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 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 *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).[1] In particular, an ANDA applicant generally must submit to the Food and Drug Administration (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 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. In order for FDA to timely convert 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).

POLICY

FDA considers certain factors when determining whether it is appropriate to convert the approval status of an approved ANDA to TA. 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 Deputy 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 Deputy 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 Deputy Director

  - Drafts "Conversion to ANDA Tentative Approval" letters

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

  - Reviews assessment conducted by the Patent and Exclusivity Team (PET) for concurrence

  - Reviews "Conversion to ANDA Tentative Approval" letter

- **DLRS 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

  - Updates the status of the ANDA that has undergone conversion from final approval to TA status in the relevant FDA databases and informs the Orange Book staff of the conversion

- **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 in the ORO DPM notifies the PET and provides either an electronic link to or an electronic copy of the submission. If the submission is made by the NDA holder or patent owner to the Office of Generic Drugs on paper, the submission is forwarded to the PET by the document room. 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 Deputy Director and makes a recommendation regarding approval status. The DLRS Deputy Director determines whether it is appropriate to convert 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.

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

If the DLRS Deputy 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 Deputy Director for review. Upon completion of the DLRS Deputy Director review, the DLRS Director performs a secondary review of the "Conversion to ANDA Tentative Approval" letter. Upon approval of the conversion letter by the DLRS Director, the PET provides the final letter to the appropriate regulatory project manager in the ORO DPM. The letter is generally transmitted for review and clearance by email. Once the letter is signed by the ORO Immediate Office, the "Conversion to ANDA Tentative Approval" letter is issued to the ANDA holder by the ORO DPM. The ORO DPM will update the status of an ANDA that has undergone conversion from final approval to TA status in the relevant FDA databases and inform the Orange Book staff of the conversion so that the application can be removed from the Orange Book.

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 § 316.31 of this chapter, 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 § 314.107(b)(1)(iii), (b)(3), or (c) are met; because there is a period of exclusivity for the listed drug under § 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]

[8] 21 CFR 314.3(b).

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
6/11/2020	Initial	N/A

ATTACHMENT 1

ANDA ######

CONVERSION TO ANDA
TENTATIVE APPROVAL

APPLICANT NAME
ADDRESS
Attention: CONTACT NAME
TITLE

Dear CONTACT:

This is in reference to your abbreviated new drug application (ANDA) for ESTABLISHED NAME DOSAGE FORM AND STRENGTH(S), approved on APPROVAL DATE pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). We are writing to inform you that, consistent with the COURT DECISION issued on DATE OF COURT ORDER, the Agency hereby converts the final approval of ANDA ##### to a tentative approval, and considers that this conversion occurred on the date of that decision. Thus, FDA regards ANDA #####, as having been tentatively approved as of DATE OF COURT ORDER. This action conforms the ANDA's status to the court's final judgement, as described in detail below.

The reference listed drug (RLD) upon which your ANDA is based, PROPRIETARY DRUG NAME DOSAGE FORM AND STRENGTH(S), of RLD HOLDER, is subject to periods of patent protection. The following patents and expiration dates are listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent No.	Expiration Date

Your ANDA contained a paragraph IV certification(s) under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the PATENT #(s) patent(s) is/are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of ESTABLISHED NAME DOSAGE FORM AND STRENGTH(S), under this ANDA.[i] As noted in your APPROVAL DATE approval letter, you notified the Agency that ANDA HOLDER complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and that litigation was initiated against ANDA HOLDER for infringement of the PATENT #(s) patent(s) within the statutory 45-day period in the COURT [INCLUDE COURT CASE NAME Plaintiff v. Defendant, Civil Action No. CASE #].

INCLUDE HISTORY OF COURT CASE[ii]

Section 505(j) of the FD&C Act does not expressly provide for a change in approval status of an approved ANDA when the patent litigation results in a finding that one or more listed patents is infringed; however, when a court orders that the approval of an ANDA is not effective before a certain date pursuant to 35 U.S.C. 271(e)(4)(A), FDA may convert an approved ANDA to tentative approval status to reflect the court's order.[iii] Further, pursuant to 21 CFR 314.107(g), if a court enters an order requiring, in the case of an already approved ANDA, that the date of approval be delayed, FDA will convert the approval to a tentative approval, if appropriate.

Therefore, after consideration of the COURT'S ORDER DATE ORDER that the date of approval for ANDA #####, is not effective before DATE OF PATENT EXPIRATION, FDA is converting the APPROVAL DATE, final approval of ANDA HOLDER'S ANDA ##### for ESTABLISHED NAME DOSAGE FORM AND STRENGTHS(S), to a tentative approval.

Please be aware that any approved supplemental ANDAs filed to this ANDA since APPROVAL DATE are considered tentatively approved. Any unapproved supplemental ANDAs and any Annual Report changes filed to the ANDA are considered WITHDRAWN and should be resubmitted in full as either a "MINOR/MAJOR Amendment to the Original," or as a new supplemental ANDA once final approval has been obtained again. We note that this is an administrative conversion only and does not reflect any review of the ANDA subsequent to its original approval or approval of any supplements.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed
drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-
1(i) of the FD&C Act. [DELETE REMS SENTENCE IF ANDA HAS REMS OR IF OTC ANDA]

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS (if applicable)

Send to REMS Coordinator Team for language

RESUBMISSION

To request final approval, please submit an amendment titled "FINAL APPROVAL REQUESTED" with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 90 days for Agency review. Accordingly,

such a request for final approval should be submitted no later than 90 days prior to the date on which you seek approval. A request for final approval that contains substantive changes to the ANDA or changes in the status of the manufacturing and testing facilities' compliance with CGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available Agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of the court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data, as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a "FINAL APPROVAL REQUESTED."

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to DATE OF PATENT EXPIRATION, you should amend your ANDA accordingly.

Annual Facility Fees

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[iv] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dose forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations
listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

For further information on the status of this ANDA, or prior to submitting additional amendments, please contact NAME, Regulatory Project Manager, at (XXX) XXX-XXXX.

Sincerely,

{See appended electronic signature page}

NAME
Director/Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

[i] The Agency notes the X patent(s) were submitted to the Agency after the submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.
[ii] *List relevant court decision(s), as appropriate*
[iii] *Mylan Laboratories, Inc. v. Thompson, 389 F.3d 1272, 1281-82 (D.C. Cir. 2004)*.
[iv] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).