Orange Book Patent Listing and Patent Certifications: Key Provisions in FDA's Proposed Regulations Implementing the Medicare Modernization Act of 2003

On February 6, 2015, the United States Food and Drug Administration (FDA) issued long-awaited proposed regulations to implement portions of the Medicare Modernization Act of 2003 (MMA). Consisting of almost one hundred pages in the Federal Register, the proposed rule and its preamble contain a vast number of provisions concerning the submission of patent information by NDA holders, patent certifications by 505(b)(2) and ANDA applicants, notices of paragraph IV certifications, 30-month litigation stays, and amendments and supplements to 505(b)(2) and ANDA applications.[1] While many of the proposals are intended to codify the Agency's current practices and policy with respect to MMA, some proposals lay out entirely new approaches that are particularly noteworthy. This Alert focuses only on certain provisions that represent a significant departure from current practice, and specifically, proposals concerning method-of-use patents, reissued patents, and paragraph IV certifications.

Method-of-Use Patents

Submission of Patent Information to the Orange Book. In the event that the scope of a patent's method-of-use claim(s) does not cover every use of the drug, FDA proposes to expressly require that the NDA applicant identify *only* the certain sections of product labeling that correspond to the specific portion(s) of the indication or other condition of use claimed by the patent.[2] This revision would address situations in which the scope of the method of use claimed by the patent is narrower than the indication described in the product labeling.[3] In such cases, the NDA holder is *not* to identify the broader indication or other condition of use.[4] Similarly, and in furtherance of the Supreme Court's caution against overbroad use codes in *Caraco Pharm. Labs. v. Novo Nordisk A/S*,[5] the proposed rule specifies that the use code for such a patent must contain "adequate information"; 505(b)(2) and ANDA applicants will use this information to determine whether a method-of-use patent claims a use for which the applicant is not seeking approval, and, should the patent not cover every approved use of the drug, the use code can only contain the specific portion of the indication or other condition of use claimed by the patent.[6]

Timing of Submission of Method-of-Use Patent Information. The proposed rule also makes clear that an NDA holder's amendment to the description of the approved method(s) of use claimed by a patent will be considered untimely filed if the amendment is submitted more than 30 days after (1) patent issuance and is not related to a corresponding change in the approved product labeling; or (2) a corresponding change in approved product labeling.[7] FDA generally does not require an applicant with a pending 505(b)(2) or ANDA application to provide a patent certification to an untimely filed patent. For applicants with pending 505(b)(2) or ANDA applications that seek to confirm that a newly listed patent was untimely filed, the preamble to the proposed rule advises those applicants to contact the Orange Book staff.[8]

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[1] The proposed rule does not address matters related to forfeiture of 180-day exclusivity.
[2] Abbreviated New Drug Applications and 505(b)(2) Applications, 80 Fed. Reg. 6802, 6884 (proposed Feb. 6, 2015) (to be codified at 21 CFR pt. 314) (Proposed 314.53(c)(2)(ii)(P)(2)).
[3] *Id.* at 6820.
[4] *Id.* at 6820-21.
[5] 132 S. Ct. 1670, 1684 (2012) ("An overbroad use code . . . throws a wrench into the FDA's ability to approve generic drugs as the statute contemplates").
[6] Abbreviated New Drug Applications and 505(b)(2) Applications, 80 Fed. Reg. at 6884 (Proposed 314.53(c)(2)(ii)(P)(3)).
[7] *Id.* at 6880 (Proposed 314.50(i)(4)); *id.* at 6888 (Proposed 314.94(a)(12)(vi)).
[8] *Id.* at 6824.

Challenging the Accuracy or Relevance of Method-of-Use Patent Listings. The proposed rule also enhances the mechanism for challenging the accuracy or relevance of method-of-use patents listed in the Orange Book. Under the current regulations, if a person disputes the accuracy or relevance of patent information or believes that an NDA holder has failed to submit required patent information, FDA, after receiving notification from the person, requests the NDA to confirm the correctness of the patent information or omission of patent information.[9] The proposed rule would establish a 30-day timeframe in which the NDA holder must respond to FDA's request.[10]

The proposed rule also specifies that, with respect to method-of-use patents, FDA will request that the NDA holder (1) confirm the correctness of the approved indication or method of use that has been included in the use code, and (2) provide information on the specific approved use claimed by the patent that enables FDA to determine whether the scope of the proposed labeling carve-out would be appropriate. If the NDA holder confirms the accuracy of the patent information, fails to timely respond, or submits a revision that does not provide adequate clarity for FDA to make such a determination, FDA proposes to review the proposed carve-out with deference to the 505(b)(2) or ANDA applicant's interpretation of the scope of the patent. FDA believes this approach for enhancing the mechanism to challenge overbroad use codes "may cause NDA holders to be more circumspect in their original submission of patent information to FDA."[11]

Reissued Patents

Requirement to Submit Reissued Patents for Listing. The proposed regulations add new provisions explicitly directed to reissued patents.[12] Although the Agency currently receives submissions of patent information for reissued patents and lists such patents, the proposal would *require* the NDA applicant or holder to include information on whether a patent submitted for listing is a reissuance of a patent previously submitted for listing, and such submission would be subject to the 30-day time frame for timely filed patent information. This proposal would treat the original patent and the issued patent as a "single bundle" of patent rights for purposes of administering the patent certification requirements and associated 30-month stay and 180-day exclusivity period.[13]

Certifications to a Reissued Patent. If a 505(b)(2) or ANDA applicant is not required to provide a patent certification or statement to the original patent because it was untimely filed and late-listed as to the pending 505(b)(2) application or ANDA, then under the proposed regulations, the applicant would not be required to provide a patent certification or statement to the reissued patent, even if the reissued patent is timely submitted for listing.[14] Otherwise, an amendment to a pending 505(b)(2) application or ANDA is necessary to provide an appropriate patent certification or statement to the reissued patent, even if the type of patent certification does not differ from that submitted for the original patent.

Reissued Patents and 30-Month Stay. An amended patent certification to the reissuance of an original patent for which a paragraph IV certification was previously submitted may have implications for the 30-month stay. For instance,

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[9] 21 C.F.R. § 314.53(f) (2014).
[10] Abbreviated New Drug Applications and 505(b)(2) Applications, 80 Fed. Reg. at 6885 (Proposed 314.53(f)(1)).
[11] *Id.* at 6828.
[12] *Id.* at 6883 (Proposed 314.53(c)(2)(i)(J)); *id.* at 6884 (Proposed 314.(c)(2)(ii)(K)); *id.* at 6821.
[13] The fact that the original patent is technically surrendered upon reissuance is not relevant to FDA's assessment of a first applicant's eligibility for 180-day exclusivity. *Id.* at 6846.
[14] *Id.* at 6845.

- if the 505(b)(2) or ANDA applicant submitted a paragraph IV certification to the original patent and a patent suit was initiated within 45 days of notice of the paragraph IV certification, the resulting 30-month stay would not be affected solely by reissuance of the patent or recertification;

- if the 505(b)(2) or ANDA applicant submitted a section viii statement or paragraph III certification and subsequently submitted a paragraph IV certification to the reissued patent, a 30-month stay would be available; and

- if the 505(b)(2) or ANDA applicant submitted a paragraph IV certification to the original patent and no patent suit was initiated within 45 days of notice of the paragraph IV certification, no subsequent patent suit with respect to the reissued patent could give rise to a 30-month stay.[15]

Reissued Patents and 180-Day Exclusivity. An amended patent certification to the reissuance of an original patent for which a paragraph IV certification was previously submitted may also have implications for 180-day exclusivity. In particular,

- if one or more first applicants is eligible for 180-day exclusivity based on a paragraph IV certification to the original patent, the first applicant would be required to submit a paragraph IV certification to the reissued patent within 30 days of listing to lawfully maintain its paragraph IV certification for 180-day exclusivity eligibility;[16] and

- if no applicant had submitted a paragraph IV certification to the original patent, then the first ANDA applicant to submit a paragraph IV certification to the reissued patent could be eligible for 180-day exclusivity, as long as no other applicant had already qualified as a first applicant based on an earlier paragraph IV certification to another listed patent.[17]

Notice of Paragraph IV Certification

Requirement to Give Notice. Under the proposed rule, where a listed patent is challenged by the applicant in an amendment or supplement to a 505(b)(2) application or ANDA, a paragraph IV notice must be provided, regardless of (1) whether the applicant has already given notice with respect to another paragraph IV certification (i.e., a previous paragraph IV certification to a different patent or a previous paragraph IV certification to the same patent) and (2) even if patent infringement litigation has been initiated in response to a previous notice.[18]

Date Before Which Notice Cannot Be Given. The proposed rule also clarifies the time frame within which notice of a paragraph IV certification to a listed patent can be provided to the NDA holder and each patent owner. First, the proposed rule clarifies the "longstanding" practice that any notice sent before the receipt of an FDA acknowledgment letter[19] or paragraph IV acknowledgment letter[20] is invalid (and thus does not

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[15] *Id.* at 6846.
[16] *Id.* at 6889 (Proposed 314.94(a)(12)(viii)(B)); *id.* at 6846.
[17] *Id.* at 6846.
[18] *Id.* at 6890 (Proposed 314.95(d)(1)); *id.* at 6881 (Proposed 314.52(d)(1)); *id.* at 6850.
[19] The proposed rule defines an "acknowledgment letter" as a written, postmarked communication from FDA to an applicant stating that the agency has determined that a 505(b)(2) application or ANDA is sufficiently complete to permit a substantive review. *Id.* at 6876 (Proposed 314.3(b)).
[20] The proposed rule defines a "paragraph IV acknowledgment letter" as a written, postmarked communication from FDA to an applicant stating that the Agency has determined that a 505(b)(2) application or ANDA containing a paragraph IV certification is sufficiently complete to permit a substantive review. *Id.* at 6877 (Proposed 314.3(b)).

trigger the 45-day period in which the NDA holder and each patent owner may initiate a patent infringement action and obtain a 30-month stay).[21] For patents issued after NDA approval, the proposed rule would render any notice sent before the first working day after the patent is published in the Orange Book as similarly invalid.[22]

Date by Which Notice Must Be Given. The proposed rule also specifies how the 20-day period for delivering notice is calculated. Specifically, the Agency proposes that the first day of the 20-day period begin on the day after the date of the postmark[23] on the acknowledgment letter or paragraph IV acknowledgment letter.[24] The 20-day period is proposed to include all calendar days, except that if the 20th day falls on a Saturday, Sunday, or federal holiday, the last day of the 20-day period will be considered the next day that is not a Saturday, Sunday, or federal holiday.[25]

Consequence for Failure to Timely Give Notice. Where an ANDA applicant fails to send a paragraph IV certification notice within the required statutory time frame of 20 days after the date of the postmark on a paragraph IV acknowledgment letter, FDA proposes that it will move forward the date of submission of the ANDA by the number of days beyond the required time frame that the applicant delayed in sending its notice.[26] Similarly, if an ANDA applicant does not provide a paragraph IV notice on the date that an amendment or supplement containing a paragraph IV certification is submitted to FDA, FDA will not consider the paragraph IV certification to be effective until the notice is sent.[27]

Consequently, an ANDA applicant may lose its first applicant status and thus its eligibility for 180-day exclusivity if it fails to timely provide notice of paragraph IV certification.[28] Such an applicant may also experience a delay in the review queue for its ANDA consistent with the revised date of submission.

No similar administrative consequence is proposed for 505(b)(2) applicants that fail to timely provide notice of a paragraph IV certification because such applicants are not eligible for 180-day exclusivity and FDA is unable to extend the review clock for an NDA subject to PDUFA performance goals and procedures.[29]

Implications

The proposed rule contains a wealth of information concerning the manner in which FDA has interpreted and proposes to interpret various Hatch-Waxman issues, including Orange Book patent listing, patent certifications, amendments and supplements to 505(b)(2) applications and ANDAs, and the 30-month stay. Although the proposed rules, if finalized, will only apply to submissions received by FDA after the effective date of the final rule, some companies may begin conforming their practices to certain aspects of the proposed rules in advance of finalization (e.g., ensuring that notice of paragraph IV certifications in

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[21] *Id.* at 6881 (Proposed 314.52(b)(2)); *id.* at 6890 (Proposed 314.95(b)(2)).
[22] *Id.* at 6890 (Proposed 314.95(b)(2)).
[23] For purposes of determining the time frame for sending a paragraph IV notice, FDA considers the date of the "postmark" on a paragraph IV acknowledgment letter for a 505(b)(2) application to be four calendar days after the date on which the filing communication is signed by the signatory authority, unless the filing communication is sent to the applicant via electronic transmission. *Id.* at 6833.
[24] *Id.* at 6881 (Proposed 314.52(b)(1)); *id.* at 6890 (Proposed 314.95(b)(1)).
[25] *Id.* This is the same way that FDA calculates the 45-day period within which the patent owner and NDA holder may initiate a patent suit and trigger a 30-month stay.
[26] *Id.* at 6892 (Proposed 314.101(b)(4)); *id.* at 6840.
[27] *Id.* at 6835.
[28] *Id.* at 6840.
[29] *Id.* at 6841.

amendments or supplements to 505(b)(2) applications or NDAs is provided). In any case, the proposals are likely to encourage debate among innovator and generic companies alike.

FDA will be accepting comments on the proposed regulations through May 7, 2015.

If you would like to discuss the foregoing or any related matter, please contact any member of Ropes & Gray's FDA regulatory practice or your usual Ropes & Gray advisor.