxcarbazepine tablets was based on U.S. Patent No. 7,037,525, which was submitted to FDA in May 2006, after ANDAs referencing the innovator drug had been submitted. The paragraph IV certifications that were the basis for exclusivity were submitted in amendments to the pending ANDAs.

which the substantially complete application containing a paragraph IV certification was submitted *for purposes of assessing first applicant status*, but it is not the date the application was submitted for other purposes. By rendering all applicants with pending ANDAs that timely submit paragraph IV certifications to a listed patent for an old antibiotic "first applicants," the QI Act effectively treats the applicants' amendments containing paragraph IV certifications as having been submitted on the first day on which any ANDA applicant submitted a substantially complete application that contains a paragraph IV certification to a patent for the listed drug. The QI Act does not, however, recalculate the date on which the ANDAs were submitted to FDA.

Petitioners' analysis would require adjusting the submission date of every ANDA that is amended to contain the first paragraph IV certification to a later-listed patent on the listed drug, whether the patent at issue was submitted after the ANDA because it was a patent claiming an old antibiotic, a patent issued by the Patent and Trademark Office after the ANDA was submitted, or a pre-existing patent that the NDA holder had not submitted before the ANDA was submitted to FDA. In each case, the recalculation of the submission date would grant the NDA holder a 30-month stay, an outcome that is in conflict with the MMA provisions limiting the 30-month stay to instances when litigation arises from patents that had been submitted to FDA before the ANDA was submitted. Moreover, the date the ANDA is submitted (and then "received" as described in 21 CFR 314.101) is used by the Agency for many regulatory purposes (e.g., to calculate the application's place in the review queue, to calculate review time). Therefore, recalculation of submission dates would further complicate and disrupt the review of applications.[21]

Finally, petitioners are incorrect that recalculating the ANDA submission date so as to grant the NDA holder a 30-month stay is required to justify eligibility for 180-day exclusivity. As has been noted on numerous occasions, 180-day exclusivity is an incentive to generic drug applicants to undertake the risk of challenging patents claiming the listed drug (see, e.g., *Teva Pharmaceuticals, USA, Inc. v. Leavitt*, 548 F.3d 103, 104 (D.C.Cir. 2008); *Ranbaxy Laboratories, Ltd. v. Leavitt*, 469 F.3d 120, 122 (D.C.Cir. 2006)). Although the MMA contains numerous requirements for 180-day exclusivity, it

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[21] FDA's paragraph IV certification information available on its website at http://www.fda.gov/cder/ogd/ppiv.htm does not have the substantive effect of readjusting the submission date of ANDAs that is ascribed to it in petitions. The website states "[b]elow is a list of drug products for which an Abbreviated New Drug Application (ANDA) has been received by the Office of Generic Drugs (OGD) containing a "Paragraph IV" patent certification. This list includes the name of the drug product, dosage form, strength (subject of Paragraph IV certification), reference listed drug (RLD), **and the date on which the first substantially complete generic drug application was submitted to the Agency (on a prospective basis beginning 3/2/04)**." Although perhaps inartfully worded, the website thus identifies the date the substantially complete ANDA that contain the paragraph IV certification was submitted. For example, for oxcarbezapine, the list notes the date of submission as 5/05/2006. This was the date the first paragraph IV certification to the newly listed patent was submitted in an amendment to the ANDA, not the date the original ANDA was submitted. The list notes certain paragraph IV certifications as having been submitted before 2/5/2009, because that is the date established in the transition rules at section (b) of the QI Act for submission of paragraph IV certifications for certain ANDA applicants who will be deemed "first applicants" under the transition rules; for these drugs, the precise date of the paragraph IV submission is irrelevant.

does not limit eligibility for 180-day exclusivity to applicants that are subject to a possible 30-month stay. Had Congress intended to impose a 30-month stay requirement for exclusivity related to later-listed patents in the same legislation in which it expressly limited the availability of 30-month stays for such patents, it is reasonable to expect that it would have done so specifically. The Agency will not impose an additional requirement for 180-day exclusivity in the absence of a clear congressional signal that such a requirement is intended (*Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060 (D.C.Cir. 1998) (finding FDA's successful defense requirement for 180-day exclusivity not supported by statutory language)).

C. Submission of Patents With the NDA

Petitioners also assert that section 4(b)(1) of the QI Act should be interpreted to treat patents listed for old antibiotic drugs as if the patents had been submitted to FDA when the old antibiotic NDA was originally submitted, rather than submitted to FDA after passage of the QI Act. To support this interpretation, petitioners point to the language in section 4(b)(1) stating that "patent information required to be filed ... under [505(b)(1) or (c)(2) of the Act]" must be filed with FDA within 60 days after enactment of the QI Act and argue that, because section 505(b)(1) and (c)(2) require that patent information be filed with the NDA when it is filed, the date of the submission of the patent information must — of necessity — be moved to the date of submission of the NDA, even if the NDA was submitted to FDA years ago. This is a tortured reading of a statutory provision that is more reasonably read to mean that patent information *of the type* required to be filed under 505(b)(1) and (c)(2) is to be submitted to FDA by the identified date. The type of patent information required to be filed under 505(b)(1) and (c)(2) is

> the patent number and expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

Petitioners do not dispute that this is the type of patent information they submitted to FDA within the time frame identified in section 4(b)(1) of the QI Act. There is no need to adopt the strained reading proposed by petitioners to give the reference to sections 505(b)(1) and (c)(2) meaning; they already have a reasonable and well established regulatory meaning.

D. Fairness and Regulatory Change

Petitioners make much of the argument that the failure of the QI Act to apply a 30-month stay for old antibiotic ANDAs that were pending when the QI Act was passed would be unfair because it would deprive them — sponsors of NDAs for old antibiotics — of a benefit that NDA sponsors for other drugs have under the Hatch-Waxman Amendments. Whether petitioners consider the legislative choice made in the QI Act regarding 30-month stays as "fair" to their interests is irrelevant. FDA is implementing the statute

based on its interpretation of the plain language, and on the basis of its experience with the complex generic drug approval program as described over the years in the Hatch-Waxman Amendments.

At each point in its evolving approach to drug regulation, Congress has made express choices about how to apply the newest regulatory regime, and in each instance some group of drugs or applications has fallen outside the scope of the new statute. When Congress enacted the Hatch-Waxman Amendments in 1984, it did not provide antibiotic drugs approved under section 507 of the Act with the various marketing exclusivity, patent listing, patent certification, and 30-month stay protections accorded to drugs approved under section 505. Likewise, when FDAMA was enacted in 1997, even though all antibiotics would be considered approved under section 505 of the Act, Congress chose to apply the various marketing exclusivity, patent listing, patent certification, and 30-month stay protections only to applications that did not contain any antibiotic drug that was the subject of an application received by FDA before FDAMA was enacted. In that case, Congress expressly enumerated the statutory benefits that would not apply to old antibiotic drugs (section 125(d)(2)). And in the QI Act, Congress appears to have made 3- and 5-year exclusivity available only to certain applications for old antibiotics when the application was submitted to FDA after enactment of the QI Act; any NDA for an old antibiotic submitted before the QI Act appears to be ineligible for the exclusivity protections. Each legislative action reflects particular public policy judgments regarding the appropriate balance of incentives and protections needed to encourage development of antibiotic drugs and the prompt approval of generic drug products.

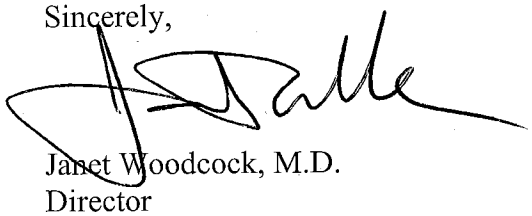
Finally, to the extent that the QI Act was intended to provide an incentive to antibiotic innovation (see discussion of QI Act at p. 7 above),, petitioners' interpretation would not further that goal. Incentives encourage the development of innovative new drug products. Petitioners, in contrast, are seeking benefits under the QI Act for old antibiotic drug products developed and approved well before Congress enacted the QI Act.

V. CONCLUSION

Petitioners have asserted a number of grounds to support their view that they are entitled to a 30-month stay on approval of certain ANDAs referencing their old antibiotic applications. After careful consideration of petitioners' arguments and related materials, FDA has concluded that the QI Act does not impose a 30-month stay of approval on

ANDA applicants that have been sued by the NDA holder or patent owner as a result of notice of a paragraph IV certification to a patent, when the patent was submitted to an old antibiotic NDA and the ANDA was pending with the FDA at the time the patent was submitted. Therefore, your petitions are denied.

Sincerely,



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