Guidance for Industry

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

DRAFT GUIDANCE

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For questions regarding this draft document, contact Martin Shimer, 301-827-5710.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Questions and Answers

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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

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

On December 8, 2003, President Bush signed into law the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Public Law 108-173) (MMA). Title XI of the MMA amends sections 505(b), (c), and (j) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 355(b), (c), and (j)). Among other things, the MMA directs FDA to issue guidance defining the term *listed drug* with respect to amendments and supplements to abbreviated new drug applications (ANDAs). This guidance is intended to clarify when a change to an ANDA should reference a listed drug ***different*** from the drug referenced in the original ANDA, thus requiring the change to be made through an entirely new application. As directed by the MMA, this document (in the form of questions and answers) provides guidance on the definition of *listed drug*.

Further, as indicated in our March 3, 2004, *Federal Register* notice,[2] we have been considering what other steps we should take in light of the MMA. As one such step, this document provides guidance to industry on certain sections of the MMA that significantly change provisions of the Act that were originally added by the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (Hatch-Waxman). These changes relate, in substantial part, to 30-month stays and to the timing of approval of ANDAs and new drug applications (NDAs) described in section 505(b)(2) of the Act (505(b)(2) applications). Specifically, this guidance clarifies changes made by the MMA with respect to (1) the availability and termination of 30-month stays of

[1] This guidance has been prepared by the Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research (CDER) in cooperation with the Office of Regulatory Policy (ORP) and the Office of the Chief Counsel (OCC) at the Food and Drug Administration.

[2] See *Generic Drug Issues; Request for Comments* (69 FR 9982).

approval on ANDAs and 505(b)(2) applications under section 505(j)(5)(B)(iii) and 505(c)(3)(C) of the Act, respectively, and (2) requirements for notice of patent certifications described in sections 505(b)(2)(A)(iv) and 505(j)(2)(A)(vii)(IV) of the Act (paragraph IV certifications). It also clarifies the applicability of certain changes made by the MMA regarding the period during which ANDAs that were not the first to challenge a patent on the listed drug cannot be approved (180-day exclusivity), as described in section 505(j)(5)(B)(iv) of the Act. Finally, this guidance explains the various effective dates that apply to the MMA's provisions.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. QUESTIONS AND ANSWERS

A. Listed Drug

1. Why is a guidance needed on the definition of *listed drug*?

The MMA, among other things, generally prohibits an ANDA applicant from amending or supplementing its application to refer to a listed drug which is different from that referred to in the application when originally submitted. Such a change can be made only by the submission of an entirely new application.

Title XI of the MMA states in part that the Secretary will issue guidance defining the term *listed drug* for purposes of section 1101(a)(1)(B) of the MMA. That section, which is now section 505(j)(2)(D)(i) of the Act, provides that "[a]n applicant may not amend or supplement an [ANDA] to seek approval of a drug referring to a different listed drug from the listed drug identified in the application as submitted to the Secretary."[3] FDA's definition of *listed drug* is contained in § 314.3 (21 CFR 314.3).[4] The Agency does not intend to amend that definition.

[3] The MMA added a related provision to the Act with respect to 505(b)(2) applications: "An applicant may not amend or supplement [a 505(b)(2) application] to seek approval of a drug that is a different drug than the drug identified in the application as submitted to the Secretary" (section 505(b)(4)(A) of the Act). This guidance does not pertain to the foregoing provision on 505(b)(2) applications because that provision does not use the term *listed drug*, and the MMA only directs FDA to issue guidance with respect to the provision applicable to 505(j) applications.

[4] This definition reads:

> *Listed drug* means a new drug product that has an effective approval under section 505(c) of the [A]ct for safety and effectiveness or under section 505(j) of the [A]ct, which has not been withdrawn or suspended under section 505(e)(1) through (e)(5) or (j)(5) of the [A]ct, and which has not been withdrawn fromsale 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" [commonly referred to as the Orange Book] or any current supplement thereto…. A drug product is deemed to be a listed drug on the date of effective approval of the application or abbreviated application for that drug product (21 CFR 314.3(b)).

2. Generally, when should a separate ANDA be submitted for a different listed drug?

The appropriate choice of whether to submit a new ANDA for a proposed product — as opposed to submitting an amendment or supplement to a previously submitted or already approved ANDA — is governed by a number of considerations. All changes that would have the effect of seeking approval for a drug product different from the listed drug cited in the initial submission (e.g., different active ingredient, dosage form, route of administration) should be made in a new application. When the Orange Book identifies as a separate listed drug a product with the characteristics (e.g., active ingredient, dosage form, route of administration) for which the applicant is seeking approval, the applicant should submit a separate ANDA referencing the corresponding listed drug.[5] The applicant should not submit a supplement or amendment to its pending or approved application to seek approval for such a change.

3. Can an amendment or supplement be submitted for different strengths?

Each strength of an approved drug is a separate listed drug. Each strength proposed in an ANDA should reference the corresponding listed drug (although the reference standard for purposes of bioequivalence may be only one strength). Generally, a single application can be used to seek approval for different strengths of the same listed drug. Also, an applicant may submit an amendment or supplement to seek approval of a different strength from that for which the application was initially submitted and is not required to file a separate application for such a change. This is expressly permitted under the Act, as amended by the MMA (see section 505(j)(2)(D)(ii) of the Act, as amended).

B. Role of Court Decisions and Other Judicial Action

1. What court decisions and other judicial actions are relevant for lifting 30-month stays of approval on ANDAs and 505(b)(2) applications?

Hatch-Waxman amended the Act to establish up to a 30-month stay of approval on an ANDA or 505(b)(2) application if:

- The application includes a paragraph IV certification challenging a patent listed in the Orange Book (a listed patent) that claims the approved drug (listed drug) on which the ANDA or 505(b)(2) application relies or claims the use of the listed drug, and

[5] Separate approved drug products, other than products with different strengths, will ordinarily have different NDA numbers.

- The patent owner or NDA holder for the listed drug sues the ANDA or 505(b)(2) applicant for patent infringement within 45 days of receiving notice of the paragraph IV certification.

The 30-month stay may be shortened or lengthened by the court if "either party to the action fail[s] to reasonably cooperate in expediting the action."[6]

The MMA further amends the Act to specify what actions by what courts will terminate a 30-month stay of approval. (The MMA also amends the Act to alter the circumstances under which a 30-month stay can arise, as discussed below in questions 1 and 2 in subsection II.D of this document.) The provisions of the MMA that identify the relevant court actions apply to any proceeding under section 505 of the Act that is pending on or after December 8, 2003.[7] Under the MMA, a 30-month stay will be terminated and approval of an ANDA or 505(b)(2) application may be made effective, as of any of the following:

- The **date that the district court enters judgment** reflecting its decision that the patent at issue is invalid or not infringed (including any substantive determination that there is no cause of action for patent infringement or invalidity), [8] **or**

- The **date of a settlement order or consent decree signed and entered by the district court** stating that the patent that is the subject of the certification is invalid or not infringed, [9] **or**

- If the district court decides that the patent has been infringed, and this decision is reversed on appeal, the **date on which the court of appeals decides that the patent is invalid or not infringed** (including any substantive determination that there is no cause of action for patent infringement or invalidity),[10] **or** the **date of a settlement order or consent decree signed and entered by the court of appeals** stating that

[6] Section 505(c)(3)(C) and 505(j)(5)(B)(iii) of the Act.

[7] See MMA Title XI section 1101(c)(1).

[8] See MMA Title XI section 1101(a)(2)(A)(ii)(II)(aa) and 1101(b)(2)(B)(ii)(II) (creating new section 505(j)(5)(B)(iii)(I)(aa) and 505(c)(3)(C)(i)(I) of the Act, respectively); see also MMA Title XI section 1101(a)(2)(A)(ii)(II)(cc) and 1101(b)(2)(B)(ii)(IV) (amending section 505(j)(5)(B)(iii)(III) and 505(c)(3)(C)(iii) of the Act, respectively).

[9] See MMA Title XI section 1101(a)(2)(A)(ii)(II)(aa) and 1101(b)(2)(B)(ii)(II) (creating new section 505(j)(5)(B)(iii)(I)(bb) and 505(c)(3)(C)(i)(II) of the Act, respectively); see also MMA Title XI section 1101(a)(2)(A)(ii)(II)(cc) and 1101(b)(2)(B)(ii)(IV) (amending section 505(j)(5)(B)(iii)(III) and 505(c)(3)(C)(iii) of the Act, respectively).

[10] See MMA Title XI section 1101(a)(2)(A)(ii)(II)(bb) and 1101(b)(2)(B)(ii)(III) (creating new section 505(j)(5)(B)(iii)(II)(aa)(AA) and 505(c)(3)(C)(ii)(I)(aa) of the Act, respectively); see also MMA Title XI section 1101(a)(2)(A)(ii)(II)(dd) and 1101(b)(2)(B)(ii)(V) (creating new section 505(j)(5)(B)(iii)(IV) and 505(c)(3)(C)(iv) of the Act, respectively).

the patent that is the subject of the certification is invalid or not infringed.[11]

If the district court hearing a patent infringement suit resulting from a paragraph IV certification decides that the patent at issue is infringed, and this decision is not appealed or is affirmed on appeal, the ANDA or 505(b)(2) application may be approved based on the district court's ruling in accordance with the patent's expiration and any extension or exclusivity that remains.[12]

2. What court decisions are relevant for triggering 180-day exclusivity for ANDAs?

As established by Hatch-Waxman, if an applicant (or applicants) is the first to submit a substantially complete ANDA containing a paragraph IV certification to a listed patent that claims the listed drug on which the application relies or claims a use of the listed drug (a paragraph IV ANDA), the applicant (or applicants) can be eligible for a 180-day period during which no other ANDA with a paragraph IV certification for the same drug may be approved.[13] This period is commonly referred to as *180-day exclusivity*.[14] Under Hatch-Waxman before the MMA, the 180-day exclusivity period was triggered by the earlier of the first commercial marketing of the drug described in the first applicant's ANDA, or the first court decision holding invalid or not infringed the patent that was the subject of the first applicant's paragraph IV certification.[15]

The MMA changes the relevance of court decisions for 180-day exclusivity in the following ways:

- For paragraph IV ANDAs filed after December 8, 2003, for a listed drug for which no paragraph IV certification was made in any ANDA before that date, **court decisions will no longer trigger the period of 180-day exclusivity**; and

- For all other ANDAs, **a court decision can still trigger the period of 180-day exclusivity. However, if the exclusivity was not already triggered before December 8, 2003, the triggering court decision must be one from which no appeal has been or can be taken**, other than a

[11] See MMA Title XI section 1101(a)(2)(A)(ii)(II)(bb) and 1101(b)(2)(B)(ii)(III) (creating new section 505(j)(5)(B)(iii)(II)(aa)(BB) and 505(c)(3)(C)(ii)(I)(bb) of the Act, respectively); see also MMA Title XI section 1101(a)(2)(A)(ii)(II)(dd) and 1101(b)(2)(B)(ii)(V) (creating new section 505(j)(5)(B)(iii)(IV) and 505(c)(3)(C)(iv) of the Act, respectively).

[12] See MMA Title XI section 1101(a)(2)(A)(ii)(II)(bb) and 1102(b)(2)(B)(ii)(III) (creating new section 505(j)(5)(B)(iii)(II)(bb) and 505(c)(3)(C)(ii)(II) of the Act, respectively); see also MMA Title XI section 1101(a)(2)(A)(ii)(II)(dd) and 1101(b)(2)(B)(ii)(V) (creating new section 505(j)(5)(B)(iii)(IV) and 505(c)(3)(C)(iv) of the Act, respectively).

[13] See section 505(j)(5)(B)(iv) of the Act.

[14] 505(b)(2) applications do not qualify for 180-day exclusivity.

[15] See section 505(j)(5)(B)(iv) of the Act; *Mylan Pharmaceuticals, Inc. v. Shalala*, 81 F. Supp. 2d 30 (D.D.C. 2000).

petition to the Supreme Court for a writ of certiorari (generally a decision of an appellate court).[16] (This is a transitional provision that redefines the court decision that can begin the 180-day period of exclusivity for any product for which there was a paragraph IV ANDA before enactment of the MMA.)

3. An ANDA was submitted on September 6, 2003, and was the first substantially complete ANDA to be submitted with a paragraph IV certification to the only listed patent for the listed drug. The ANDA applicant is sued for patent infringement. After December 8, 2003, the district court issues a decision finding the patent at issue invalid. This decision is appealed. Can the ANDA be approved? Does the applicant's 180-day exclusivity start to run on the date of the district court's decision?

As explained in the response to question 1 in subsection II.B of this document, for any proceeding under section 505 of the Act pending on or after December 8, 2003, the district court's decision that the patent at issue is invalid or not infringed terminates the 30-month stay of approval. Thus, if it is otherwise ready for approval, the ANDA in this question can be approved at the time of the district court's decision. However, as explained in response to question 2 in subsection II.B, as a result of the MMA, 180-day exclusivity for ANDAs filed before December 8, 2003, can now be triggered by a court decision only if it is a decision that has not been, or cannot be, appealed. Therefore, the district court's decision does not trigger 180-day exclusivity in the scenario described in this question because that decision has been appealed. Note that this result is a departure from prior law. Before enactment of the MMA, a district court decision finding a listed patent invalid or not infringed would have both terminated a 30-month stay and, in the case of an ANDA that qualified for 180-day exclusivity, triggered the start of such exclusivity as to that patent (if the exclusivity was not already triggered by commercial marketing).

4. What is the status of FDA's guidance for industry entitled *Court Decisions, ANDA Approvals, and 180-Day Exclusivity Under the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act*?

That guidance addresses the types of court decisions relevant for ANDA approvals and 180-day exclusivity under Hatch-Waxman before enactment of the MMA. The MMA supersedes relevant provisions of Hatch-Waxman in effect at the time that guidance was published and thus supersedes the guidance.

C. Notice of Paragraph IV Certifications

1. Are ANDA and 505(b)(2) applicants required to give notice for paragraph IV certifications made between August 18, 2003, and December 8, 2003?

[16] See MMA Title XI section 1102(b)(3) (defining, for this purpose, *decision of a court* as used in section 505(j)(5)(B)(iv) of the Act).

Yes. The MMA requires ANDA and 505(b)(2) applicants to provide notice for ***all*** paragraph IV certifications submitted to FDA on or after August 18, 2003.[17] Notice is to be provided:

- If the certification is included in the original application, not later than 20 days after the date of the postmark on the notice from FDA informing the applicant that the application has been filed, or

- If the certification is in an amendment or supplement, at the time the applicant submits the amendment or supplement, regardless of whether the applicant has already given notice of a prior paragraph IV certification contained in the application or an amendment or supplement to the application.[18]

We recognize that our final rule which became effective on August 18, 2003 (Final Rule),[19] stated that notice was not required for a paragraph IV certification made by an ANDA or 505(b)(2) applicant if the applicant had already provided notice of another paragraph IV certification in its application or an amendment or supplement to the application. However, as discussed above, the MMA's provisions regarding notice are retroactive to August 18, 2003, and supersede the Final Rule's provisions concerning this subject. On March 10, 2004, FDA revoked the Final Rule's notice-related provisions.[20]

We are also aware that compliance with the MMA's time frame for providing notice of a paragraph IV certification made in an amendment to an ANDA or 505(b)(2) application is not possible for ANDA and 505(b)(2) applicants who submitted paragraph IV certifications in amendments between August 18, 2003, and December 8, 2003, for which no notice was required under the Final Rule, and who have not yet provided notice of these certifications. We emphasize, however, that the MMA's requirement for notice is now in effect for all paragraph IV certifications made on or after August 18, 2003, [21] including those paragraph IV certifications previously excluded from notice requirements by the recently revoked provisions of the Final Rule. Accordingly, all applicants with pending ANDAs or 505(b)(2) applications that include paragraph IV certifications made on or after August 18, 2003, but before December 8, 2003, should have provided notice to NDA holders and patent owners in a timely manner.

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[17] See MMA Title XI section 1101(a)(1)(A) and 1101(b)(1)(A) (amending section 505(j)(2)(B)(i) and 505(b)(3)(A) of the Act, respectively); see also MMA Title XI section 1101(c)(2).

[18] See MMA Title XI section 1101(a)(1)(A) and 1101(b)(1)(A) (amending section 505(j)(2)(B)(ii) and 505(b)(3)(B) of the Act, respectively).

[19] See *Applications for FDA Approval to Market a New Drug: Patent Submission and 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*; Final Rule (68 FR 36676; June 18, 2003).

[20] See *Application of 30-Month Stays on Approval of Abbreviated New Drug Applications and Certain New Drug Applications Containing a Certification That a Patent Claiming the Drug Is Invalid or Will Not Be Infringed*; Technical Amendment (69 FR 11309; March 10, 2004).

[21] See MMA Title XI section 1101(c)(2).

2. If, between August 18, 2003, and December 8, 2003, an ANDA or 505(b)(2) applicant provided voluntary notice with respect to a paragraph IV certification for which notice was not required under the Final Rule, is the applicant considered to have satisfied the MMA's notice requirement?

The applicant will have satisfied the MMA's notice requirement if the notice it gave complies with all applicable provisions of the MMA (e.g., provisions specifying to whom notice must be given and the notice's required contents). [22]

D. Multiple 30-Month Stays

1. Does the MMA preclude ANDAs and 505(b)(2) applications from being subject to more than one 30-month stay of approval?

The MMA generally precludes multiple 30-month stays for those applications to which it applies. The relevant provisions of the MMA apply to patents submitted to FDA on or after August 18, 2003.[23] For ANDAs and 505(b)(2) applications with paragraph IV certifications to a patent submitted to FDA on or after August 18, 2003, the MMA provides that a 30-month stay may be available for litigation related to that patent only if the patent was submitted to FDA before the date that the ANDA or 505(b)(2) application (excluding an amendment or supplement) was submitted.[24] In other words, the MMA precludes 30-month stays for *later listed* patents, that is, those patents submitted to FDA on or after the date the ANDA or 505(b)(2) application was submitted. Because of this limitation, in most cases, ANDAs and 505(b)(2) applications will be subject to no more than one 30-month stay. [25]

Multiple 30-month stays, however, still may be possible in certain cases. For instance, an ANDA or 505(b)(2) application may contain a paragraph IV certification to a patent at the time of first submission that gives rise to one 30-month stay. If the same application also contains a paragraph III certification to a different patent that was submitted to FDA (1) on or after August 18, 2003, and (2) before the ANDA or 505(b)(2) application was submitted, and the applicant subsequently converts this certification to a paragraph IV

[22] See MMA Title XI section 1101(a)(1)(A) and 1101(b)(1)(A) (amending section 505(j)(2)(B) and 505(b)(3) of the Act, respectively).

[23] See MMA Title XI section 1101(c)(3). The effective date for this provision means that the MMA supersedes FDA's Final Rule with respect to the availability of 30-month stays. As noted earlier in response to question 1 in subsection II.C of this document, on March 10, 2004, FDA revoked provisions of the Final Rule superseded by the MMA (see footnote 20, supra).

[24] See MMA Title XI section 1101(a)(2)(A)(ii)(I) and 1101(b)(2)(B)(i) (amending section 505(j)(5)(B)(iii) and 505(c)(3)(C) of the Act, respectively).

[25] Under the regulations in effect before FDA adopted its August 18, 2003, Final Rule, multiple 30-month stays could arise in the case of later-listed patents if (1) an ANDA or 505(b)(2) application had already been subject to one such stay based on a paragraph IV certification to a patent listed before the application's submission, and (2) the ANDA or 505(b)(2) applicant made a subsequent paragraph IV certification to a patent listed after the application's submission that triggered another timely patent infringement lawsuit.

certification, a second 30-month stay could be possible. This is because the new paragraph IV certification is subject to the MMA and references a patent submitted to FDA before the applicant's ANDA was submitted.

2. Does the MMA ensure that a patent owner or NDA holder can obtain one 30-month stay of approval on an ANDA or 505(b)(2) application containing a paragraph IV certification to a listed patent when the patent owner or NDA holder sues the ANDA or 505(b)(2) applicant for patent infringement?

No. The MMA does not guarantee that any patent owner or NDA holder will receive a 30-month stay, even if it sues for patent infringement. Rather, the MMA provides the opportunity to obtain a stay only in certain situations. As noted in response to question 1 in subsection II.D of this document, the amendments made by the MMA with respect to the availability of 30-month stays apply to patents submitted to FDA on or after August 18, 2003. With respect to such patents, a 30-month stay of approval on an ANDA or 505(b)(2) application containing a paragraph IV certification to the patent will ensue if:

- The patent was submitted before the date that the ANDA or 505(b)(2) application (excluding an amendment or supplement) was submitted to FDA, **and**

- The patent owner or NDA holder initiates a patent infringement action on the patent within 45 days of the date that it receives notice of the certification.[26]

No 30-month stay of approval will result from a patent subject to the MMA, even if litigation is initiated based on a paragraph IV certification to the patent, if either of the conditions described above is not satisfied. That is, no 30-month stay of approval will apply if the patent was submitted to FDA *on or after* the date the ANDA or 505(b)(2) application with a paragraph IV certification to the patent was submitted. (Note that this is the case even if the later-submitted patent is the first listed patent to claim the drug described in the ANDA or 505(b)(2) application.) In addition, a 30-month stay will not ensue if litigation is initiated more than 45 days after the date that the patent owner or NDA holder receives notice of the certification.

3. An ANDA was submitted to FDA in November 2003 with multiple patent certifications, including a paragraph IV certification to at least one patent. No patent infringement lawsuit was initiated, but a new patent was submitted to FDA on December 27, 2003. What are the ANDA applicant's certification and notification obligations? Is a 30-month stay of approval possible based on the December 27 patent?

[26] See MMA Title XI section 1101(a)(2)(A) and 1101(b)(2)(B) (amending section 505(j)(5)(B)(iii) and 505(c)(3)(C) of the Act, respectively); see also MMA Title XI section 1101(c)(3).

Under section 505(j)(2)(A)(vii) of the Act (which was not amended by the MMA), the ANDA applicant would be required to provide a certification with respect to the December 27, 2003, patent. With regard to notice, as discussed in response to question 1 in subsection II.C of this document, the MMA amends section 505 of the Act to make clear that ANDA and 505(b)(2) applicants must provide notice of all paragraph IV certifications.[27] Accordingly, if the applicant amends its ANDA to include a paragraph IV certification to the December 27, 2003, patent, it would be required by the MMA to notify the patent owner and NDA holder of its certification at the time its amendment is submitted.[28]

As previously discussed, the MMA provides that a 30-month stay cannot arise from a patent submitted on or after August 18, 2003, unless the patent was also submitted to FDA before the ANDA or 505(b)(2) application was submitted.[29] Accordingly, no 30-month stay of approval would be possible based on the December 27, 2003, patent in this question.

4. Is a 30-month stay based on a patent possible if the patent (1) is submitted to FDA on or after August 18, 2003, and before an ANDA or 505(b)(2) application with a paragraph IV certification to the patent is submitted, and (2) is not published in the Orange Book before the application's submission?

The patent described in this question could provide the basis for a 30-month stay if the other conditions for a stay, as discussed above, are satisfied. As previously noted, under the MMA, a patent that is submitted to FDA on or after August 18, 2003, could potentially trigger a 30-month stay if it is also "submitted . . . before the date on which the [ANDA] application (excluding an amendment or supplement to the application) is submitted."[30] Eligibility for a 30-month stay thus turns on when the patent is *submitted* to FDA, as opposed to when it is published in the Orange Book. Because the patent in this question meets the time frames for submission specified in the MMA, it can result in a 30-month stay, regardless of when it is published in the Orange Book.

E. 180-Day Exclusivity

What ANDAs are subject to the MMA's new 180-day exclusivity provisions?

With two exceptions, the new provisions relating to 180-day exclusivity govern only ANDAs filed after the date of the MMA's enactment (December 8, 2003) that reference a listed drug for which no paragraph IV certification was made in any ANDA before that date.[31] The two exceptions concern the forfeiture of 180-day exclusivity by entering into

[27] See MMA Title XI section 1101(a)(1)(A) and 1101(b)(1)(A) (amending section 505(j)(2)(B)(i) and 505(b)(3)(A) of the Act, respectively); see also MMA Title XI section 1101(c)(2).
[28] See MMA Title XI section 1101(a)(1) (creating new section 505(j)(2)(B)(ii)(II) of the Act).
[29] See MMA Title XI section 1101(a)(2)(A)(ii)(I) (amending section 505(j)(5)(B)(iii) of the Act).
[30] MMA Title XI section 1101(a)(2)(A)(ii)(I) (amending section 505(j)(5)(B)(iii) of the Act).
[31] See MMA Title XI section 1102(b)(1).

a collusive agreement and the triggering of the exclusivity period by judicial action.[32] All other ANDAs remain subject to the 180-day exclusivity provisions in effect before the MMA's enactment. Thus, for example, FDA's guidance for industry, *180-Day Exclusivity When Multiple ANDAs Are Submitted on the Same Day*, still applies to ANDAs submitted before, on, or after December 8, 2003, that reference a listed drug for which a paragraph IV certification had been made in any ANDA before December 8, 2003. FDA will further interpret provisions of the MMA relating to 180-day exclusivity in future regulations and/or guidances.

F. Applicability and Effective Dates

What are the effective dates of the various provisions of the MMA?

MMA Section	Amended or Added Sections of the Act	Effective Date or Scope of Applicability
1101(a)(1) and (b)(1) (Amending or supplementing an application)	505(j)(2)(D) and 505(b)(4)	A change in listed drug or proposed drug made on or after December 8, 2003
1101(a)(1) and (b)(1) (Notice provisions)	505(j)(2)(B) and 505(b)(3)	Any paragraph IV certification submitted on or after August 18, 2003 in an application, amendment, or supplement
1101(a)(2)(A)(ii)(I) and (b)(2)(B)(i) (30-month stay provisions)	505(j)(5)(B)(iii) and 505(c)(3)(C)	Retroactive to patent information submitted to FDA on or after August 18, 2003
1101(a)(2)(A)(ii)(II) and (b)(2)(B)(ii) (Court decision provisions for approval)	505(j)(5)(B)(iii) and 505(c)(3)(C)	Any proceeding pending on or after December 8, 2003, regardless of the date on which the proceeding was or is commenced

[32] The exception relating to forfeiture based on a first ANDA applicant's entry into an anti-competitive agreement applies if conditions specified in the MMA are met, regardless of when the first ANDA paragraph IV certification for the listed drug was made (see MMA Title XI section 1102(b)(2)). The second exception relates to the MMA's definition of the term *decision of a court* for purposes of section 505(j)(5)(B)(iv) of the Act. As discussed in response to question 2 in subsection II.B of this document, the MMA's definition of this term applies to alter the court decision trigger for 180-day exclusivity for all ANDAs other than those filed after December 8, 2003, for a listed drug for which no paragraph IV certification was made in any ANDA before that date (see MMA Title XI section 1102(b)(3)).

MMA Section	Amended or Added Sections of the Act	Effective Date or Scope of Applicability
1101(a)(2)(C) and (b)(2)(D) (Civil action to obtain patent certainty)	505(j)(5)(C) and 505(c)(3)(D)	Any proceeding pending on or after December 8, 2003, regardless of the date on which the proceeding was or is commenced
1102(a) (180-day exclusivity period)	505(j)(5)(B)(iv) and 505(j)(5)(D)	ANDAs filed after December 8, 2003 for a listed drug for which no paragraph IV certification had been made in any ANDA before December 8, 2003, except as provided in the box immediately following
1102(a)(2) (Collusive agreement forfeiture provision)	New 505(j)(5)(D)(i)(V)	ANDAs filed after December 8, 2003, regardless of when the first paragraph IV certification was made for the listed drug referenced in any ANDA
1102(b)(3) (Meaning of *decision of a court* that will trigger the beginning of 180-day exclusivity for certain ANDAs)	505(j)(5)(B)(iv)	ANDAs for a listed drug for which a paragraph IV certification was made in any ANDA before December 8, 2003, and for which there was no court decision or commercial marketing that triggered 180-day exclusivity (under the Act pre-MMA) on or before December 8, 2003
1103(a) (Bioavailability/ bioequivalence)	505(j)(8)	December 8, 2003