Best Practices for 505(b)(2) and ANDA Applicants

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Learning Objectives

- Explain types of patent certifications
- Discuss how & when to respond to changes to patent information
- Review other best practices for ANDAs
- Apply what was discussed in a case study
- Bring it all together with challenge questions

Patent Certifications

- Applicants must ‘certify’ with respect to each patent listed for the reference listed drug (RLD) in the Orange Book
  - 314.50(i)(1) for 505(b)(2)s & 314.94(a)(12) for ANDAs
- If there are no patents listed, or they are expired:
  - Patent information has not been filed (Paragraph I certification)
  - The patent has expired (Paragraph II certification)
  - No relevant patents

Patent Certifications (continued)

- If there are unexpired patents listed:
  - The date on which the patent will expire (Paragraph PIII certification)
  - That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted (Paragraph PIV certification)
  - Method-of-use (MOU) patent
    - For ANDAs, also known as a section viii statement
  - PIV certification/method-of-use
    - Some times referred to as a split certification

Notice of Paragraph IV Certification

- 314.52 for 505(b)(2)s & 314.95 for ANDAs
  - a. Notice of certification
  - b. Sending the notice
  - c. Content(s) of a notice
  - d. Amendment or supplement
  - e. Documentation of timely sending & receipt of notice
  - f. Forty-five day period after receipt of notice

Notice of Paragraph IV Certification

- Sending the notice
  - Applicant must provide notice of Paragraph PIV certification to the RLD holder/patent owner(s) within 20 days after the date of the postmark on the PIV acknowledgment letter
- Documentation of timely sending & receipt of notice
  - Applicant must submit documentation to FDA
  - 21 CFR 314.52(e) & 21 CFR 314.95(e)
- Forty-five day period after receipt of notice
  - NDA holder/patent owner(s) have 45 days from the receipt of notification to initiate a lawsuit against the 505(b)(2) or ANDA applicant

Common Issues with Sending Notice

- Notice documents missing, not provided to FDA
- Notice documents don’t align or are incomplete – was notice appropriately provided?
- Licensure agreement but notice documents missing
- Notifying FDA if litigation is filed within the 45-day period after receipt of notice

Changes in Patent Information

Changes in Patent Information

- Newly listed patents
- New use codes
- Revised use codes

Newly Listed Patents

- An Applicant must address all new, timely filed patents listed in the Orange Book after its application has been filed with one of the previously discussed patent certifications
  - Applicant must also comply with regulations (i.e., sending notice & documentation of delivery of notice)
  - No stay of approval associated with patents listed after application has been acknowledged for filing

Timely vs Untimely Filed Patent

- A patent is deemed untimely filed if the patent is submitted for listing more than 30 days after:
  - the NDA is approved,
  - the patent is issued, or
  - approval of a supplement that allows for the listing of the patent
- An Applicant whose application has been acknowledged for filing is not required to certify to untimely filed patents
  - If an Applicant provides a patent certification to an untimely filed patent, they can withdraw the certification

New Use Codes

- Similar to new patents, the RLD can list new use codes for previously submitted patents
  - If the new use code is timely filed, Applicant must address it

Revised Use Codes

- RLDs can revise use codes
- Applicants must update their patent certification if the revised use code is timely filed & the applicant has submitted a PIV certification, method-of-use statement, or split certification to that patent
- Use codes that are the basis of 180-day exclusivity for ANDAs cannot be delisted until after 180-day has been forfeited or expired

Sending Notice of PIV Certification

- If an applicant elects to certify PIV to a newly listed or revised use code, they are required to send notice of PIV certification
- Must follow appropriate regulations
  - 314.52 for 505(b)(2)
  - 314.95 for ANDAs

Case Study – Revised Use Code

- The RLD is Gilenya (fingolimod) 0.5 mg capsule, NDA 22527
- Patent ‘405 added to Orange Book 12/2/2015 with the patent use code U-1086 (Treatment of autoimmune disease)
- ANDA X is submitted on 01/01/2018 with a PIV certification to patent ‘405 & the associated use code U-1086, ANDA X is sued

Case Study – Revised Use Code

- On 8/16/2019, a supplement is approved for the RLD, SUPPL-29
  - Within 30 days of supplement approval, RLD submits a Form FDA-3542 to revise the U-1086 use code to U-2613 (Treatment of relapsing-remitting Sclerosis (MS))
  - ANDA X submits a labeling amendment on 12/01/2019 in response to latest RLD labeling update; labeling amendment seeks to add a new indication or other condition of use

Case Study – Revised Use Code

- Since the RLD has revised their use code (U-1086 revised to be U-2613), ANDA X's original PIV cert to patent '405 is no longer valid
- If the applicant for ANDA X wishes to maintain the PIV certification to patent '405, they must recertify & renotify under 21 CFR 314.96(d)(1), since their labeling amendment seeks, 'to add a new indication or other condition of use'

Other Best Practices for ANDAs

Other Best Practices for ANDAs

- Pediatric Exclusivity
  - ANDA Sponsors may not maintain a PIV certification to an expired patent
  - Pediatric exclusivity waivers
    - Waiver is on the NDA holders' letterhead
    - Waiver is signed by NDA's responsible agent
    - Wavier has an effective date

Other Best Practices for ANDAs

- Court Documents
  - Notify FDA of the entry of all final court orders or judgments (314.107(e))
  - Please provide complete copy of first civil action complaint with civil action number
- Commercial Marketing for first filers
  - Notify FDA within 30 days of marketing (314.107(c)(2))
  - Includes marketing of an authorized generic!

Challenge Question #1

Which of the following can be addressed with a section viii statement?

A. Drug product patent

B. Drug substance patent

C. Method-of-use patent

D. None of the above

Challenge Question #2

An ANDA applicant is a first filer & the basis for their 180-day exclusivity is patent ‘222, a method of use patent with use code U-111. Which of the following statements is NOT true?

A. The RLD can delist their use code, & the first filer will lose their 180-day seat

B. The ANDA applicant can revise their PIV certification to a section viii statement and retain eligibility to 180-day exclusivity

C. If the RLD lists a new use code for patent ‘222 & the ANDA applicant submits a PIV certification there will be a new stay of approval

D. All of the above

Summary

- All applicants must address all patents listed in the Orange Book
- If a new patent or use code is timely filed & listed in the Orange Book after an application is submitted but before it is approved, Applicants must address it with an appropriate patent certification or statement
- There is no additional stay of approval for PIV certifications to newly listed patents or use codes

ANDA Questions?

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