FDA’s Final MMA Regulations
Section-by-Section Redline Guide for Industry

This document tracks changes to the FDA’s regulations, primarily in 21 C.F.R. Part 314, governing various aspects of the Hatch-Waxman Amendments, as amended by the Medicare Prescription Drug Improvement and Modernization Act of 2003 (the “MMA”). These revised regulations were announced in a Final Rule published on October 6, 2016 (81 Fed. Reg. 69580) and became effective on December 5, 2016. The Final Rule modifies, among other things, the rules and procedures applicable to: the submission of patent information (including “Use Codes”) to the FDA by holders of New Drug Applications (NDAs); challenges to the appropriateness of such patent information as submitted to FDA; products for which an ANDA may be approved; permissible changes to a pending or approved ANDA or 505(b)(2) NDA; the submission of patent certifications in ANDAs and 505(b)(2) NDAs; the provision of Paragraph IV Notifications by ANDA and 505(b)(2) NDA applicants to NDA holders and patent owners; which listed drug products must be referenced in a 505(b)(2) NDA or an ANDA; and the 180-day generic drug exclusivity period. Many of the substantive changes to the regulations are not in fact new, but rather codify practices and policies that FDA has already been following in the 13 years since passage of the MMA. Numerous other changes are merely editorial or organizational in nature and do not reflect substantive policies or procedures.

This document is meant as a reference tool for clients to help them more easily identify and evaluate regulatory changes potentially applicable to approved or pending NDAs. Other changes that most directly impact generic drug applicants and ANDA holders are identified in the redline but are not, in most cases, addressed by associated commentary. Neither the redline nor the associated comments constitute legal advice or a legal opinion by DLA Piper LLP or any of its attorneys.

§ 314.3 Definitions.
(a) The definitions and interpretations contained in section 201 of the Federal Food, Drug, and Cosmetic Act apply to those terms when used in this part and part 320 of this chapter.
(b) The following definitions of terms apply to this part and part 320 of this chapter: 180-day exclusivity period is the 180-day period beginning on the date of the first commercial marketing of the drug (including the commercial marketing of the reference listed drug) by any first applicant. The 180-day period ends on the day before the date on which an ANDA submitted by an applicant other than a first applicant could be approved.

505(b)(2) application is an NDA submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for a drug for which at least some of the investigations described in section 505(b)(1)(A) of the Federal Food, Drug, and Cosmetic Act and relied upon by the applicant for approval of the NDA 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.

Abbreviated application means an NDA (including a 505(b)(2) application) or abbreviated application ANDA.

Application means a new drug application, or NDA is the application described under § 314.94, including all amendments and supplements to the application. "Abbreviated application" applies to both an abbreviated new drug application and an abbreviated antibiotic application.

Acknowledgment letter is a written, postmarket communication from FDA to an applicant stating that the Agency has determined that an ANDA is sufficiently complete to permit a substantive review. An acknowledgment letter indicates that the ANDA is regarded as received.

Active ingredient is any component that is intended to furnish pharmacological activity, or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.

Active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or cation) of the molecule, responsible for the physiologic or pharmacological action of the drug substance.

ANDA holder is the applicant that owns an approved ANDA.

Applicant means any person who submits an NDA (including a 505(b)(2) application) or abbreviated application ANDA or an amendment or supplement to an NDA or ANDA under this part to obtain FDA approval of a new drug or an antibiotic drug and any person who owns an approved NDA (including a 505(b)(2) application) or abbreviated application ANDA.

Application means new drug application, or NDA is the application described under § 314.95, including all amendments and supplements to the application.

505(b)(2) Application means an application. An NDA refers to "stand-alone” applications submitted under section 505(b)(1) of the act for a drug for which the investigations described in section Federal Food, Drug, and Cosmetic Act and to 505(b)(1)(A) of the act and 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.

Approval letter means a written communication to an applicant from FDA approving an application NDA or an abbreviated application ANDA.

Assess the effects of the change means to evaluate the effects of a manufacturing change on the identity, strength, quality, purity, and potency of a drug product as these factors may relate to the safety or effectiveness of the drug product.

Authorized generic drug means is a listed drug, as defined in this section, that has been approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and is marketed, sold, or distributed directly or indirectly to the retail class of trade with labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trademark that differs from that of the listed drug.

Bioavailability is the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of drug action. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of drug action.

Bioequivalence is the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. Where there is an intentional difference in rate (e.g., in certain extended-release dosage forms), certain pharmaceutical equivalents or alternatives may be considered bioequivalent if there is no...
significant difference in the extent to which the active ingredient or moiety from each product becomes available at the site of drug action. This applies only in the case where the active ingredient or moiety becomes available at the site of drug action in a manner that is not intentional and is reflected in the proposed labeling. Bioequivalence may be assessed by scientifically valid measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of drug action.

Bioequivalence requirements are imposed by FDA for in vitro and or in vivo testing of specified drug products that must be satisfied as a condition of marketing.

Class 1 resubmission means is the resubmission of an application, NDA or efficacy supplement, following receipt of a complete response letter, that contains one or more of the following: Final printed labeling, draft labeling, certain safety updates, stability updates to support provisional or final dating periods, commitments to perform postmarketing studies (including proposals for such studies), assay validation data, final release testing on the last lots used to support approval, minor reanalyses of previously submitted data, and other comparatively minor information.

Class 2 resubmission means is the resubmission of an application, NDA or efficacy supplement, following receipt of a complete response letter, that includes any item not specified in the definition of “Class 1 resubmission,” including any item that would require presentation to an advisory committee.

Commercial marketing is the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA, outside the control of the ANDA applicant, except that the term does not include transfer of the drug product for investigational use under part 312 of this chapter or transfer of the drug product to parties identified in the ANDA for reasons other than sale. Commercial marketing includes the introduction or delivery for introduction into interstate commerce of the reference listed drug by the ANDA applicant.

Component is any ingredient intended for use in the manufacture of a drug product, including those that may not appear in such drug product.

Date of approval is the date on the approval letter from FDA stating that the NDA or ANDA is approved, except that the date of approval for an NDA described in section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act is determined as described in section 505(x)(2) of the Federal Food, Drug, and Cosmetic Act. “Date of approved” refers only to a final approved and not to a tentative approval.

Dosage form is the physical manifestation containing the active and inactive ingredients that delivers a dose of the drug product. This includes such factors as:

(1) The physical appearance of the drug product;
(2) The physical form of the drug product prior to dispensing to the patient;
(3) The way the product is administered; and
(4) The design features that affect frequency of dosing.

Drug product means is a finished dosage form, for example, e.g., tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.

Drug substance means is an active ingredient, the active moiety, an intermediate use in the synthesis of the drug, a pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body, but does not include intermediates used in the synthesis of such ingredient.

Efficacy supplement means is a supplement to an approved application, NDA proposing to make one or more related changes from among the following changes to product labeling:

(1) Add or modify an indication or claim;
(2) Revise the dose or dose regimen;
(3) Provide for a new route of administration;
(4) Make a comparative efficacy claim naming another drug product;
(5) Significantly alter the intended patient population;
(6) Change the marketing status from prescription to over-the-counter use;
(7) Provide for, or provide evidence of effectiveness necessary for, the traditional approval of a product originally approved under subpart H of this part 314, or
(8) Incorporate other information based on at least one adequate and well-controlled clinical study.

FDA means is the Food and Drug Administration.

First applicant is an ANDA 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 for which the applicant lawfully maintains, a paragraph IV certification for the drug.

Inactive ingredient is any component other than an active ingredient.

Listed drug means a new drug product that has an effective approval been approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act for safety and effectiveness or under section 505(i) of the Federal Food, Drug, and Cosmetic Act, which has not been withdrawn or suspended under section 505(c)(1) through (c)(5) or section 505(i)(26) of the Federal Food, Drug, and Cosmetic 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 as an approved drug with an effective approval. A drug product is deemed to be a listed drug on the date of effective approval of the application or abbreviated application for the NDA or ANDA for that drug product.

NDA holder is the applicant that owns an approved NDA.

Newly acquired information means is data, analyses, or other information not previously submitted to the Agency, which may include (but at not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

Original application means is an application, NDA for which FDA has never issued a complete response letter or approval letter, or an application, ANDA that was submitted again after FDA had refused to file it or after it was withdrawn without being approved.

Paragraph IV acknowledgment letter is 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. A paragraph IV acknowledgment letter indicates that the 505(b)(2) application is regarded as filed or the ANDA is regarded as received.

Paragraph IV certification is a patent certification of invalidity, unenforceability, or non infringemen in § 314.94(a)(2)(i)(B), and § 314.94(a)(2)(i)(D). Patent owner is the owner of the patent for which information is submitted for an NDA.

Pharmaceutical equivalents are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form, or in the same salt or ester. Each drug product individually meets either the identical or its own respective standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, dissolution times, and/or dissolution rates.

Pharmaceutical alternatives are drug products in identical dosage forms, and route(s) of administration that contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified-release formulations, dissolution rates.

Content uniformity, disintegration times, and/or dissolution rates.

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§ 314.50 Content and format of an applicationNDA.

ApplicationsNDA and supplements to approved applicationsNDA are required to be submitted in the form and contain the information, as appropriate for the particular submission, required under this section. Three copies of the applicationNDA are required: An archival copy, a review copy, and a field copy. An applicationNDA for a new chemical entity will generally contain an application form, an index, a summary, five or six technical sections, case report tabulations of patient data, case report forms, drug samples, and labeling, including, if applicable, any Medication Guide required under part 208 of this chapter. Other applicationsNDA will generally contain only some of those items, and information will be limited to that needed to support the particular submission. These include an applicationNDA of the type described in section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, an amendment, and a supplement. The applicationNDA is required to contain reports of all investigations of the drug product sponsored by the applicant, and all other information about the drug pertinent to an evaluation of the applicationNDA that is received or otherwise obtained by the applicant from any source. FDA will maintain guidance documents on the format and content of applicationNDA to assist applicants in their preparation.

(a) *   *   *   *   *   *
(1) The name and address of the applicant; the date of the applicationNDA; the applicationNDA number if previously issued (for example, if the applicationNDA is a resubmission, or an amendment, or a supplement); the name of the drug product, including proprietary, code, and chemical names; the dosage form and strength, the route of administration; the identification numbers of all investigational new drug applications as defined in § 312.3(b) of this chapter) that are referenced in the applicationNDA; the identification numbers of all drug master files and other applications under this part that are referenced in the applicationNDA; and the drug product’s proposed indications for use.

(e) *   *   *   *   *   *
(1) Upon request from FDA, the applicant shall submit the samples described below to the places identified in the agency’s Agency’s request: FDA will generally ask applicants to submit samples directly to two or more Agency laboratories that will perform all necessary tests on the samples and validate the applicant’s analytical procedures.

*   *   *   *   *   *

(i) Patent certification—certification—(1) Contents. A 505(b)(2) application is required to contain the following:

(ii) Patents claiming drug substance, drug product, or method of use. (A) Except as provided in paragraphs (ii)(2) of this section, an appropriate patent certification or statement with respect to each patent issued by the United States Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, there are no patents described in (B) If the drug on which investigations that are relied upon by the applicant were conducted is itself a licensed generic drug of a patented drug first approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act, the applicant shall provide an appropriate patent certification or statement under this section with respect to each patent that claims the first-approved patented drug or that claims an approved use for such a drug.

(C) If, before the date of submission of an original 505(b)(2) application, there is a drug product approved in an NDA that is pharmaceutically equivalent to the drug product for which the original 505(b)(2) application is submitted, an appropriate patent certification or statement under this section with respect to each patent that claims the drug substance or drug product or that claims an approved use for such drug product.

(ii) Nonobvious patents. If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (i)(1)(i) of this section, a certification in the following form:

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DLA Piper LLP (US)
application is submitted for a drug or method of use that the applicant is seeking approval includes an indication or other condition of use that is covered by the method-of-use patent, a statement explaining that the method-of-use patent does not claim any of the drug or method of use that the applicant has made a licensing agreement for which the applicant is seeking approval includes an indication or other condition of use that, according to the patent information submitted under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act and § 314.53 or in the opinion of the applicant, is claimed by a method-of-use patent, the applicant shall submit an applicable certification under paragraph (i)(1)(i) of this section as to that patent or patent information.

(2) Method of manufacturing patent. An applicant is not required to make a certification with respect to any patent that claims only a method of manufacturing the drug product for which the applicant is seeking approval unless:

(A) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of patent issuance;

(B) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision;

(C) An amendment to the description of the approved method(s) of use claimed by the patent is submitted after the NDA holder's patent, and the amendment contains a copy of the decision.

(3) Licensing agreements. If a 505(b)(2) application is submitted for a drug or method of using a drug claimed by a patent and the applicant has a licensing agreement with the patent owner, the applicant shall submit a certification under paragraph (i)(1)(i) or (ii) of this section as to that patent and a statement that the applicant has been granted a patent license. If the patent owner consents to an immediate effective date upon approval of the 505(b)(2) application, the certification under paragraph (i)(1)(i) or (ii) shall contain a statement from the patent owner that it has a licensing agreement with the applicant and that it consents to an immediate effective date of approval of the 505(b)(2) application as of a specific date.

(4) Late submission. (a) Unintended filing of patent information. If a patent described in paragraph (i)(1)(i)(A) of this section is issued and the holder of the approved application NDA for the patented drug does not submit with the application the required information on the patent within 30 days of issuance of the patent, an applicant who submitted a 505(b)(2) application that, before the submission of the patent information, contained an appropriate patent certification or statement is not required to submit an amended patent certification or statement to address the patent or patent information that is late-listed with respect to the pending 505(b)(2) application. Except as provided in § 314.53(i)(1), an NDA holder’s amendment to the description of the approved method(s) of use claimed by the patent will be considered untimely filing of patent information, unless:

(A) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of patent issuance;

(B) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision.

(ii) After finding of infringement. An applicant who has submitted a paragraph IV certification under paragraph (i)(1)(i)(A)(4) of this section and is sued for patent infringement within 45 days of the receipt of notice sent under § 314.52 shall amend the certification to list the patent as no longer eligible for approval and file a lawsuit to change the certification if a court enters a final judgment or decree from which no appeal has been or can be taken, or signs and enters a settlement order or consent decree in the action entered that includes a finding that the patent to be infringed is invalid or not infringed by the method(s) of use claimed by the patent. Once the amendment or decree becomes final, the applicant shall amend the paragraph IV certification to reflect the patent is no longer infringed, unless:

(A) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision;

(B) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision.

(5) Disputed patent information. If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent information is withdrawn or changed, the applicant must submit an appropriate certification or statement for each patent listed.

(6) Amended certifications. A patent certification or statement submitted under paragraphs (i)(1)(i) through (i)(1)(iii) of this section may be amended at any time before the effective date of the approval of the 505(b)(2) application. An applicant shall submit an amended certification as an amendment to a pending application or by letter to an approved 505(b)(2) application. If an applicant with a pending 505(b)(2) application voluntarily makes a patent certification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely filed patent. Once an amendment or letter for the change is submitted to change the certification that has been submitted, the 505(b)(2) application will no longer be considered to contain the prior certification.

(i) After filing of enforcement. An applicant who has submitted a paragraph IV certification under paragraph (i)(1)(i)(A)(4) of this section and is sued for patent infringement within 45 days of the receipt of notice sent under § 314.52 shall amend the certification to list the patent as no longer eligible for approval and file a lawsuit to change the certification if a court enters a final judgment or decree from which no appeal has been or can be taken, or signs and enters a settlement order or consent decree in the action entered that includes a finding that the patent to be infringed is invalid or not infringed by the method(s) of use claimed by the patent. Once the amendment or decree becomes final, the applicant shall amend the paragraph IV certification to reflect the patent is no longer infringed, unless:

(A) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision;

(B) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the U.S. Patent and Trademark Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court that is specific to the patent and alters the construction of a method-of-use claim(s) of the patent, and the amendment contains a copy of the decision.

(ii) After removal of request to remove a patent or statement of information from the list. If the list reflects that an NDA holder has requested that a patent or patent information be removed from the list, and no ANDA applicant is eligible for 180-day exclusivity based on a paragraph IV certification to that patent, the patent or patent information will be removed and any applicant with a pending 505(b)(2) application (including a tentatively approved 505(b)(2) application with a delayed effective date) who has made a certification with respect to such patent shall amend its certification to reflect the certification is no longer applicable.
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The name and address of the patent owner or its attorney, agent, or authorized official may be obtained by sending a written or electronic communication to the Orange Book Staff, Office of Generic Drugs, 2500+7620 Standish Pl., Rockville, MD 20855, or to the Orange Book Staff at the email address listed on the Agency’s Web site at http://www.fda.gov. (3) This paragraph (a) does not apply to a method-of-use patent that claims no use, and a method-of-use patent that claims a use for which the applicant is seeking approval.

(4) An applicant may send notice by an alternative method only if FDA has agreed in advance that the method will produce an acceptable form of documentation.

(b) Sending the notice. (1) Except as provided under paragraph (d) of this section, the applicant must send the notice required by paragraph (a) of this section on or after the date of filing described in §314.101(a)(2) or (3), as applicable, but not later than 20 days after the date of the postmark on the IV acknowledgment letter. The 20-day clock described in this paragraph (b) begins on the day after the date of the postmark on the IV acknowledgment letter. When the 20th day falls on Saturday, Sunday, or a Federal holiday, the 20th day will be the next day that is not a Saturday, Sunday, or Federal holiday.

(2) Any notice required by paragraph (a) of this section is invalid if it is sent before the date of filing described in §314.101(a)(2) or, if FDA notifies the applicant that FDA has refused to file the 505(b)(2) application, before the date described in §314.101(a)(3) on which the 505(b)(2) application is filed. The applicant will not have complied with this paragraph (b) until it sends valid notice.

(b) Sending the notice. The applicant shall send the notice required by paragraph (a) of this section when it receives from FDA an acknowledgment letter stating that its application has been filed. At the same time, the
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applicant shall amend its application to include (3) The applicant must submit to FDA an amendment to its 505(b)(2) application that includes a statement certifying that the notice has been provided to each person identified under paragraph (a) of this section and that the notice met the content requirement under paragraph (c) of this section. A copy of the notice itself need not be submitted to the Agency. (c) Content of a notice. In the notice, the applicant shall cite section 505(b)(3)(D) of the Federal Food, Drug, and Cosmetic Act and shall the notice must include, but is not be limited to, the following information: (1) A statement that a 505(b)(2) application that contains any required bioavailability or bioequivalence studies has been submitted by the applicant has been filed by FDA. (2) The application NDA number. (3) The established name, if any, as defined in section 502(e)(3) of the Federal Food, Drug, and Cosmetic Act, of the proposed drug product. (4) The active ingredient, strength, and dosage form of the proposed drug product. (5) The patent number and expiration date, as submitted to the agency or as known to the applicant, of each patent on the list alleged to be invalid, unenforceable, or not infringed. (6) A detailed statement of the factual and legal basis of the applicant’s opinion that the patent is not valid, unenforceable, or will not be infringed. The applicant shall include in the detailed statement: (i) For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed. (ii) For each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation. (7) If the applicant alleges that the patent will not be infringed and the applicant seeks to preserve the option to later file a civil action for declaratory judgment in accordance with section 505(c)(3)(D) of the Federal Food, Drug, and Cosmetic Act, then the notice must be accompanied by an offer of confidential access to the 505(b)(2) application for the sole and limited purpose of evaluating possible infringement of the patent that is the subject of the paragraph IV certification. (8) If the applicant does not reside or have a place of business in the United States, the name and address of an agent in the United States authorized to accept service of process for the applicant. (d) Amendment to an or supplement to a 505(b)(2) application. If an application is amended to include the certification described in § 314.101(a)(2) or (3), as applicable, an applicant submits an amendment or supplement to its 505(b)(2) application that includes a paragraph IV certification, the applicant shall send the notice required by paragraph (a) of this section at the same time that the amendment or supplement to the 505(b)(2) application is submitted to FDA, regardless of whether the applicant has already been given notice with respect to another such certification contained in the 505(b)(2) application or in an amendment or supplement to the 505(b)(2) application. (e) Documentation of timely sending and receipt of notice. The applicant shall amend its 505(b)(2) application to document the date of receipt of the notice required under paragraph (a) of this section by each person provided the notice. The amendment must be submitted to FDA within 30 days after the last date on which notice was received by a person described in paragraph (d)(1) of this section. The amendment also must include a copy of the return receipt or other similar evidence documentation that its notice was sent on a date that complies with the timeframe required by paragraph (b) or (d) of this section, as applicable. FDA will accept as adequate documentation of the date the notification was received or notice was sent, a copy of the registered mail receipt, certified mail receipt, or receipt from a designated delivery service, as defined in paragraph (e) of this section. FDA will accept as adequate documentation of the date of receipt a return receipt, a signature proof of delivery, or a letter acknowledgment receipt by the person provided the notice. An applicant may rely on another form of documentation only if FDA has agreed to such documentation in advance. A copy of the notice itself need not be submitted to the Agency. (f) Approval. Forty-five day period after receipt of notice. If the requirements of this section are met, the Agency will presume the notice to be complete and sufficiently detailed to count the day following the date of receipt of the notice by the patent owner or its representative and by the approved application holder NDA holder or its attorney, agent, or other authorized official as the first day of the 45- day period provided for in section 505(c)(3)(C) of the Federal Food, Drug, and Cosmetic Act. FDA may, if the applicant amends its 505(b)(2) application with a written statement that a later date should be used, count from such later date. (g) Designated delivery services. (1) For purposes of this section, the term “designated delivery service” is any delivery service provided by a trade or business that the Agency determines: (i) Is available to the general public throughout the United States; (ii) Records electronically to its database, kept in the regular course of its business, marks on the cover in which any item referred to in this section is to be delivered, the date on which such item was given to such trade or business for delivery; and (iii) Provides overnight or 2-day delivery service throughout the United States. (2) FDA may periodically issue guidance regarding designated delivery services.

§ 314.53 Submission of patent information.
(a) Who must submit patent information. This section applies to any applicant who submits to FDA a new drug application NDA or an amendment to it under section 505(b) of the Federal Food, Drug, and Cosmetic Act and § 314.50 or a supplement to an approved application NDA under § 314.70, except as provided in paragraph (d)(2) of this section. (b) Patents for which information must be submitted and patents for which information must not be submitted—(1) General requirements. An applicant described in paragraph (a) of this section shall submit to its NDA the required information, on the required FDA declaration form set forth in paragraph (c) of this section for each patent that claims the drug or a method of using the drug that is the subject of the new drug application NDA or amendment or supplement to it and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. For purposes of this part, such patents consist of drug substance (active ingredient) patents, drug product (formulation
and composition) patents, and method-of-use patents. For patents that claim the drug substance, the applicant shall submit information only on those patents that claim the drug substance that is the subject of the pending or approved application NDA. For patents that claim only a polymorph that is the same as the active ingredient described in the approved or pending application NDA, the applicant shall certify in the required FDA declaration form that the applicant has test data, as set forth in paragraph (b)(2) of this section, demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the approved application NDA. For patents that claim a drug product, the applicant shall submit information only on those patents that claim the drug product, as is defined in § 314.3, that is described in the pending or approved application NDA. For patents that claim a method of use, the applicant shall separately identify each pending or approved method of use and related patent claim or claims. For approved applications, the NDA holder’s description of the patented method of use required by paragraph (c)(2)(ii)(P) of this section must describe only the approved method(s) of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. If the method(s) of use claimed by the patent does not cover an indication or other condition of use in its entirety, the applicant must describe only the specific approved method of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. For approved NDAs, the NDA holder submitting information on the method-of-use patent shall identify with specificity the section(s) and subsection(s) of the approved labeling that corresponds to the method(s) of use claimed by the patent submitted. Process patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates are not covered by this section, and information on these patents must not be submitted to FDA.

(2) Test data for submission of patent information for patents that claim only a polymorph. The test data, referenced in paragraph (b)(1) of this section, must include the following:

(i) A full description of the polymorphic form of the drug substance, including its physical and chemical characteristics and stability; the method of synthesis (or isolation) and purification of the drug substance; the process controls used during manufacture and packaging; and such specifications and analytical methods as are necessary to assure the identity, strength, quality, and purity of the polymorphic form of the drug substance;

(ii) The executed batch record for a drug product containing the polymorphic form of the drug substance and documentation that the batch was manufactured under current good manufacturing practice requirements;

(iii) Demonstration of bioequivalence between the executed batch of the drug product that contains the polymorphic form of the drug substance and the drug product as described in the NDA;

(iv) A list of all components used in the manufacture of the drug product containing the polymorphic form and a statement of the composition of the drug product; a statement of the specifications and analytical methods for each component; a description of the manufacturing and packaging procedures and in-process controls for the drug product; such specifications and analytical methods as are necessary to assure the identity, strength, quality, purity, and bioavailability of the drug product, including release and stability data complying with the approved product specifications to demonstrate pharmaceutical equivalence and comparable product stability; and

(v) Comparative in vitro dissolution testing on 12 dosage units each of the executed test batch and the new drug application NDA product.

(c) Reporting requirements—

(1) General requirements. An applicant described in paragraph (a) of this section shall submit the required patent information described in paragraph (c)(2) of this section for each patent that meets the requirements described in paragraph (b) of this section. We will not accept the patent information unless it is complete and submitted on the appropriate form, Form FDA Forms 3542 or 3542a, and contains the information required in paragraph (c)(2) of this section. These forms may be obtained on the Internet at http://www.fda.gov by searching for “forms”.

(2) Drug substance (active ingredient), drug product (formulation and composition), and method-of-use patents—

(i) Original declaration. For each patent that claims a drug substance (active ingredient), drug product (formulation and composition), or method of use, the applicant shall submit Form FDA Forms 3542a. The following information and verification is required, subject to the exceptions listed in paragraph (c)(2)(i)(S) of this section:

(A) New drug application NDA number;

(B) Name of new drug application sponsor;

(B) The NDA applicant’s name, full address, phone number, if available, fax number and email address;

(C) Trade name (or proposed trade name) of new drug;

(D) Active ingredient(s) of new drug;

(E) Strength(s) of new drug;

(F) Dosage form(s) and route(s) of administration of new drug, and whether the applicant proposes to market the new drug for prescription use or over-the-counter use;

(G) United States; U.S. patent number, issue date, and expiration date of patent submitted;

(H) The patent owner’s name, full address, phone number and, if available, fax number and email address of an agent or representative who resides or maintains a place of business within the United States; and

(I) The name, full address, phone number and, if available, fax number and email address of the applicant described in paragraph (a) of this section:

(j) Information on whether the patent has been submitted previously for the new drug application NDA or supplement:

(K) Information on whether the expiration date is a new expiration date; and

(L) Information on whether the patent is a product-by-process patent in which the product claimed is novel;

Internet address, Form FDA Form FDA 3542 or 3542a, and completes the Form FDA Form FDA 3542 or 3542a, and contains the information required in paragraph (c)(2) of this section. These forms may be obtained on the Internet at http://www.fda.gov by searching for “forms”.

(2) Drug substance (active ingredient), drug product (formulation and composition), and method-of-use patents—

(i) Original declaration. For each patent that claims a drug substance (active ingredient), drug product (formulation and composition), or method of use, the applicant shall submit Form FDA Forms 3542a. The following information and verification is required, subject to the exceptions listed in paragraph (c)(2)(i)(S) of this section:

(A) New drug application NDA number;

(B) Name of new drug application sponsor;

(B) The NDA applicant’s name, full address, phone number, if available, fax number and email address;

(C) Trade name (or proposed trade name) of new drug;

(D) Active ingredient(s) of new drug;

(E) Strength(s) of new drug;

(F) Dosage form(s) and route(s) of administration of new drug, and whether the applicant proposes to market the new drug for prescription use or over-the-counter use;

(G) United States; U.S. patent number, issue date, and expiration date of patent submitted;

(H) The patent owner’s name, full address, phone number and, if available, fax number and email address of an agent or representative who resides or maintains a place of business within the United States; and

(I) The name, full address, phone number and, if available, fax number and email address of the applicant described in paragraph (a) of this section:

(j) Information on whether the patent has been submitted previously for the new drug application NDA or supplement:

(K) Information on whether the expiration date is a new expiration date; and

(L) Information on whether the patent is a product-by-process patent in which the product claimed is novel;
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(M) Information on the drug substance (active ingredient) patent, including the following:

(1) Whether the patent claims the drug substance that is the active ingredient in the drug product described in the new drug application NDA or supplement;

(2) Whether the patent claims only a polymorph that is the same active ingredient that is described in the pending application NDA or supplement;

(3) Whether the applicant has test data, described in paragraph (b)(2) of this section, demonstrating that a drug product containing only the polymorph will perform the same as the drug product described in the new drug application NDA or supplement, and a description of the polymorphic form(s) claimed by the patent for which such test data exist;

(4) Whether the patent claims only a metabolite of the active ingredient; and

(5) Whether the patent claims only an intermediate;

(N) Information on the drug product (composition/formulation) patent, including the following:

(1) Whether the patent claims the drug product for which approval is being sought, as defined in § 314.3; and

(2) Whether the patent claims only an intermediate;

(O) Information on each method-of-use patent, including the following:

(1) Whether the patent claims one or more methods of using the drug product for which use approval is being sought and a description of each pending method of use or related indication and related patent claim of the patent being submitted; and

(2) Identification of the specific section(s) and subsection(s) of the proposed labeling for the drug product that corresponds to the method of use claimed by the patent submitted; and

(3) An applicant that submits information for a patent that claims one or more methods of using the drug product must also submit information described in either paragraph (c)(2)(i)(M) or (N) of this section, regarding whether that patent also claims either the drug substance (active ingredient) or the drug product (composition/formulation);

(P) Whether there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition), or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product;

(Q) A signed verification stating:

The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

(R) Information on whether the applicant, patent owner or attorney, agent, representative, or other authorized official signed the form; the name of the person; and the full address, phone number and, if available, the fax number and email address.

(S) Exceptions to required submission of patent information:

(1) If an applicant submits the information described in paragraph (c)(2)(i)(M) of this section for a patent that claims the drug substance (active ingredient) and meets the requirements for listing on that basis, then the applicant is not required to provide the information described in paragraph (c)(2)(i)(N) of this section on whether that patent also claims the drug product (composition/formulation);

(2) If an applicant submits the information described in paragraph (c)(2)(i)(N) of this section for a patent that claims the drug product (composition/formulation) and meets the requirements for listing on that basis, then the applicant is not required to provide the information described in paragraph (c)(2)(i)(M) of this section on whether that patent also claims the drug substance (active ingredient).

(T) If the applicant submits a supplement for a change other than one of the changes listed under paragraph (d)(2)(ii) of this section, then the patent information submission requirements of paragraph (d)(2)(ii) of this section apply.

(ii) Submission of patent information upon and after approval. Within 30 days after the date of approval of its application NDA or supplement, the applicant must submit Form FDA 3542 for each patent that claims the drug substance (active ingredient), drug product (formulation and composition), or approved method of use. FDA will rely only on the information submitted on this form and will not list or publish patent information if it is not provided on this form or if the patent declaration is incomplete or does not contain the required information or indicates the patent is not eligible for listing. Patent information must also be submitted for patents issued after the date of approval of the new drug application NDA as required in paragraph (c)(2)(ii) of this section. As described in paragraph (d)(3) of this section, to be timely filed, patent information for patents issued after the date of approval of the NDA must be submitted to FDA within 30 days of the date of issuance of the patent. If the applicant submits the required patent information within the 30 days, but we notify an applicant that a declaration form is incomplete or shows that the patent is not eligible for listing, the applicant must submit an acceptable declaration form within 15 days of FDA notification to be considered timely filed. The following information and verification statements required are subject to the exceptions listed in paragraph (c)(2)(ii)(T) of this section:

(A) New drug application NDA number;

(B) Name of new drug application sponsor;

(C) Trade name of new drug;

(D) Active ingredient(s) of new drug;

(E) Strength(s) of new drug;

(F) Dosage form(s) and route(s) of administration of new drug and whether the new drug is approved for prescription use or over-the-counter use;

(G) Approval date of new drug application NDA or supplement;

(H) United States U.S. patent number, issue date, and expiration date of patent submitted;

(I) The patent owner’s name, full address, phone number and, if available, fax number and email address;

(J) The name, full address, phone number and, if available, fax number and email address of an agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under sections 505(b)(3) and 505(j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and §§ 314.52 and 314.95 (if patent owner or new drug application NDA applicant or holder does not reside or have a place of business within the United States);

(K) Information on whether the patent has been submitted previously for the new drug application NDA or supplement;

(L) Information on whether the expiration date is a new expiration date if the patent has been submitted previously for listing.
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identify all change(s) from the previously submitted patent information and specify whether the change is related to the patent or related to an FDA action or procedure;

(M) Information on whether the patent is a product-by-process patent in which the product claimed is novel;

(N) Information on the drug substance (active ingredient) patent, including the following:

(1) Whether the patent claims drug substance that is the same active ingredient in the drug product described in the approved application NDA;

(2) Whether the patent claims only a polymorph that is the same as the active ingredient that is described in the approved application NDA;

(3) Whether the applicant has test data, described at paragraph (b)(2) of this section, demonstrating that a drug product containing only the polymorph will perform the same as the drug product described in the approved application NDA and a description of the polymorphic form(s) claimed by the patent for which such test data exist;

(4) Whether the patent claims only a metabolite of the active ingredient; and

(5) Whether the patent claims only an intermediate;

(O) Information on the drug product (composition/formulation) patent, including the following:

(1) Whether the patent claims the approved drug product as defined in § 314.3; and

(2) Whether the patent claims only an intermediate;

(P) Information on each method-of-use patent, including the following:

(1) Whether the patent claims one or more approved methods of using the approved drug product and a description of each approved method of use or indication and related patent claim of the patent being submitted;

(2) Identification of the specific section(s) and subsection(s) of the approved labeling for the drug product that corresponds to describes the method of use claimed by the patent submitted; and

(3) The description of the patented method of use as required for publications which must contain adequate information to assist 505(b)(2) and ANDA applicants in determining whether a listed method-of-use patent claims a use for which the 505(b)(2) or ANDA applicant is not seeking approval (for example, if the method(s) of use claimed by the patent does not cover an indication or other approved condition of use in its entirety, then the applicant must describe only the specific approved method of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product); and

(4) An applicant that submits information for a patent that claims one or more methods of using the drug product must also submit information on whether that patent also claims the drug substance (active ingredient) or the drug product (composition/formulation).

(Q) Whether there are no relevant patents that claim the approved drug substance (active ingredient), the approved drug product (formulation or composition), or approved method(s) of use and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product;

(R) A signed verification that states:

The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement approved under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information or response to a request under 21 CFR 314.53(f)(1) is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the information described in paragraph (c) of this section is true, correct, and complete. I further certify that the information is not a false statement or response to a request under 21 CFR 314.53(f)(1) or a false declaration required by this section shall must submit patent information required by this section on each drug (substance (active ingredient), drug product (formulation and use or sale of the drug product); and

(S) Information on whether the applicant, patent owner or attorney, agent, representative, or other authorized official signed the form; the name of the person; and the full address, phone number and, if available, the fax number and email address, and

Exception to required submission of patent information:

(1) If the applicant submits the information described in paragraph (c)(2)(ii)(N) of this section for a patent that claims the drug substance (active ingredient) and meets the requirements for listing on that basis, then the applicant is not required to provide the information described in paragraph (c)(2)(ii)(O) of this section on whether that patent also claims the drug product (composition/formulation).

(2) If an applicant submits the information described in paragraph (c)(2)(ii)(O) of this section for a patent that claims the drug product (composition/formulation) and meets the requirements for listing on that basis, then the applicant is not required to provide the information described in paragraph (c)(2)(ii)(N) of this section on whether that patent also claims the drug substance (active ingredient).

(T) Exceptions to required submission of patent information:

(1) If an applicant submits the original application NDA, an applicant shall must submit with its original application NDA submitted under this part— including an application, described in section 505(b)(2) of the act, the information described in paragraph (c) of this section on each drug (substance (active ingredient), drug product (formulation and composition), and method of method of use patent issued before the application NDA is filed with FDA and for which patent information is required to be submitted under this section. If a patent is issued after the application NDA is filed with FDA but before the application NDA is approved, the applicant shall must within 30 days of the date of issuance of the patent, submit the required patent information in an amendment to the application NDA under § 314.60. and

(2) Supplements. (i) An applicant shall must submit patent information required under paragraph (c) of this section for a patent that claims the drug substance, drug product, or method of use for which approval is sought in any of the following supplements:

(A) To change the formulation;

(B) To add a new indication or other condition of use, including a change in price change the dosage form or route of administration;

(E) To add or change the strength: or

James N. Czaban, Chairman
FDA and Medical Products Regulatory Practice Group
james.czaban@dlapiper.com; T 202.799.4045
DLA Piper LLP (US)
(DC) To make any other patented change regarding the drug, drug product, or any method of use to over-the-counter use.

(ii) If the applicant submits a supplement for a change other than one of the changes listed under paragraph (d)(2)(i) of this section and/or, for example, to change the formulation, to add a new indication or other condition of use, or to make any other patented change regarding the drug substance, drug product, or any method of use, the following patent information submission requirements apply:

(A) If existing patents for which information required by paragraph (c) of this section has already been submitted to FDA for the product approved in the original NDA claim the changed product, the applicant shall submit a certified copy of the applicable patent(s), and a description of the change(s) to FDA no later than the date on which the applicant submits the supplement.

(B) If one or more existing patents for which information has already been submitted to FDA no longer claim the changed drug, drug product, or any method of use, the applicant shall submit a request under paragraph (f)(2)(iv) of this section to remove that patent information from the list at the time of approval of the supplement.

(C) If one or more existing drug substance (active ingredient), drug product (formulation and composition), or method-of-use patents claim the changed product for which approval is sought in the supplement and such patent information has not been submitted to FDA, the applicant shall submit the patent information required under paragraph (c) of this section.

(iii) If the applicant submits a supplement for one of the changes listed under paragraph (d)(2)(i) of this section and no existing patents, including previously submitted patents, claim the changed product, it shall so certify.

(a) The applicant shall comply with the requirements for amendment of formulation or composition and method of use patent information under paragraphs (c)(2)(ii) and (d)(3) of this section.

(b) Patient information deadlines--Newly issued patents. If a patent is issued for a drug substance, drug product, or method of use after an application NDA is approved, the applicant shall submit to FDA, as described in paragraph (d)(4) of this section, the required patent information within 30 days of the date of issuance of the patent. If the required patent information is not submitted within 30 days of the issuance of the patent, FDA will list the patent, but patent certifications or statements will be governed by the provisions regarding unexpired filed patent information at § 314.50(k)(1)(i)(A), (B), and (l), and § 314.94(a)(12)(vii) and (viii).

(4) Copies Submission of Forms FDA 3542a and 3542--(i) Patent information submitted with the filing of an NDA, amendment, or supplement. The applicant shall submit two copies of each submission of patent information, an archival copy, and a copy for the chemistry, manufacturing, and controls required by paragraphs (c)(1) and (c)(2)(ii) of this section of the review copy and § 314.50(h) or § 314.70(h) on Form FDA 3542a to the Central Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, 5901 Beltsville Rd., Beltsville, MD 20705-1266. The applicant shall submit the patent information by letter separate from but at the same time as, submission of the supplement, or to FDA in an electronic format submission that complies with § 314.50(k)(5). Form FDA 3542a should not be submitted to the Orange Book Office in the Office of Generic Drugs.

(ii) Patent information submitted upon and after approval of an NDA or supplement. The applicant shall submit patent information required by paragraphs (c)(1) and (c)(2)(ii) of this section on Form FDA 3542 to the Central Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266, or to FDA in an electronic format submission that complies with § 314.50(k)(5). Form FDA 3542 should not be submitted to the Orange Book Office in the Office of Generic Drugs.

(iii) Submission date. Patent information shall be considered to be submitted to FDA for purposes of paragraph (d)(3) of this section as of the earlier of the date the information is received on Form FDA 3542 is date-stamped by the Central Document Room, or officially received by FDA in an electronic format submission that complies with § 314.50(k)(5).

(iv) Identification. Each submission of patent information, except information submitted with an original application, and its mailing cover sheet, must bear prominent identification as to its contents, i.e., Patent Information, or, if submitted after approval of an application NDA, “Time Sensitive Patent Information.”

(v) Public disclosure of patient information. FDA will publish in the list the patent number and expiration date of each patent that is required to be, and is, submitted to FDA by an applicant, and for each use method-of-use patent, the approved indication or other conditions of use as covered by a patent, description of the method of use claimed by the patent as required by § 314.53(c)(2)(ii) (Pr3). FDA will publish such patent information upon approval of the application NDA, or, if the patent information is submitted by the applicant after approval of an application NDA as provided under paragraph (d)(2) of this section, as soon as possible after the submission to the Agency of the patent information. Patent information submitted by the last working day of the month will be published in that month’s supplement to the list. Patent information received by the Agency between monthly publications of supplements without the required delay may be placed in public display in FDA’s Division of Freedom of Information. A request for copies of the file shall be submitted patent information must be sent in writing to the Freedom of Information Staff at the address listed on the Agency’s Agency’s Web site at http://www.fda.gov. The submitted patent information, and requests to remove a patent or patent information from the list, may be subject to public disclosure.

(j) Correction of patent information. The applicant or person other than the NDA holder may request corrections of the accuracy or relevance of patent information submitted to the Agency under this section and published by FDA in the list, or believes that an applicant NDA holder has failed to submit required patent information, that person must first notify the Agency in writing stating the written or electronic communication titled “§ 314.53(h) Patent Listing Dispute.” The patent listing dispute communication must include a statement of dispute that describes the specific grounds for disagreement. Each notification regarding the accuracy or relevance of patent information for FDA to send to the applicable NDA holder. For a dispute regarding the accuracy or relevance of patent information, regarding an approved method of using the drug, drug product, this statement of dispute must be only a narrative description (no more than 250 words) of the person’s interpretation of the scope of the patent. This statement of dispute must only contain information for which the person consents to disclosure because FDA will send the text of the statement to the applicable NDA holder without review or reduction. The patent listing dispute communication should be directed to the Office of Generic Drugs, OGD Document Room, Attention: Orange Book Staff, 7500 07620 Standish Pl., Rockville, MD 20855, or to the Orange Book Staff at the email address.

[1] Communication with the NDA holder.-(A) Drug substance or drug product claim. For requests submitted under this paragraph (f)(1) that are directed to the accuracy or relevance of submitted patent information regarding a drug substance or drug product claim, the Agency will then request the statement of dispute to the applicable new drug application NDA holder. The NDA holder must confirm the correctness of the patent information, omission(s), and include the signed verification required by paragraph (c)(2)(i)(R) of this section or withdraw or amend the patent information within 30 days of receipt of the statement of dispute. Unless the application NDA holder withdraws or amends its patent information in response to FDA’s request for the patent listing dispute, the Agency will not change the patent information in the list. If the new drug application holder does not change the patent information submitted to FDA, a 505(b)(2) application or an abbreviated new drug application under section 505(t) of the act submitted for a drug that is claimed by a patent for which information has been submitted must, despite any disagreement as to the correctness of the patent information, contain an appropriate certification or statement for each listed patent Orange Book.

(B) Method of use claim. For requests submitted under this paragraph (f)(1) that are directed to the accuracy or relevance of submitted patent information regarding an approved method of using the drug product, FDA will send the statement of dispute to the NDA holder. The NDA holder must confirm the correctness of its description of the approved method of use claimed by the patent that has been included as the “Use Code” in the Orange Book, or withdraw or amend the patent information in accordance with paragraph (f)(2) of this section, provide a narrative description (no more than 250 words) of the NDA holder’s interpretation of the scope of the patent that explains why the existing or amended “Use Code” describes only the specific approved method of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent cannot use the manufacture, use, or sale of the drug product, and include the signed verification required by paragraph (c)(2)(ii)(R) of this section within 30 days of the date on which the Agency sends the statement of dispute. The narrative description must only contain information for which the NDA holder consents to disclosure because FDA will send the text of the statement to the person who submitted the patent listing dispute without review or redaction.

(7) If the NDA holder confirms the correctness of the patent information, provides the narrative description required by paragraph (f)(1)(i)(B) of this section, and includes the signed verification required by paragraph (c)(2)(ii)(R) of this section within 30 days of the date on which the Agency sends the statement of dispute, the Agency will not change the patent information in the Orange Book.

(2) If the NDA holder responds to the patent listing dispute with amended patent information in accordance with paragraph (f)(2), the Agency will update the Orange Book to reflect the amended patent information.

(i) Patent certification or statement during and after patent listing dispute. A 505(b)(2) application or ANDA must contain an appropriate certification or statement for each listed patent, including the disputed patent, during and after the patent listing dispute.

(iii) Information on patent listing dispute. FDA will promptly post information on its Web site regarding whether a patent listing dispute has been submitted for a description of a patented method of use for a drug product and whether the NDA holder has timely responded to the patent listing dispute.

(2) Requests by the NDA holder.—(i) Patents or patent claims that no longer meet the statutory requirements for listing. If the NDA holder determines that a patent or patent claim no longer meets the requirements for listing in section 505(b)(1) or (c)(2) of the Federal Food, Drug, and Cosmetic Act (including if there has been a judicial finding of invalidity for a listed patent, from which no appeal has been or can be taken), the NDA holder is required to promptly notify FDA to amend the patent information or withdraw the patent information and request that the patent or patent information be removed from the list. If the NDA holder is required by court order to amend patent information or withdraw a patent from the list, it must submit an amendment to its NDA that includes a copy of the order, within 14 days of the date the order was entered, to the Center, Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266. The amendment to the NDA must bear the identification described in paragraph (d)(6) of this section. FDA will remove a patent or patent information from the list if there is not an applicant eligible for 180-day exclusivity based on a paragraph IV certification to that patent or after the 180-day exclusivity period of a first applicant based on that patent has expired or has been extinguished.

(ii) Patent term restoration. If the term of a listed patent is extended pursuant to 35 U.S.C. 156(e), the NDA holder must submit on Form FDA 3542 a correction to the expiration date of the patent. This correction must be submitted within 30 days of receipt of a certificate of extension as described in 35 U.S.C. 156(e)(1) or documentation of an extension of the term of the patent under 35 U.S.C. 156(e)(2).

(iii) Submission of corrections or changes to patent information. Corrections or changes to previously submitted patent information, other than withdrawal of a patent and requests to remove a patent from the list, must be submitted on Form FDA 3542 or 3542a, as appropriate, in an amendment or supplemental to the NDA. The amendment or supplement to the NDA must bear the identification described in paragraph (d)(6) of this section. We will not accept the corrections or changes unless they are submitted on the appropriate forms.

(iv) Submission of patent withdrawals and requests to remove a patent from the list. Withdrawal of a patent and requests to remove a patent from the list must be submitted to the same addresses described in paragraph (d)(4)(ii) of this section, except that the withdrawal request to remove a patent from the list is not required to be submitted on Form FDA 3542 and may be submitted by letter. Withdrawal of a patent and requests to remove a patent from the list must contain the following information:

(A) The NDA number to which the request applies.

(B) Each product(s) approved in the NDA to which the request applies, and

(C) The patent number.

§ 314.54 Procedure for submission of ana 505(b)(2) application requiring investigations for approval of a new indication for, or other change from, a listed drug.

(a) The Federal Food, Drug, and Cosmetic Act does not permit approval of an abbreviated new drug application ANDA for a new indication, nor does it permit approval of other changes in a listed drug if investigations, other than bioavailability or bioequivalence studies, are essential to the approval of the change. Any person seeking approval of a drug product that represents a modification of a listed...
drug (e.g., a new indication or new dosage form) and for which investigations, other than bioavailability or bioequivalence studies, are essential to the approval of the changes may, except as provided in paragraph (b) of this section, submit a 505(b)(2) application. This 505(b)(2) application need contain only that information needed to support the modification(s) of the listed drug.

(1) Identification of the listed drug for which FDA has made a finding of safety and effectiveness and on which finding the applicant relies in seeking approval of its proposed drug product by established name, if any, proprietary name, dosage form, strength, route of administration, name of listed drug (i.e., drug's application holder, and listed drug (ii.e., drug's approved application NDA number). The listed drug(s) identified as relied upon must include a drug product approved in an NDA that:

(A) Is pharmaceutically equivalent to the drug product for which the original 505(b)(2) application was submitted; and
(B) Was approved before the original 505(b)(2) application was submitted.

(v) Any patent information required under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act with respect to any patent which claims the drug for which approval is sought or a method of using such drug and to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

(vi) Any patent certification or statement required under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act with respect to any relevant patent that claim the listed drug or that claim any other drug(s) on which investigations relied on by the applicant for approval of the application were conducted, or that claim a use for the listed drug or other drug(s). A 505(b)(2) applicant seeking approval of a drug that is pharmaceutically equivalent to a listed drug approved in an NDA implicitly relies upon one such pharmaceutically equivalent listed drug.

(2) The applicant shall submit a review copy that contains the technical sections described in § 314.50(d)(1), except that the section described in § 314.50(d)(1)(i)(c) shall contain the proposed or actual master production record, including a description of the equipment, to be used for the manufacture of a commercial lot of the drug product, and paragraphs § 314.50(d)(3), and the technical sections described in paragraphs § 314.50(d)(2), (d)(4), (d)(5), (d) through (6), and (f) when needed to support the modification. Each of the technical sections in the review copy is required to be separately bound with a copy of the information required under § 314.50(a), (b), and (c) and a copy of the proposed labeling.

(4) The applicant shall submit a field copy of the 505(b)(2) application that contains the technical section described in § 314.50(d)(1), a copy of the information required under § 314.50(a) and (c), and certification that the field copy is a true copy of the technical section described in § 314.50(d)(1) contained in the archival and review copies of the 505(b)(2) application.

(b) A 505(b)(2) application may not be submitted under this section for a drug product whose only difference from the reference listed drug is that:

(1) The extent to which its active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug; or
(2) The rate at which its active ingredient(s) is absorbed or otherwise made available to the site of action is unintentionally less than that of the reference listed drug.

§ 314.60 Amendments to an unapproved application NDA, supplement, or resubmission.

(a) Submission of NDA. FDA generally assumes that when an original application NDA, supplement to an approved application NDA, or resubmission of an application NDA or supplement is submitted to the Agency for review, the applicant believes that the Agency can approve the application NDA, supplement, or resubmission as submitted. However, the applicant may submit an amendment to an application NDA, supplement, or resubmission that has been filed under § 314.101 but is not yet approved.

(b)(1) Submission of a major amendment.

(4)(i) An unapproved application may not be amended if all of the following conditions apply.

(c) Limitation on certain amendments.

(1) * * *
(2) * * *
(iii) The applicant has not obtained a right of reference or use to the investigation described in paragraph (c)(1)(iii) of this section; and

(d) Field copy. The applicant shall submit a field copy of each amendment to a section of the NDA described in § 314.50(d)(1). The applicant shall include in its submission of each such amendment to FDA a statement certifying that a field copy of the amendment has been sent to the applicant’s home FDA district office.

(e) Different drug. An applicant may not amend a 505(b)(2) application to seek approval of a drug that is a different drug from the drug in the original submission of the 505(b)(2) application. For purposes of this paragraph (e), a drug is a different drug if it has been modified to have a different active ingredient, different route of administration, different dosage form, or difference in excipients that requires either a separate clinical study to establish safety or effectiveness or, for topical products, that requires a separate in vivo demonstration of bioequivalence. However, notwithstanding the limitation described in paragraph (e), an applicant may amend the 505(b)(2) application to seek approval of a different strength.

(f) Patent certification requirements. (1) An amendment to a 505(b)(2) application is required to contain an appropriate patent certification or statement described in § 314.50(c) or a recertification for a previously submitted paragraph IV certification if approval is sought for any of the following types of amendments:

(1) To add a new indication or other condition of use;
(2) To add a new strength;
(3) To make other than minor changes in product formulation; or
(4) To change the physical form or crystalline structure of the active ingredient.

(2) If the amendment to the 505(b)(2) application does not contain a patent certification or statement, the applicant must verify that the proposed change described in the amendment is not one of the types of amendments described in paragraph (f)(1) of this section.

§ 314.70 Supplements and other changes to an approved application NDA.

(a) The NDA holder of an approved application under section 505 of the act must, within 30 days of the receipt by the Agency of any submission from a sponsor, assess the effects of the change before distributing a drug product made with a manufacturing change.

(b) * * *

(c) Limitation on certain amendments.

(1) * * *
(2) * * *
(iii) The applicant has not obtained a right of reference or use to the investigation described in paragraph (c)(1)(iii) of this section; and

(d) Field copy. The applicant shall submit a field copy of each amendment to a section of the NDA described in § 314.50(d)(1). The applicant shall include in its submission of each such amendment to FDA a statement certifying that a field copy of the amendment has been sent to the applicant’s home FDA district office.

(e) Different drug. An applicant may not amend a 505(b)(2) application to seek approval of a drug that is a different drug from the drug in the original submission of the 505(b)(2) application. For purposes of this paragraph (e), a drug is a different drug if it has been modified to have a different active ingredient, different route of administration, different dosage form, or difference in excipients that requires either a separate clinical study to establish safety or effectiveness or, for topical products, that requires a separate in vivo demonstration of bioequivalence. However, notwithstanding the limitation described in paragraph (e), an applicant may amend the 505(b)(2) application to seek approval of a different strength.

(f) Patent certification requirements. (1) An amendment to a 505(b)(2) application is required to contain an appropriate patent certification or statement described in § 314.50(c) or a recertification for a previously submitted paragraph IV certification if approval is sought for any of the following types of amendments:

(1) To add a new indication or other condition of use;
(2) To add a new strength;
(3) To make other than minor changes in product formulation; or
(4) To change the physical form or crystalline structure of the active ingredient.

(2) If the amendment to the 505(b)(2) application does not contain a patent certification or statement, the applicant must verify that the proposed change described in the amendment is not one of the types of amendments described in paragraph (f)(1) of this section.

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approval of a drug that is a different drug from the drug in the approved 505(b)(2) application. For purposes of this paragraph (b), a drug is a different drug if it has been modified to have a different active ingredient, different route of administration, different dosage form, or difference in excipients that requires either a separate clinical study to establish safety or effectiveness or, for topical products, that requires a separate in vivo demonstration of bioequivalence. However, notwithstanding the limitation described in this paragraph (b), an applicant may supplement the 505(b)(2) application to seek approval of a different strength.

§ 314.90 Waivers.

(c) If FDA grants the applicant’s waiver request with respect to a requirement under §§ 314.50 through 314.81, the waived requirement will not constitute a basis for refusal to approve an NDA under § 314.125.

§ 314.93 Petition to request a change from a listed drug.

(2) If, after approval of a petition and before approval of an ANDA submitted pursuant to the approved petition, a drug product is approved in an NDA for the change described in the petition, the petition and the listed drug identified in the petition can no longer be the basis for an ANDA submission, irrespective of whether FDA has withdrawn approval of the petition. A person seeking approval for such drug product must submit a new ANDA that identifies the pharmacologically equivalent reference listed drug as the basis for ANDA submission and comply with applicable regulatory requirements.

§ 314.94 Content and format of an abbreviated application ANDA.

(a) Abbreviated new drug application ANDAs.

(1) Table of contents. The archival copy of the abbreviated new drug application ANDA is required to contain a table of contents that shows the volume number and page number of the contents of the submission.

(2) Basis for abbreviated new drug application ANDA submission. An abbreviated new drug application ANDA must refer to a listed drug. Ordinarily, that listed drug will be the drug product selected by the Agency as the reference standard for conducting bioequivalence testing. The application ANDA must contain:

(i) The name of the reference listed drug, including its dosage form and strength. For an Abbreviated new drug application ANDA based on an approved petition under § 10.30 of this chapter and § 314.93, the reference listed drug must be the same as the listed drug referenced in the approved petition.

(ii) A statement as to whether, according to the information published in the list, the reference listed drug is entitled to a period of marketing exclusivity under section 505(j)(4)(D) of the Federal Food, Drug, and Cosmetic Act.

(iii) For an abbreviated new drug application ANDA based on an approved petition under § 10.30 of this chapter and § 314.93, a reference to the FDA-assigned docket number for the petition and a copy of FDA’s correspondence approving the petition.

(iv) The information required under § 314.50(d)(1), except that the information required under § 314.50(d)(1)(ii)(c) shall contain the proposed or actual master production record, including a description of the equipment, to be used for the manufacture of a commercial lot of the drug product.

(4)(i) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the abbreviated new drug application ANDA is submitted. The applicant shall entitle such a certification “Paragraph IV Certification”. This certification shall be submitted in the following form:

I, (name of applicant), certify that Patent No. (is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of) (name of proposed drug product) for which this application ANDA is submitted.

(ii) The certification shall be accompanied by a statement that the applicant will comply with the requirements under § 314.95(a) with respect to providing a notice to each owner of the patent or their representative and to the NDA holder of the approved application or, if the NDA holder does not reside or maintain a place of business within the United States, its attorney, agent, or other authorized official for James N. Czaban, Chairman FDA and Medical Products Regulatory Practice Group james.czaban@lapiper.com; T 202.799.4045 DLA Piper LLP (US)
In paragraph (a)(12)(i) of this section, a certification as to that patent and a statement under paragraph (a)(12)(i)(A) that the applicant is not required to make a certification or statement at the time of filing an ANDA refers to a listed drug that is a drug or method of using a drug claimed by a patent information submitted to FDA, the applicant and to the best of its knowledge, is claimed by a patent that claims only a method of manufacturing the listed drug, and to the best of its knowledge, is a method of manufacturing patent.

(ii) No relevant patents. If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (a)(12)(i) of this section, a certification in the following form:

In the opinion and to the best knowledge of (name of applicant), there are no patents that claim the listed drug referred to in this application OR that claim a use of the listed drug.

(iii) Method-of-use Patent. An applicant who submitted an abbreviated new drug application ANDA for that drug that contained an appropriate patent certification or statement at the time of filing an ANDA as of a specific date, the ANDA must contain a written statement from the patent owner that it has a licensing agreement with the applicant and that it consents to approval of the ANDA as of a specific date.

(iv) Intimacy of filing of patent information. (A) If a patent on the listed drug is issued and the holder of the approved ANDA for the listed drug does not submit with FDA the required information on the patent within 30 days of issuance of the patent, an applicant who submitted an abbreviated new drug application ANDA for that drug that contained an appropriate patent certification or statement before the submission of the patent information is not required to submit an amended patent certification. An or statement to address the patent or patent information that is late-listed with respect to the pending ANDA. Except as provided in § 314.53(f)(1), an ANDA holder’s amendment to the description of the approved method(s) of use claimed by the patent will be considered untimely filing of patent information unless:

(1) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of patent issuance;

(2) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of approval of a corresponding change to product labeling; or

(3) The amendment to the description of the approved method(s) of use claimed by the patent is submitted within 30 days of a decision by the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court which specifies the method of use claimed by the patent, and the amendment contains a copy of the decision.

(B) An applicant whose abbreviated new drug application ANDA is submitted after a late submission of the NDA holder’s untimely filing of patent information, or whose pending abbreviated application ANDA was previously submitted but did not contain an appropriate patent certification or statement at the time of the patent submission, shall submit an amendment to the application under paragraph (a)(12)(i) of this section and/or a statement under paragraph (a)(12)(iii) of this section as to that patent. Disputed patent information. If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent information is withdrawn or changed, the applicant shall submit a statement for each relevant listed patent.

(viii) Amended certifications. A patent certification or statement submitted under paragraphs (a)(12)(i) through (a)(12)(iii) of this section may be amended at any time before the effective date of the approval of the application. However, an applicant who has submitted a paragraph IV patent certification may not change it to a paragraph III certification. A patent infringement suit has been filed against another paragraph IV applicant unless the applicant has demonstrated that the applicant is entitled to 180-day exclusivity or the patent expires before the lawsuit is resolved or expires after the suit is resolved but before the end of the 180-day exclusivity period ANDA. If an applicant with a pending application ANDA voluntarily makes a patent certification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely filed patent. An applicant shall submit an amended certification by letter or as an amendment to a pending application or by letter to an approved application ANDA. Once an amendment or letter is submitted to change a certification, the application ANDA will no longer be considered to contain the prior certification.

(A) After finding of infringement. An applicant who has submitted a paragraph IV certification under paragraph (a)(12)(ii)(A) of this section and is sued for patent infringement within 45 days of the receipt of notice sent by the Patent Office or by a Federal district court, the Court of Appeals for the Federal Circuit, or the U.S. Supreme Court which specifies the method of use claimed by the patent, the applicant shall submit an amendment to change its certification if a court enters a final judgment which finds the patent to be infringed or invalid. In its amendment, the applicant shall not withdraw or change the certification unless the amendment includes a finding that the patent is invalid.

In its amendment, the applicant shall not withdraw or change the certification unless the amendment includes a finding that the patent is invalid.

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longer seeking approval for a method of use claimed by the patent. Once an amendment for the change has been submitted, the ANDA will no longer be considered to contain a paragraph IV certification to the patent. If a final judgment finds the patent to be invalid and infringed, an amended certification is not required.

(B) After removal of request to remove a patent or patent information from the list. If the list reflects that an NDA holder has requested that a patent or patent information be removed from the list, and no ANDA applicant is eligible for 180-day exclusivity based on a paragraph IV certification to that patent, the patent or patent information will be removed and any applicant with a pending application ANDA (including a tentatively approved application with a delayed effectiveness) claims a certification with respect to such patent shall submit an amendment to withdraw its certification. The applicant shall certify under paragraph (a)(12)(iv)(B) of this section that no patents described in paragraph (a)(12)(iv)(i) of this section claim the drug or, if other relevant patents claim the drug, shall amend the certification to refer only to those relevant patents. In the amendment, the applicant shall state the reason for withdrawing the change in certification or statement (that the patent is or has been removed from the list). If the list reflects that an NDA holder has requested that a patent that is the subject of a lawsuit under §314.107(c) shall not be removed from the list until FDA determines either that no delay in effective dates of approval is required under that section as a result of the lawsuit, that the patent is no longer applicable 180-day exclusivity has expired or that any such period of delay in effective dates of approval is ended. An applicant shall be extinguished. After any applicable 180-day exclusivity has expired or has been extinguished, the patent or patent information will be removed and any applicant with a pending ANDA (including a tentatively approved ANDA) who has made a certification with respect to such patent must submit an amended certification to withdraw its certification. Once an amendment or letter to withdraw the change in certification has been submitted, the application ANDA will no longer be considered to contain a certification under paragraph (a)(12)(viii)(A)(4) of this section. A certification under paragraph (a)(12)(viii)(A)(4) of this section contains two separate sections. One section contains the information described under paragraphs (a)(2) through (a)(6), (a)(8) and (a)(9) of this section if FDA's laboratories to perform tests on samples of the proposed drug product and to validate the applicant’s analytical procedures. The applicant must submit an amended certification reflecting that there are no relevant patents. Other amendments. (1) Except as provided in paragraphs (a)(12)(vi) and (a)(12)(viii)(C)(2) of this section, (i) An applicant shall amend a submitted certification or statement if, at any time before the effective date of approval of the ANDA, the applicant learns that the submitted certification or statement is no longer accurate, and (ii) An applicant shall submit an appropriate patent certification or statement under paragraph (a)(12)(i) and/or (iii) of this section if, after submission of the ANDA, a new patent is issued by the U.S. Patent and Trademark Office that, in the opinion of the applicant ANDA, contains a reference listed drug or that claims the reference listed drug or that claims an approved use for such reference listed drug and for which information is required to be filed under section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act and §314.53. For a paragraph IV certification, the certification must not be submitted earlier than the first working day after the day the patent is published in the list.

(2) An applicant is not required to amend a supplement to change a submitted certification when information on a patent on the listed drug is submitted after the effective date of approval of the abbreviated application ANDA.

(d) Format of an ANDA. (1) The applicant must submit a complete archival copy of the ANDA as required under paragraphs (a) and (c) of this section. FDA will maintain the archival copy during the review of the ANDA to assist in the review process. The information that is not contained in the particular technical sections of the ANDA, to give other Agency personnel access to the ANDA for official business, and to maintain in one place a complete copy of the ANDA.

(2) For abbreviated new drug application ANDAs, the applicant shall submit a review copy of the abbreviated application ANDA that contains two separate sections. One section shall contain the information described under paragraphs (a)(2) through (a)(6), (a)(8) and (a)(9) of this section if FDA's laboratories to perform tests on samples of the proposed drug product and to validate the applicant’s analytical procedures. The other section shall contain the information described under paragraphs (a)(3), (a)(7), and (a)(8) of this section. Each of the sections in the review copy is required to contain a copy of the application form described under §314.50 paragraph (a) of this section.

§314.95 Notice of certification of invalidity, unenforceability, or noninfringement of a patent.

(a) Notice of certification. For each patent that claims the listed drug or that claims a use for such listed drug for which the applicant is seeking approval and that for which the applicant certifies under §314.94(a)(12) is invalid, unenforceable, or will not be infringed by a submission of a paragraph IV certification, the applicant shall send notice of such certification by registered or certified mail, return receipt requested, or by a designated delivery service, as defined in paragraph (g) of this section to each of the following persons:

(1) Each owner of the patent that is the subject of the certification or the representative designated by the owner to receive the notice. The name and address of the patent owner or its representative may be obtained from the United States Patent and Trademark Office; and

(2) The holder of the approved application NDA under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the listed drug that is claimed by the patent and for which the applicant is seeking approval, or, if the application NDA holder does not reside or maintain a place of business within the United States, the application NDA holder’s attorney, agent, or other authorized official. The name and address of the application NDA holder or its attorney, agent, or authorized official may be obtained from by sending a written or electronic communication to the Orange Book Staff, Office of Generic Drugs, 2500 7620 Standish Pl., Rockville, MD 20855, or to the Orange Book Staff at the email address listed on the Agency’s Web site at http://www.fda.gov.

(3) This paragraph (a) does not apply to a use-method-of-use patent that claims no use or does not claim a use for which the applicant is seeking approval.

(4) An applicant may send notice by an alternative method only if FDA has agreed in advance that the method will produce an acceptable form of documentation.

(b) Sending the notice. (1) Except as provided under paragraph (d) of this section, the applicant shall send the notice required by paragraph (a) of this section when or after the date it receives from FDA a paragraph IV certification.
acknowledgment letter stating that its abbreviated new drug application is sufficiently complete to permit a substantive review. At the same time, the applicant identified under paragraph IV of an ANDA, but not later than 20 days after the date of the postmark on the paragraph IV acknowledgment letter. The 20-day clock described in this paragraph (b) begins on the day after the date of the postmark on the paragraph IV acknowledgment letter. When the 20th day falls on a Saturday, Sunday, or a Federal holiday, the 20th day will be the next day that is not a Saturday, Sunday or Federal holiday.

(2) Any notice required by paragraph (a) of this section is invalid if it is sent before the applicant’s receipt of a paragraph IV acknowledgment letter, or before the first working day following the day the patent is published in the list. The applicant will not have complied with this paragraph (b) until it sends valid notice.

its abbreviated new drug application to include:

(3) The applicant must submit to FDA an amendment to its ANDA that includes:

(a) A statement certifying that the applicant has not submitted a previous paragraph IV certification.
(b) Any notice required by paragraph (a) of this section. If an ANDA amendment or supplement to the abbreviated new drug application is submitted to FDA AND MEDICAL PRODUCTS REGULATORY PRACTICE GROUP James N. Czaban, Chairman FDA and Medical Products Regulatory Practice Group james.czaban@dlapiper.com; T 202.799.4045 DLA Piper LLP (US)

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unenforceable, or will not be infringed. The applicant shall must include in the detailed statement:

(i) For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed.
(ii) For each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation.

(a) If the applicant alleges that the patent will not be infringed and the applicant seeks to preserve the option to later file a civil action for declaratory judgment in accordance with section 505(i)(5)(B)(i) of the Federal Food, Drug, and Cosmetic Act, then the notice must be accompanied by an offer of confidential access to the ANA of the applicant to provide documentation of the possible infringement of the patent that is the subject of the paragraph IV certification.

(b) If the applicant does not reside or have a place of business in the United States, the name and address of an agent in the United States authorized to accept service of process for the applicant.

(c) The applicant shall must include in the detailed statement:

(1) A statement that FDA has received an abbreviated new drug application ANDA submitted by the applicant containing any required bioavailability or bioequivalence data or information.
(2) The abbreviated application ANDA number.
(3) A statement that the applicant has received the paragraph IV acknowledgment letter for the ANDA.
(4) The established name, if any, as defined in section 502(e)(3) of the Federal Food, Drug, and Cosmetic Act, of the proposed drug product.
(5) The active ingredient, strength, and dosage form of the proposed drug product.
(6) The patent number and expiration date on the patent for the reference listed drug alleged to be invalid, unenforceable, or not infringed.
(7) A detailed statement of the factual and legal basis of the applicant’s opinion that the patent is not valid,

unenforceable, or will not be infringed. The applicant shall must include in the detailed statement:

(i) For each claim of a patent alleged not to be infringed, a full and detailed explanation of why the claim is not infringed.
(ii) For each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation.

(a) If the applicant alleges that the patent will not be infringed and the applicant seeks to preserve the option to later file a civil action for declaratory judgment in accordance with section 505(i)(5)(B)(i) of the Federal Food, Drug, and Cosmetic Act, then the notice must be accompanied by an offer of confidential access to the ANA of the applicant to provide documentation of the possible infringement of the patent that is the subject of the paragraph IV certification.

(b) If the applicant does not reside or have a place of business in the United States, the name and address of an agent in the United States authorized to accept service of process for the applicant.

(c) The applicant shall must include in the detailed statement:

(1) A statement that FDA has received an abbreviated new drug application ANDA submitted by the applicant containing any required bioavailability or bioequivalence data or information.
(2) The abbreviated application ANDA number.
(3) A statement that the applicant has received the paragraph IV acknowledgment letter for the ANDA.
(4) The established name, if any, as defined in section 502(e)(3) of the Federal Food, Drug, and Cosmetic Act, of the proposed drug product.
(5) The active ingredient, strength, and dosage form of the proposed drug product.
(6) The patent number and expiration date on the patent for the reference listed drug alleged to be invalid, unenforceable, or not infringed.
(7) A detailed statement of the factual and legal basis of the applicant’s opinion that the patent is not valid,
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§ 314.97 Supplements and other changes to an approved abbreviated application ANDA.

(a) General requirements. The applicant must comply with the requirements of §§ 314.70 and 314.71 regarding the submission of supplemental applications ANDAs and other changes to an approved abbreviated application ANDA.

(b) Different listed drug. An applicant may not supplement an ANDA to seek approval of a drug referring to a listed drug that is different from the current reference listed drug identified in the ANDA. This paragraph (b) applies if changes are proposed in a supplement to the ANDA such that the proposed product is a pharmaceutical equivalent to a different listed drug than the reference listed drug identified in the ANDA. A change of reference listed drug must be submitted in a new ANDA. However, notwithstanding the limitation described in this paragraph (b), an applicant may supplement the ANDA to seek approval of a different strength.

§ 314.99 Other responsibilities of an applicant of an abbreviated application ANDA.

(a) An applicant must comply with the requirements of § 314.65 regarding withdrawal by the applicant of an unapproved abbreviated application ANDA and § 314.72 regarding a change in ownership of an abbreviated application ANDA.

(b) An applicant may ask FDA to waive under this section any requirement that applies to the applicant under §§ 314.92 through 314.99. The applicant must comply with the requirements for a waiver under § 314.90. If FDA grants the applicant’s waiver request with respect to a requirement under §§ 314.92 through 314.99, the waived requirement will not constitute a basis for refusal to approve an ANDA under § 314.127.

§ 314.101 Filing an application ANDA and receiving an abbreviated new drug application ANDA.

(a) Filing an ANDA. (1) Within 60 days after FDA receives an application ANDA, the Agency will determine whether the application ANDA may be filed. The filing of an application ANDA means that FDA has made a threshold determination that the abbreviated application ANDA is sufficiently substantially complete to permit a substantive review.

(2) If FDA finds that none of the reasons in paragraphs (d) and (e) of this section for considering the abbreviated new drug application ANDA not to have been received applies, the ANDA is substantially complete, and the Agency will receive the abbreviated new drug application ANDA and notify the applicant in writing. If FDA determines, upon evaluation, that an ANDA was substantially complete as of the date it was submitted to FDA, FDA will consider the ANDA to have been received as of the date of submission. In the case of an ANDA that contains a paragraph IV certification, the applicant will be notified via a paragraph IV acknowledgment letter. The date of filing will be the date 60 days after the date FDA received the application ANDA. The date of filing begins the 180-day period described in section 505(c) of the Federal Food, Drug, and Cosmetic Act. This 180-day period is called the “filing clock.”

(3) If FDA refuses to file the application ANDA, the Agency will notify the applicant in writing and state the reason under paragraph (d) or (e) of this section for the refusal. If FDA refuses to file the application ANDA under paragraph (d) of this section, the applicant may request in writing within 30 days of the agency’s notification an informal conference with the Agency about whether the Agency should file the application ANDA. If, following the informal conference, the applicant requests that FDA file the application ANDA (with or without amendments to correct the deficiencies), the Agency will file the application ANDA over protest under paragraph (a)(2) of this section, notify the applicant in writing, and review it as filed. If the application ANDA is filed over protest, the date of filing will be the date 60 days after the date the applicant requested the informal conference. The applicant need not resubmit a copy of an application ANDA that is filed over protest. If FDA refuses to file the application ANDA under paragraph (e) of this section, the applicant may amend the application ANDA and resubmit it, and the Agency will make a determination under this section whether it may be filed.

(b) (1) An abbreviated new drug application will be considered Receiving an Abbreviated New Drug Application. An Abbreviated New Drug Application ANDA not to have been received after it is submitted to determine whether the abbreviated application ANDA may be received. Receipt of an Abbreviated New Drug Application ANDA means that FDA has made a threshold determination that the abbreviated application ANDA is sufficiently substantially complete to permit a substantive review. 

(2) If FDA finds that none of the reasons in paragraphs (d) and (e) of this section for considering the Abbreviated New Drug Application ANDA not to have been received applies, the ANDA is substantially complete, and the Agency will receive the Abbreviated New Drug Application ANDA and notify the applicant in writing. If FDA determines, upon evaluation, that an ANDA was substantially complete as of the date it was submitted to FDA, FDA will consider the ANDA to have been received as of the date of submission. In the case of an ANDA that contains a paragraph IV certification, the applicant will be notified via a paragraph IV acknowledgment letter. The date of filing will be the date 60 days after the date FDA received the application ANDA. The date of filing begins the 180-day period described in section 505(c) of the Federal Food, Drug, and Cosmetic Act. This 180-day period is called the “filing clock.”
IV certification, the applicant will be notified, via a paragraph IV acknowledgment letter.

(3) If FDA considers the abbreviated new drug application ANDA not to have been received under paragraph (d) or (e) of this section, FDA will notify the applicant—ordinarily by telephone of the refuse-to-receive decision. The applicant may then:

(i) Withdraw the abbreviated new drug application ANDA under § 314.49; or

(ii) Amend the abbreviated new drug application ANDA to correct the deficiencies and resubmit the ANDA; or

(iii) Take no action, in which case FDA will refuse to receive the abbreviated new drug application. FDA may consider the ANDA withdrawn after 1 year.

(6) [Reserved]

(d) ND A or ANDA deficiencies. FDA may refuse to file an application NDA or may not consider an abbreviated new drug application ANDA to be received if any of the following applies:

(1) The application NDA or ANDA does not contain a completed application form.

(2) The application NDA or ANDA is not submitted in the form required under §314.50 or §314.94.

(3) The application or abbreviated application NDA or ANDA is incomplete because it does not on its face contain information required under section 505(b), or section 505(j), or section 522 of the Federal Food, Drug, and Cosmetic Act and §314.50 or §314.94. In determining whether an ANDA is incomplete on its face, FDA will consider the nature (e.g., major or minor) of the deficiencies, including the number of deficiencies in the ANDA.

(4) The applicant fails to submit a complete environmental assessment, which addresses each of the items specified in the applicable format under § 25.40 of this chapter or fails to provide sufficient information to establish that the requested action is subject to categorical exclusion under § 25.30 or § 25.31 or fails to provide sufficient information to establish that the application is complete environmental assessment, which was conducted in compliance with the institutional review board regulations in part 56 of this chapter, or was not subject to those regulations, and that it was conducted in compliance with the informed consent regulations in part 50 of this chapter, or, if the study was subject to but was not conducted in compliance with those regulations, the application NDA or ANDA does not contain a brief statement of the reason for the noncompliance.

(7) The application NDA or ANDA does not contain a statement for each clinical study that "the study was conducted in compliance with the institutional review board regulations in part 56 of this chapter, or was not subject to those regulations, and that it was conducted in compliance with the informed consent regulations in part 50 of this chapter, or, if the study was subject to but was not conducted in compliance with those regulations, the application NDA or ANDA does not contain a brief statement of the reason for the noncompliance."

(8) The drug product that is the subject of the submission is already covered by an approved application or abbreviated application NDA or ANDA and the applicant of the submission:

(i) Has an approved application or abbreviated application NDA or ANDA for the same drug product;

(ii) Is merely a distributor and/or repackager of the already approved drug product.

(9) The application NDA is submitted as a 505(b)(2) application for a drug that is a duplicate of a listed drug and is eligible for approval under section 505(j) of the Federal Food, Drug, and Cosmetic Act.

(e) Regulatory deficiencies. The Agency will refuse to file an application NDA or will consider an abbreviated new drug application ANDA not to have been received if any of the following applies:

(1) The drug product is subject to licensing by FDA under the Public Health Service Act (42 U.S.C. 201 et seq.) and paragraph F of this chapter.

(2) In the case of a 505(b)(2) application, an abbreviated new drug application, the drug product contains the same active moiety as a drug that:

(i) Was approved after September 24, 1984, in an application under section 505(b) of the act, and

(ii) Is entitled to a 5-year period of exclusivity.

(3) Submission of a 505(b)(2) application or an abbreviated new drug application, the drug product contains a certification of patent invalidity or non infringement, described in §314.50(c)(1)(i), (ii), (iii), 505(j)(4)(I)(a)(v)(I), 505(j)(6)(A)(vi), or §314.94(a), and §314.94(b)(1)(ii), (iii), or §314.94(b)(a), (1), (ii), (iii), (iv) of the Federal Food, Drug, and Cosmetic Act.

(f) Outcome of FDA review. (1) Within 180 days after the date of filing, plus the period of time the review period was extended (if any), FDA will either:

(i) Approve the application NDA; or

(ii) Issue a notice of opportunity for a hearing if the applicant asked FDA to provide it an opportunity for a hearing on an application NDA in response to a complete response letter.

(2) Within 180 days after the date of receipt, plus the period of time the review clock was extended (if any), FDA will either approve or disapprove the abbreviated new drug application ANDA. If FDA disapproves the abbreviated new drug application ANDA, FDA will issue a notice of opportunity for hearing if the applicant asked FDA to provide it an opportunity for a hearing on an abbreviated new drug application ANDA in response to a complete response letter.

(3) This paragraph (f) does not apply to applications or abbreviated applications NDA, or ANDAs that have been withdrawn from FDA review by the applicant.

§314.105 Approval of an application NDA and an abbreviated application ANDA.

(a) The Food and Drug Administration will approve an application and send the applicant an approval letter if none of the reasons in §314.125 for refusing to approve the application applies. An approval becomes effective on the date of the issuance of the approval letter, except with regard to an application under section 505(b)(2) of the act with a delayed effective date. An approval with a delayed effective date is tentative and does not become final until the effective date. A new drug product or antibiotic approved under this paragraph may not be marketed until an approval is effective.

(b) FDA will approve an NDA and send the applicant an approval letter if none of the reasons in §314.125 for refusing to approve the NDA applies. FDA will issue a tentative approval letter if an NDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved because there is a 7-year period of orphan exclusivity for the listed drug under section 527 of the Federal Food, Drug, and Cosmetic Act and §316.31 of this chapter, or if a 505(b)(2) application otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved until the conditions in §314.107(b)(3) are met.

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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 Federal Food, Drug, and Cosmetic Act; or because there is a period of exclusivity for the listed drug under section 505E of the Federal Food, Drug, and Cosmetic Act. A drug product that is granted tentative approval is not an approved drug and will not be approved until FDA issues an approval letter. A new drug product is based on information available to FDA at the time of the tentative approval letter (i.e., the information in the 505(b)(2) application and the status of current good manufacturing practices of the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to FDA's attention. A new drug product may not be marketed until the date of approval.

(b) FDA will approve an application NDA and issue the applicant an approval letter on the basis of draft labeling if the only deficiencies in the labeling are typographical, editorial, or minor in nature as directed, and upon the applicant submitting to FDA a copy of the final printed labeling prior to marketing.

(c) FDA will approve an application NDA after it determines that the drug meets the statutory standards for safety and effectiveness, manufacturing and controls, and labeling, and an abbreviated application ANDA after it determines that the drug meets the statutory standards for manufacturing and controls, labeling, and, whenever possible, bioequivalence. While the statutory standards apply to all drugs, the many kinds of drugs that are subject to the statutory standards and the wide range of uses for those drugs demand flexibility in applying the standards. Thus FDA is required to exercise its scientific judgment to determine the kind and quantity of data and information an applicant is required to provide for a particular drug to meet the statutory standards. FDA makes its views on drug products and classes of drugs available through guidance documents, recommendations, and other statements of policy.

(d) FDA will approve an abbreviated new drug application ANDA and send the applicant an approval letter if none of the reasons in § 314.127 for refusing to approve the abbreviated new drug application ANDA applies. The approval becomes effective on the date of the issuance of the agency's approval letter unless the approval letter provides for a delayed effective date. An approval with a delayed effective date is tentative and does not become final until the effective date. FDA will issue a tentative approval letter for an ANDA only if the ANDA otherwise meets the requirements for approval under the Federal Food, Drug, and Cosmetic Act, but cannot be approved because there is a 7-year, period of orphan exclusivity for the listed drug under section 527 of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter, or cannot be approved because the conditions in § 314.107(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 Federal Food, Drug, and Cosmetic Act, or because there is a period of exclusivity for the listed drug under section 505E of the Federal Food, Drug, and Cosmetic Act. A drug product that is granted tentative approval is not an approved drug and will not be approved until FDA issues an approval after any necessary additional review of the ANDA. FDA's tentative approval of a drug product is based on information available to FDA at the time of the tentative approval letter (i.e., the information in the ANDA and the status of current good manufacturing practices of the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to FDA's attention. A drug product may not be marketed until the date of approval.

§ 314.107 Effective Date of approval of a 505(b)(2) application or abbreviated new drug application under section 505(j) of the act.

(a) General. A drug product may be introduced or delivered for introduction into interstate commerce when approval of the 505(b)(2) application or abbreviated new drug application ANDA for the drug product becomes effective. Except as provided in this section, approval of an application ANDA for a drug product becomes effective on the date FDA issues an approval letter under § 314.105 for the 505(b)(2) application or abbreviated application ANDA.

(b) Effect of patent on the listed drug. If approval of an abbreviated new drug application submitted under section 505(j) of the act or of a 505(b)(2) application is granted, that approval will become effective in accordance with the following:

(1) Timing of approval based on patent application. As described in paragraphs (b)(1) and (2) of this section, the status of patents listed for the listed drug(s) relied upon or reference listed drug, as applicable, must be considered in determining the first possible date on which a 505(b)(2) application or ANDA can be approved. The criteria in paragraphs (b)(1) and (2) of this section will be used to determine, for each relevant patent, the date that patent will no longer prevent approval. The first possible date on which the 505(b)(2) application or ANDA can be approved will be calculated for each patent, and the 505(b)(2) application or ANDA may be approved on the last applicable date.

(2) Timing of approval based on patent certification or statement. If none of the reasons in § 314.125 or § 314.127, as applicable, for refusing to approve the 505(b)(2) application or ANDA applies, and none of the reasons in paragraph (d) of this section for delaying approval applies, the 505(b)(2) application or ANDA may be approved as follows:

(1) Date of approval letter. Except as provided in paragraphs (b)(3), (b)(4), and (c) of this section, approval will become effective on the date FDA issues an approval letter under § 314.105(i). Immediately, if the applicant certifies under § 314.50(i) or § 314.94(a)(12) that:

(i) There are no relevant patents; or

(iiA) The applicant is aware of a relevant patent but the patent is unenforceable, or will not be infringed, except as provided in paragraphs (b)(3) and (c) of this section, and the 45-day period provided for in section 505(c)(3)(C) and (j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act has expired.

(iiB) There are no relevant patent is invalid, unenforceable, or will not be infringed patents.

(1) Immediately, if the applicant submits an appropriate statement under § 314.50(i) or § 314.94(a)(12) explaining that a method-of-use patent does not claim an indication or other condition of use for which the applicant is seeking approval, except that if the applicant also submits a paragraph IV certification to the patent, then the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(1)(i)(C) of this section.

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(2) Patent expiration: (iii) On the date specified, if the applicant certifies under § 314.50(t) or § 314.94(a)(12) that the relevant patent will expire on a specified date, approval must become effective on the specified date.

(2) Patent information filed after submission of 505(b)(2) application or ANDA: If the holder of the approved NDA for the listed drug submits patent information required under § 314.53 after the date on which the 505(b)(2) application or ANDA was submitted to FDA, the 505(b)(2) applicant or ANDA applicant must comply with the requirements of §§ 314.50(ii)(4) and (6) and §§ 314.94(a)(12)(vi) and (viii) regarding submission of an appropriate patent certification or statement. If the applicant submits an amendment certifying under § 314.50(i)(4) or § 314.94(a)(12)(vi), that the relevant patent is invalid, unenforceable, or will not be infringed, and complies with the requirements of §§ 314.52 or § 314.95, the 505(b)(2) application or ANDA may be approved immediately upon submission of documentation of receipt of notice of paragraph IV certification under § 314.53(e) or § 314.95(g). The 45-day period provided for in section 505(c)(3)(C) and (j)(5)(B)(iii) of the Federal Food, Drug, and Cosmetic Act does not apply in these circumstances.

(3) Disposition of patent litigation: (i) Approval upon expiration of 30-month period or 71/2 years from date of listed drug approval. (A) Except as provided in paragraphs (b)(3)(ii), (b)(3)(iii), and (b)(3)(iv) through (viii) of this section, if with respect to patents for which information was submitted under § 314.53 before the date on which the 505(b)(2) application or ANDA was submitted to FDA (excluding an amendment or supplemental NDA for the applicant), the applicant certifies under § 314.50(t) or § 314.94(a)(12) that the relevant patent is invalid, unenforceable, or will not be infringed, and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement within 45 days of receipt of the notice of certification from the applicant under § 314.52 or § 314.95, approval may be made effective on the 30-month period or 71/2 years from the date of approval of the application NDA for the patented drug product.

(B) If the patented drug product qualifies for 5 years of exclusive marketing under § 314.108(b)(2) and the patent owner or its representative or the exclusive patent licensee brings suit for patent infringement during the 1-year period beginning 4 years after the date of approval of the patented drug, approval may be made effective on the date the court enters a final order or judgment that the patent is invalid, unenforceable, or not infringed.

(ii) Federal district court decision of invalidity, unenforceability, or non-infringement. If before the expiration of the 30-month period, or 71/2 years where applicable, the district court issues a final order or judgment that the patent is invalid, unenforceable, or not infringed, approval may be made effective on the date the court enters a final order or judgment determining that there is no cause of action for patent infringement or invalidity, the 505(b)(2) application or ANDA may be approved on:

(A) The date on which the court enters judgment reflecting the decision; or

(B) The date of a settlement order or consent decree signed and entered by the court stating that the patent is the subject of the consent, approval may be granted on or after the date of the consent, approval may be granted on or after that date.

(iii) Appeal of Federal district court judgment of infringement. If before the expiration of the 30-month period, or 71/2 years where applicable, the district court issues a final order or judgment that the patent has been infringed, approval may be made effective on the date the court determines that enforcement of the district court’s judgment is appropriate, the 505(b)(2) application or ANDA may be approved on:

(A) The date on which the mandate is issued by the court of appeals ordering the district court to enter judgment that the patent is invalid, unenforceable, or not infringed; or

(B) The date of a settlement order or consent decree signed and entered by the court of appeals stating that the patent is the subject of the consent, approval may be granted on or after the date of the consent.

(iv) Affirmation or non-appeal of Federal district court judgment of infringement. If before the expiration of the 30-month period, or 71/2 years where applicable, the district court decides that the patent has been infringed, and if the judgment of the district court is not affirmed or is affirmed, the 505(b)(2) application or ANDA may be approved no earlier than the date specified by the district court in an order under 35 U.S.C. 221(e)(4).

(v) Grant of preliminary injunction by Federal district court. If before the expiration of the 30-month period, or 71/2 years where applicable, the district court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug product until the court decides the issues of patent validity and infringement, and if the court later decides that the patent is invalid, unenforceable, or not infringed, approval may be made effective on the date the court enters a final order or judgment that the patent is invalid, unenforceable, or not infringed.

(A) The patent is invalid, unenforceable, or not infringed, the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(3)(ii) of this section; or

(B) The patent is infringed, the 505(b)(2) application or ANDA may be approved as provided in paragraph (b)(3)(vi) or (vii) of this section, whichever is applicable.

(vi) Written consent to approval by patent owner or exclusive patent licensee. If before the expiration of the 30-month period, or 71/2 years where applicable, the patent owner or the exclusive patent licensee (or their representatives) agrees in writing that the 505(b)(2) application or ANDA may be approved any time on or after the date of the consent, approval may be granted on or after that date.

(vii) Court order terminating 30-month or 71/2-year period. If before the expiration of the 30-month period, or 71/2 years where applicable, the court enters an order requiring the 30-month or 71/2-year period to be terminated, the 505(b)(2) application or ANDA may be approved in accordance with the court’s order.

(viii) Court order of dismissal without a finding of infringement. If before the expiration of the 30-month period, or 71/2 years where applicable, the court orders dismissal without a finding of infringement in each pending suit for patent infringement brought within 45 days of receipt of the notice of paragraph IV certification sent by the 505(b)(2) or ANDA applicant, the 505(b)(2) application or ANDA may be approved on or after the date of the order.

(v) Tentative approval. FDA will issue a tentative approval letter when tentative approval is appropriate in accordance with paragraph (b)(3).
of this section, the applicant must receive an approval letter from the Agency indicating that the application has received final approval. Tentative approval of an application, NDA or ANDA, does not constitute "approval" of an ANDA for a subsequent applicant or an ANDA for a subsequent application. An application for a generic copy of the same listed drug that is both substantially complete and contains the same certification as the ANDA of a subsequent applicant will not be approved if the applicant does not submit certifications to the Agency that the same patent was invalid, unenforceable, or not infringed as of the first date of introduction or delivery for commercial marketing of its drug product; or if an application is for a generic copy of the same listed drug that is both substantially complete and contains the same certification as the ANDA of a subsequent applicant. The ANDA of a subsequent applicant will not be approved if the ANDA contains a paragraph IV certification that the patent upon which the 180-day exclusivity provisions in section 505A of the act or a 505(b)(2) application or ANDA if delay is required by the patent valid and infringed; and a copy of any subsequent court order lifting the injunction; and (vii) a copy of any court order pursuant to 25 U.S.C. 271(e)(4)(A) ordering that a 505(b)(2) application or ANDA may be approved no earlier than the date specified (irrespective of whether the injunction relates to a patent described in paragraph (b)(3)(i) of this section).

(e) Notice of court actions or written consent to approval. (1) The applicant shall submit a copy of the order or judgment to the Office of Generic Drugs (HFD-600), or to the appropriate division in the Office of New Drugs within 10 working days of a final judgment, the following information to FDA, as applicable: (i) A copy of any court order entered by the court (district court or mandate of the court of appeals) or settlement order or consent decree signed and entered by the court (district court or court of appeals) finding a patent described in paragraph (b)(3) of this section invalid, unenforceable, or not infringed, or finding the patent valid and infringed; (ii) Written notification of whether or not any action by the court described in paragraph (e)(1)(i) of this section has been appealed within the time permitted for an appeal; (iii) A copy of any order entered by the court (terminating the 50-month or 7-year period described in section 505E of the Federal Food, Drug, and Cosmetic Act; or section 505A of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act and § 316.31 of this chapter; section 505A of the Federal Food, Drug, and Cosmetic Act; or section 505E of the Federal Food, Drug, and Cosmetic Act in paragraph (b)(3)(i), (ii), (v), or (vii) of this section; (iv) A copy of any written consent to approval by the patent owner or exclusive patent licensee described in paragraph (b)(3)(vi) of this section; (v) A copy of any preliminary injunction described in paragraph (b)(3)(vi) of this section, and a copy of any subsequent court order lifting the injunction; and (vi) A copy of any court order pursuant to 25 U.S.C. 271(e)(4)(A) ordering that a 505(b)(2) application or ANDA may be approved no earlier than the date specified (irrespective of whether the injunction relates to a patent described in paragraph (b)(3)(i) of this section).

(f) Forty-five day period after receipt of notice of paragraph IV certification—(1) Computation of 45-day time clock. (i) The 45-day clock described in paragraph (b)(3) of this section as to each recipient required to receive notice of paragraph IV certification under § 314.52 or § 314.95 begins on the day after the date of receipt of the applicant’s notice of paragraph IV certification by the patent owner or its representative, and by the approved application holder/recipient. When the 45-day time period expires, the applicant shall notify FDA, as required in this paragraph (c)(1).

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infringement. The notice should contain the name(s) of the active ingredient(s), the drug product or, if no established name exists, the product's strength, and dosage form.

The notice shall include:

(iA) The abbreviated new drug application or 505(b)(2) application or ANDA number.

(iiB) The name of the abbreviated new drug 505(b)(2) application or ANDA applicant.

(iiiC) The established name of the drug product or, if no established name exists, the name(s) of the active ingredient(s), the drug product's strength, and dosage form.

(ivD) A certification statement that an action for patent infringement has been filed within 45 days of receipt of the notice of paragraph IV certification. If the applicant submitting the abbreviated new drug application or the 505(b)(2) application does not notify FDA in writing before the expiration of the 45-day time period or the completion of the agency's review and approval of the application, whichever is later, that a legal action for patent infringement was filed within 45 days of receipt of the notice of certification, approval of the abbreviated new drug application or the 505(b)(2) application, will be made effective immediately upon expiration of the 45 days or upon completion of the agency's review and approval of the application, whichever is later.

The notification to FDA of the legal action shall include:

(a) Definitions. The definitions in § 314.3 apply to this section:

(b) Submission of and effective date of approval of an abbreviated new drug application submitted under section 505(j) of the Act on a 505(b)(2) application. (1) **FDA** means the Food and Drug Administration.

(c) New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other application or approved by an applicant who is an exclusive patent licensee or its representative(s) before (date on which 45 days elapse) (Name of patent owner or NDA holder who is an exclusive patent licensee or its representative(s)) has been approved after September 24, 1984, in an application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, that a legal action for patent infringement against (name of applicant) has been filed within 45 days of receipt of the notice of certification and the patent owner or approved applicant or its representative(s) has waived its opportunity to file a legal action for patent infringement within 45 days of a receipt of the notice of certification and the patent owner or approved applicant or its representative(s) has been approved upon completion of the agency's review and approval of the application NDA or ANDA. FDA will only accept a waiver in the following form:

(Name of patent owner or NDA holder who is an exclusive patent licensee or its representative(s)) has received notice from (name of applicant) under section 505(b)(3) or 505(j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and does not intend to file an action for patent infringement against (name of applicant) concerning the drug (name of drug) before (date on which 45 days elapse). (Name of patent owner or NDA holder who is an exclusive patent licensee) waives the opportunity provided by section 505(c)(3)(C) or 505(j)(2)(B)(iii) of the Federal Food, Drug, and Cosmetic Act, and does not object to FDA's approval of (name of applicant)'s 505(b)(2) or abbreviated new drug application or ANDA for (name of drug) with an immediate approval.

(d) Conversion of approval to tentative approval. 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.

§314.108 New drug product exclusivity.

(a) Definitions. The definitions in § 314.3 and the following definitions of terms apply to this section:

Active moiety means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule responsible for the physiological or pharmacological action of the drug substance.

Approved under section 505(b) means an application submitted under section 505(b) and approved on or after October 10, 1962, or an application that was "deemed approved" under section 107(c)(2) of Pub. L. 87-78.

Bioavailability study means a study to determine the bioavailability or the pharmacokinetics of a drug.

* * * * * *

Essential to approval means, with regard to an investigation, that there are no other data available that could support approval of the application.

**FDA** means the Food and Drug Administration.

New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other application or approved under section 505(b) of the Federal Food, Drug, and Cosmetic Act.

* * * * * *

(b) Submission of and effective date of approval of an abbreviated new drug application submitted under section 505(j) of the Act on a 505(b)(2) application. (1) **FDA** means the Food and Drug Administration.

(c) New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other application or approved by an applicant who is an exclusive patent licensee or its representative(s) before (date on which 45 days elapse) (Name of patent owner or NDA holder who is an exclusive patent licensee) has been approved after September 24, 1984, in an application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, that a legal action for patent infringement against (name of applicant) has been filed within 45 days of receipt of the notice of certification and the patent owner or approved applicant or its representative(s) has waived its opportunity to file a legal action for patent infringement within 45 days of a receipt of the notice of certification and the patent owner or approved applicant or its representative(s) has been approved upon completion of the agency's review and approval of the application NDA or ANDA. FDA will only accept a waiver in the following form:

(Name of patent owner or NDA holder who is an exclusive patent licensee or its representative(s)) has received notice from (name of applicant) under section 505(b)(3) or 505(j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and does not intend to file an action for patent infringement against (name of applicant) concerning the drug (name of drug) before (date on which 45 days elapse). (Name of patent owner or NDA holder who is an exclusive patent licensee) waives the opportunity provided by section 505(c)(3)(C) or 505(j)(2)(B)(iii) of the Federal Food, Drug, and Cosmetic Act, and does not object to FDA's approval of (name of applicant)'s 505(b)(2) or abbreviated new drug application or ANDA for (name of drug) with an immediate approval.

(d) Conversion of approval to tentative approval. 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.
described in paragraph (b)(2) of this section will become effective as provided in §314.107(b)(1) or (b)(2), unless the owner of a patent that claims the drug, the patent owner’s representative, or exclusive licensee brings suit for patent infringement against the applicant during the 1-year period beginning 48 months after the date of approval of the new drug application (NDA) for the new chemical entity and within 45 days after receipt of the notice described at §314.52 or §314.95, in which case, approval of the 505(b)(2) application or abbreviated application (ANDA) will be made effective as provided in §314.107(b)(3).

(4) If an application (NDA):
(i) Was submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act;
(ii) Was approved after September 24, 1984;
(iii) Was for a drug product that contains an active moiety that has been previously approved in another application (NDA) under section 505(b) of the Federal Food, Drug, and Cosmetic Act, and
(iv) Contained reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application, the agency will not make effective for a period of 3 years after the date of approval of the application, the approval of Agency will not approve a 505(b)(2) application or an abbreviated new drug application (ANDA) for the conditions of approval of the original application, or an abbreviated new drug application (ANDA), or an ANDA submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting the conditions of approval of an original new drug application (NDA).

(5) If a supplemental application (NDA):
(i) Was approved after September 24, 1984; and
(ii) Contained reports of new clinical investigations (other than bioavailability studies) that were conducted or sponsored by the applicant that were essential to approval of the supplemental application, the agency will not make effective (NDA) for a period of 3 years after the date of approval of the supplemental application, the approval of Agency will not approve a 505(b)(2) application or an abbreviated new drug application (ANDA) for a change, or an abbreviated new drug application (ANDA) submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting a change approved in the supplemental new drug application (NDA).

§ 314.125 Refusal to approve an application (NDA)

(b) FDA may refuse to approve an application (NDA) for any of the following reasons, unless the requirement has been waived under §314.90:

(1) The 505(b)(2) application failed to contain a patent certification or statement with respect to each listed patent for a drug product approved in an NDA that:

(i) Is pharmaceutically equivalent to the drug product for which the original 505(b)(2) application is submitted; and
(ii) Was approved before the original 505(b)(2) application was submitted.

(19) The 505(b)(2) application failed to contain a patent certification or statement with respect to each listed patent for a drug product approved in an NDA that:

(1) Is pharmaceutically equivalent to the drug product for which the original 505(b)(2) application is submitted; and
(2) Was approved before the original 505(b)(2) application was submitted.

§ 314.127 Refusal to approve an abbreviated new drug application (ANDA)

(a) FDA will refuse to approve an abbreviated new drug application (ANDA) for a new drug under section 505(j) of the Federal Food, Drug, and Cosmetic Act for any of the following reasons, unless the requirement has been waived under §314.90:

(1) Information submitted with the abbreviated new drug application (ANDA) is insufficient to show that each of the proposed conditions of use has been previously approved for the listed drug referred to in the application (ANDA).

§ 314.127 Refusal to approve an abbreviated new drug application (ANDA)

(a) FDA will refuse to approve an abbreviated new drug application (ANDA) for a new drug under section 505(j) of the Federal Food, Drug, and Cosmetic Act for any of the following reasons, unless the requirement has been waived under §314.90:

(2) Information submitted with the abbreviated new drug application (ANDA) is insufficient to show that each of the proposed conditions of use has been previously approved for the listed drug referred to in the application (ANDA).

(b) FDA will consider an inactive ingredient in, or the composition of, a drug product intended for parenteral use to be unsafe and will refuse to approve the abbreviated new drug application (ANDA) unless it contains the inactive ingredients, other than preservatives, buffers, substances to adjust toxicity, or thickening agents, in the same concentration as the listed drug, and if it differs from the listed drug in a preservative, buffer, or antioxidant, the application (ANDA) contains sufficient information to demonstrate that the difference does not affect the safety or efficacy of the drug product.

§ 314.125 Refusal to approve an application (NDA)

(b) FDA may refuse to approve an application (NDA) for any of the following reasons, unless the requirement has been waived under §314.90:

(1) The 505(b)(2) application failed to contain a patent certification or statement with respect to each listed patent for a drug product approved in an NDA that:

(ii) Was approved after September 24, 1984;
(iii) Was for a drug product that contains an active moiety that has been previously approved in another application (NDA) under section 505(b) of the Federal Food, Drug, and Cosmetic Act, and
(iv) Contained reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application, the approval of Agency will not make effective for a period of 3 years after the date of approval of the application, the approval of Agency will not approve a 505(b)(2) application or an abbreviated new drug application (ANDA) for the conditions of approval of the original application, or an abbreviated new drug application (ANDA), or an ANDA submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting the conditions of approval of an original new drug application (NDA).

(5) If a supplemental application (NDA):
(i) Was approved after September 24, 1984; and
(ii) Contained reports of new clinical investigations (other than bioavailability studies) that were conducted or sponsored by the applicant that were essential to approval of the supplemental application, the agency will not make effective (NDA) for a period of 3 years after the date of approval of the supplemental application, the approval of Agency will not approve a 505(b)(2) application or an abbreviated new drug application (ANDA) for a change, or an abbreviated new drug application (ANDA) submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting a change approved in the supplemental new drug application (NDA).

§ 314.125 Refusal to approve an application (NDA)

(b) FDA may refuse to approve an application (NDA) for any of the following reasons, unless the requirement has been waived under §314.90:

(1) The 505(b)(2) application failed to contain a patent certification or statement with respect to each listed patent for a drug product approved in an NDA that:

(ii) Was approved after September 24, 1984;
(iii) Was for a drug product that contains an active moiety that has been previously approved in another application (NDA) under section 505(b) of the Federal Food, Drug, and Cosmetic Act, and
(iv) Contained reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application, the approval of Agency will not make effective for a period of 3 years after the date of approval of the application, the approval of Agency will not approve a 505(b)(2) application or an abbreviated new drug application (ANDA) for the conditions of approval of the original application, or an abbreviated new drug application (ANDA), or an ANDA submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting the conditions of approval of an original new drug application (NDA).

(5) If a supplemental application (NDA):
(i) Was approved after September 24, 1984; and
(ii) Contained reports of new clinical investigations (other than bioavailability studies) that were conducted or sponsored by the applicant that were essential to approval of the supplemental application, the agency will not make effective (NDA) for a period of 3 years after the date of approval of the supplemental application, the approval of Agency will not approve a 505(b)(2) application or an abbreviated new drug application (ANDA) for a change, or an abbreviated new drug application (ANDA) submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting a change approved in the supplemental new drug application (NDA).

§ 314.125 Refusal to approve an application (NDA)

(b) FDA may refuse to approve an application (NDA) for any of the following reasons, unless the requirement has been waived under §314.90:

(1) The 505(b)(2) application failed to contain a patent certification or statement with respect to each listed patent for a drug product approved in an NDA that:

(ii) Was approved after September 24, 1984;
(iii) Was for a drug product that contains an active moiety that has been previously approved in another application (NDA) under section 505(b) of the Federal Food, Drug, and Cosmetic Act, and
(iv) Contained reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application, the approval of Agency will not make effective for a period of 3 years after the date of approval of the application, the approval of Agency will not approve a 505(b)(2) application or an abbreviated new drug application (ANDA) for the conditions of approval of the original application, or an abbreviated new drug application (ANDA), or an ANDA submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting the conditions of approval of an original new drug application (NDA).

(5) If a supplemental application (NDA):
(i) Was approved after September 24, 1984; and
(ii) Contained reports of new clinical investigations (other than bioavailability studies) that were conducted or sponsored by the applicant that were essential to approval of the supplemental application, the agency will not make effective (NDA) for a period of 3 years after the date of approval of the supplemental application, the approval of Agency will not approve a 505(b)(2) application or an abbreviated new drug application (ANDA) for a change, or an abbreviated new drug application (ANDA) submitted pursuant to an approved petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act that relies on the information supporting a change approved in the supplemental new drug application (NDA).
patent certifications or statements), submission of patent information and requests by the NDA holder to amend or withdraw a patent or patent information, submission of a new patent listing dispute, and notification of court actions or written consent to approval) received by FDA on or after the effective date. In addition, a person (including a 505(b)(2) or ANDA applicant) may submit a request under § 314.53(f)(1) for an NDA holder to confirm the accuracy or relevance of previously submitted patent information in light of requirements for submission of patent information on and after the effective date of this final rule.