Changes to Orange Book Patent Information

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Celebrating 40 Years: An In-Depth Examination of the FDA Orange Book
October 27, 2020

Learning Objectives

1. Describe how to submit and make changes to patent information
2. Discuss patent expiration date extensions
3. Describe the patent delisting process
4. Discuss what patent information to submit for supplement approvals, including "Rx-to-OTC" switches

Regulatory Framework

- Final rule implementing portions of Title XI of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA)
- 81 FR 69580 (10/6/2016)

Form FDA 3542a vs. 3542

- Submitting patent information with an original NDA, an amendment, or a supplement prior to approval?
  - Form FDA 3542a
- Submitting information on a patent that claims an approved drug or an approved method of using the drug after approval of an NDA or supplement?
  - Form FDA 3542

Patent Information Submission

- Orange Book lists patents per Form FDA 3542
- Electronic common technical document (eCTD) format required
- Prominent submission identification:
  - "Patent Information"
  - After NDA approval: "Time Sensitive Patent Information"

Submitting Changes on Form FDA 3542

- Ensure use of most recent form
- Section 1g is generally “Yes”
- Section 1h should note all relevant changes to patent listing

g.	Has the patent referenced above been submitted previously for listing for this drug product? ☐ Yes ☐ No
h.	If the answer to question 1.g. is “Yes,” identify all change(s) from the previously submitted Form 3542 and specify whether each change is related to the patent or related to an FDA action or procedure. (See FORM FDA 3542 SUPPLEMENT – FORM INSTRUCTIONS for additional information regarding changes to the method(s) of use listed for the patent).

Submitting Changes on Form FDA 3542

- Verify completeness of form
  - Section 1e: U.S. Agent
  - Section 4: Method of use
  - Section 6: Signature

Changes to Patent Information

- Prompted by NDA holder request (314.53(f)(2))
- Reason for changes:
  i. No longer meets statutory requirements for listing
  ii. Patent term restoration (expiration date extensions)
  iii. Corrections or changes to patent information

Statutory Requirements No Longer Met

- Promptly notify FDA to amend or withdraw patent information
- If required by court order, submit copy of order within 14 days of order entry

Patent Term Restoration

- NDA holder requirement to provide prospective applicants timely notice of changes
- Expiration date correction submitted on Form FDA 3542
  - Tips for Sections 1g and 1h
- Submitted within 30 days of relevant documentation
  - Certification of extension receipt per 35 U.S.C. 156(e)(1)
  - Documented patent term extension per 35 U.S.C. 156(e)(2)

Patent Corrections or Changes

- Corrections or changes to previously submitted patent information
- Must be submitted on Form FDA 3542 or 3542a
  - Exceptions: requests for patent withdrawals

Timely Method of Use Amendments

- If submitted within 30 days of the following:
  1. Patent issuance
  2. Approval of a corresponding change to product labeling
  3. A relevant decision by the U.S. Patent and Trademark Office or a Federal court (21 CFR 314.53(f)(2))
  4. Patent listing dispute (21 CFR 314.53(f)(1))
- Outside of these circumstances, changes to approved method(s) of use are not considered timely filed

Error Correction Requests

- Contact the Orange Book staff at our mailbox orangebook@fda.hhs.gov
- Considered on case-by-case basis
- Updated as soon as practicable

Consequence of Untimely Filed Patents

Generally, applicants for pending ANDAs or 505(b)(2)'s are not required to submit a patent certification or statement to address the patent or patent information that is late-listed with respect to the pending ANDA or 505(b)(2) application

Challenge Question #1

The following are the reason(s) that an NDA holder may request changes to Orange Book patent listings:

a. Patent expiration date change

b. Patent claims no longer meet statutory requirements

c. Corrections to previously submitted patent information

d. All of the above

e. None of the above

Orange Book Patent Delisting

Patent Delisting Submissions

- May be submitted by letter or Form FDA 3542
  - Form FDA 3542 not required
- Identify as "Time Sensitive Patent Information"
- Must include:
  1. NDA number
  2. Each applicable product(s)
  3. Patent number

See *§ 314.53(f)(2)(iv)*

Patent Delisting Process

- Has all required information been submitted?
- Based on 180-day exclusivity eligibility, can patent be removed from Orange Book?
  - Yes: Patent listing is removed 
  - No: Delist flag “Y”, patent remains listed 

Orange Book Patent Listing

- Delist impermissible

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	7888362	04/12/2026	DS			Y	07/17/2015

- Patent delisted from Orange Book

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
Your search did not return any results							

Patent Delist Request Flag

- Patent delist request flag “Y”
- NDA holder has requested delist of patent
- First applicant may retain eligibility for 180-day exclusivity

Delist Requested	Submission Date
Y	07/17/2015

Patents with Delist Flag

- ANDA applicants must submit or maintain appropriate certifications to the patent
- Applicants under 505(b)(2) not required to certify when this flag is “Y”
- Removal after associated 180-day exclusivity has expired or has been extinguished or relinquished

Orange Book Delisted Patents List

- List of patents delisted since most recent Annual Edition
- Delisted Patents list

Delisted Patents List

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

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Delisted Patents

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Appl No	Active Ingredient	Proprietary Name	Dosage Form	Route	Strength	Patent No.	Patent Use	Mkt. Status	Submission Date
N202450	ACLIDINIUM BROMIDE	TUDORZA PRESSAIR	POWDER, METERED	INHALATION	0.4MG/INH	6750226	U-1264	RX	08/17/2012
N207202	ARIPIPRAZOLE	ABILIFY MYCITE KIT	TABLET	ORAL	10MG	9577864	U-2169	RX	12/12/2017
N207202	ARIPIPRAZOLE	ABILIFY MYCITE KIT	TABLET	ORAL	15MG	9577864	U-2169	RX	12/12/2017
N207202	ARIPIPRAZOLE	ABILIFY MYCITE KIT	TABLET	ORAL	20MG	9577864	U-2169	RX	12/12/2017
N207202	ARIPIPRAZOLE	ABILIFY MYCITE KIT	TABLET	ORAL	2MG	9577864	U-2169	RX	12/12/2017
N207202	ARIPIPRAZOLE	ABILIFY MYCITE KIT	TABLET	ORAL	30MG	9577864	U-2169	RX	12/12/2017
N207202	ARIPIPRAZOLE	ABILIFY MYCITE KIT	TABLET	ORAL	5MG	9577864	U-2169	RX	12/12/2017
N022250	DALFAMPRIDINE	AMPYRA	TABLET, EXTENDED RELEASE	ORAL	10MG	8007826	U-1030	RX	09/28/2011

Challenge Question #2

Patent delist or withdrawal requests may be submitted to the Agency on the following:

a. Form FDA 3542

b. Letter

c. On Form FDA 3542 or by letter

d. None of the above

Reissued Patents

- After patent reissuance, original patent ceases to have legal effect
- NDA holder required to request original patent removal from Orange book
- Original patent may remain listed due to 180-day exclusivity eligibility (21 CFR 314.53(f)(2)(i))

Including Prescription to Over-the-Counter (RX to OTC) Switches

Patents for Supplemental Approvals

Requirements for Patent Submission

- Must submit patent information when seeking supplement approval for the following:
  - To add or change dosage form or route of administration
  - To add or change the strength
  - To change the drug product from prescription use to over-the-counter use
- May need to submit patent information for other changes

Patents for Supplemental Approvals

- Form FDA 3542 must be submitted for new patents relevant to the supplemental approval
  - Supplement approval date identified
  - Select Supplement
  - Section 4.2b aligning with labeled indication
- FDA Forms - Form FDA 3542 Instructions

Timely Filed Patent Information

- ✓ Within 30 days after approval date of NDA or supplement
- ✓ Within 30 days of issuance date of a post-approval patent
- ✓ Within 15 days of FDA notification of incomplete form

RX-to-OTC Switches: General

- Prescription (RX) to over-the-counter (OTC) supplemental approvals may occur
- RX product number is retained for OTC product listing

RX-to-OTC Switches: Patent Processing

- New Form FDA 3542 for each patent must be submitted for the new OTC product listing
- Currently listed patent information is retained for 30 days after OTC approval
- If no new Form FDA 3542 is received, patents are delisted

Challenge Question #3

After an RX-to-OTC switch supplemental approval occurs, the NDA holder should do the following:

a. Submit relevant new Forms FDA 3542 for OTC product listing within 30 days of approval

b. Submit relevant new Forms FDA 3542a for OTC product listing within 30 days of approval

c. Both a and b

d. None of the above

Challenge Question #4

- **Question [True/False]:** After an RX-to-OTC switch supplemental approval occurs, the NDA holder's listed patents will automatically be retained in the Orange Book product listings after 30 days.
- Answer: False.

Summary

- Patent information and changes are submitted and listed according to Form FDA 3542
- Patent delisting requests may be submitted to the Agency by letter
- New patent forms must be submitted for each relevant patent after an RX-to-OTC switch

Questions?

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Closing Thought

Timely and complete submissions of patent changes help to ensure accurate Orange Book patent listings.


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ADMINISTRATION