POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS

Conversion of ANDA Approval to Tentative Approval Because of Court Order

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PURPOSE

- This Manual of Policies and Procedures (MAPP) describes the policies and procedures of the Office of Generic Drugs for converting the approval status of an abbreviated new drug application (ANDA) from final approval to tentative approval (TA) following a court order issued under 35 U.S.C. 271(e)(4)(A) for patent infringement.

BACKGROUND

- The timing of ANDA approval depends on, among other things, the patent and exclusivity protections for the reference listed drug (RLD) on which the applicant relies in seeking approval. An applicant must provide, in its ANDA, information related to any patents listed for the RLD in the Food and Drug Administration's (FDA's) *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).[1] In particular, an ANDA applicant generally must submit to FDA one of four specified certifications regarding the patents for the RLD under section 505(j)(2)(A)(vii) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)(2)(A)(vii)).

- With respect to each patent listed in the Orange Book for the RLD, the ANDA applicant's patent certification must state one of the following:

  – That such patent has expired (a paragraph II certification),

[1] The Orange Book is available at https://www.accessdata.fda.gov/scripts/cder/ob/.

  - The date on which such patent will expire (a paragraph III certification), or

  - That such patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted (a paragraph IV certification).[2]

- Once FDA has received an ANDA for review,[3] an applicant that submitted a paragraph IV certification to a listed patent must provide the new drug application (NDA) holder and each patent owner notice of its paragraph IV certification, including a description of the legal and factual basis for the ANDA applicant's assertion that the patent is invalid, unenforceable, or will not be infringed.[4] If a patent is listed at the time an original ANDA is submitted and, in response to a notice of a paragraph IV certification, the NDA holder or patent owner initiates a patent infringement action against the ANDA applicant within 45 days of receiving the required notice, approval of the ANDA generally will be stayed for 30 months from the later of the date of receipt of the notice by any owner of the patent or the NDA holder or such shorter or longer time as the court might order.[5]

- FDA may issue final approval to an ANDA at the conclusion of a 30-month stay if a patent infringement lawsuit about the drug product at issue in that ANDA is pending, the ANDA does not contain any paragraph III certifications, the ANDA is not blocked by any unexpired exclusivities, and all other requirements for approval have been met. However, after the ANDA is approved, the NDA holder or patent owner may be successful in its patent infringement lawsuit against the ANDA holder. In such a case, the district court may order that the patent is infringed and that the approval of the ANDA is not effective before expiration of the infringed patent pursuant to 35 U.S.C. 271(e)(4)(A). Under these circumstances, FDA must determine whether it is appropriate to convert the approval status of the ANDA to TA[6] and, if that conversion is appropriate, the timing of such conversion. To facilitate FDA's timely conversion of the approval status of an ANDA to TA, ANDA applicants are required to submit any and all documents pursuant to 21 CFR 314.107(e) within 14 days of the date of entry by the court or the date of appeal or expiration of the time for appeal.[7]

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[2] Section 505(j)(2)(A)(vii) of the FD&C Act; see also 21 CFR 314.94(a)(12)(i)(A).

[3] 21 CFR 314.101(b).

[4] Section 505(j)(2)(B) of the FD&C Act.

[5] Section 505(j)(5)(B)(iii) of the FD&C Act and 21 CFR 314.107(b)(3)(i).

[6] 21 CFR 314.107(g) ("If FDA issues an approval letter in error or a court enters an order requiring, in the case of an already approved 505(b)(2) application or ANDA, that the date of approval be delayed, FDA will convert the approval to a tentative approval if appropriate.").

[7] 21 CFR 314.107(e). We note that FDA may become aware of the court order through other means, such as receiving a copy from the patent owner or NDA holder.

POLICY

- FDA considers certain factors when determining whether it is appropriate to convert the approval status of an approved ANDA to TA and, if that conversion is appropriate, the timing of such conversion. Upon receipt of a Federal district court judgment that the patent is infringed and the approval of the ANDA is not effective before expiration of the infringed patent, as described in 35 U.S.C. 271(e)(4)(A), FDA will consider the judgment and will also consider any documents showing (1) that the district court judgment has been stayed or (2) that there is a pending motion for stay of the district court judgment.

RESPONSIBILITIES

- **Office of Generic Drug Policy Patent and Exclusivity Team**

  – Receives information from the Office of Regulatory Operations (ORO) Division of Project Management (DPM) concerning patent infringement lawsuits, which may be submitted by electronic submission by the ANDA holder or by paper submission by or on behalf of the NDA holder.

    • Verifies that any patents subject to the patent infringement lawsuits are listed in the Orange Book.

    • Assesses court orders and motions for stay related to patent infringement lawsuits to determine whether it is appropriate to convert the approval status of an ANDA from final approval to TA.

    • Notifies the Associate Director of the Office of Generic Drug Policy (OGDP) Division of Legal and Regulatory Support (DLRS) when information concerning patent infringement lawsuits is received, provides the DLRS Associate Director the information received on the status of the patent infringement lawsuits (e.g., copies of the order issued by the district court that finds patent infringement pursuant to 35 U.S.C. 271(e)(4)(A)), and provides a recommendation of approval status to the DLRS Associate Director.

    • Drafts "Conversion to ANDA Tentative Approval" letters.

- **OGDP DLRS Associate Director (or designee)**

  – Reviews assessment conducted by the Patent Exclusivity Team (PET) for concurrence.

- Reviews "Conversion to ANDA Tentative Approval" letter.

- **OGDP DLRS Division Director (or designee)**

  - Performs a secondary review of the "Conversion to ANDA Tentative Approval" letter.

- **ORO DPM**

  - Sends information received electronically about a patent infringement lawsuit to PET.

  - Issues the "Conversion to ANDA Tentative Approval" letter.

  - Ensures that the ANDA status updates from final approval to TA in relevant internal databases and notifies the Division of Orange Book Publication and Regulatory Assessment (DOBPRA) and Drugs@FDA staff of the conversion, so that the application can be removed from the Orange Book and for appropriate processing of the approval information in Drugs@FDA.

- **ORO Immediate Office**

  - Provides the final signature on the "Conversion to ANDA Tentative Approval" letter.

PROCEDURES

- **Receipt of court decisions or other documents related to patent infringement lawsuits**

  - Submissions related to patent infringement lawsuits may be submitted by or on behalf of either (1) the patent owner or NDA holder or (2) the ANDA holder. Depending on the submitter, the document may be received in electronic or paper format to the ANDA or to an office or person at FDA.

- **Triage of submissions related to patent infringement lawsuits**

  - All submissions related to patent infringement lawsuits are reviewed by the PET. If the submission is made by the ANDA holder and submitted electronically to its application, the regulatory project manager (RPM) in the ORO DPM notifies the PET and provides either an electronic link to, or an electronic copy of, the submission. If a physical or electronic submission is received from the NDA holder or patent owner by the Office of Generic Drugs, the submission is forwarded to the PET for review and archiving. The

PET will verify that any patents identified in the lawsuit are listed in the Orange Book.

- **Decision to convert the approval status of an ANDA from final approval to TA**

  – Once the verification process is complete, the PET provides the submitted documentation and verification results to the DLRS Associate Director and makes a recommendation regarding approval status. The DLRS Associate Director determines whether it is appropriate to convert, and the timing of any such conversion, by considering the factors noted in the Policy section above. If the approval status of the ANDA is converted from final approval to TA, any unapproved supplements and/or annual report changes submitted to the ANDA will be considered withdrawn, and any approved supplements will be considered TA status.

- **Creation and issuance of "Conversion to ANDA Tentative Approval" letter**

  – If the DLRS Associate Director determines that conversion is appropriate, the PET drafts the "Conversion to ANDA Tentative Approval" letter to the ANDA holder and sends the letter to the DLRS Associate Director for review. Upon completion of the DLRS Associate Director review, the DLRS Director performs a secondary review of the "Conversion to ANDA Tentative Approval" letter. Upon clearance of the conversion letter by the DLRS Director, the PET provides the final letter to the appropriate RPM in the ORO DPM. The letter is generally transmitted for review and clearance by email and uploaded, by the RPM, into the system of record. The ORO Immediate Office signs and archives the letter. The letter is issued to the ANDA holder by the ORO DPM. The ORO DPM will ensure the status of an ANDA that has undergone conversion from final approval to TA is accurate in the relevant internal FDA databases and inform DOBPRA and Drugs@FDA staff of the conversion so that the application can be removed from the Orange Book and for appropriate processing of the information in Drugs@FDA.

DEFINITIONS

- **Tentative approval**: Notification that an NDA or ANDA otherwise meets the requirements for approval under the FD&C Act, but cannot be approved because there is a 7-year period of orphan exclusivity for a listed drug under section 527 of the FD&C Act and 21 CFR 316.31, or that a 505(b)(2) application or ANDA otherwise meets the requirements for approval under the FD&C Act, but cannot be approved until the conditions in 21 CFR 314.107(b)(1)(iii), (b)(3), or (c) are met; because there is a period of exclusivity for the listed drug under 21 CFR 314.108; because there is a period of pediatric exclusivity for the listed drug under

section 505A of the FD&C Act; because there is a period of exclusivity for the listed drug under section 505E of the FD&C Act; or because a court order pursuant to 35 U.S.C. 271(e)(4)(A) orders that the NDA or ANDA may be approved no earlier than the date specified. A drug product that is granted tentative approval is not an approved drug and will not be approved until FDA issues an approval letter after any necessary additional review of the NDA or ANDA.[8]

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
06/11/2020	Initial	N/A
TBD	1	Minor revisions to reflect organizational updates.

[8] 21 CFR 314.3(b).