How Recent FDA Guidelines Impact Generic Pharma Companies

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Background

What are Rules and Guidances?

- **What is a Rule (or Regulation)?**
  - Prepared and implemented by an agency (FDA) in order to clarify and enforce its statute
  - Notice & Comment
  - Binding
- **What is a Guidance?**
  - Reflects an Agency's thinking
  - Not binding

The Final Rule

- **"Abbreviated New Drug Applications and 505(b)(2) Applications"**
- **Published October 6, 2016**
- **Two Main Purposes**
  - To implement the MMA (enacted Dec. 2003)
  - To reflect court decisions

When in Effect, and What They Affect

- **Effective Date December 5, 2016**
- **All new NDAs, 505(b)(2)s, and ANDAs submitted after that date**
- **Prior Applications**
  - Patent amendments
  - Listing of new patents
  - Challenges to patent listing
  - Reporting court decisions

New Definitions

21 C.F.R. § 314.3

New Definitions

- **"505(b)(2) Application"**
  - Defined as a subset of 505(b)(1) applications (NDAs)
  - Rules that apply to NDAs apply to 505(b)(2)s
- **"Reference Standard"**
  - The drug product selected by FDA for which an ANDA applicant must perform BE studies
  - (as opposed to RLD, which encompasses all brand dosage strengths)

New Definitions

- **"Acknowledgement Letter"**
  - Written communication from FDA that an ANDA is sufficiently complete for substantive review
- **"Paragraph IV Acknowledgement Letter"**
  - Written communication from FDA that a 505(b)(2) or ANDA with P-IV is sufficiently complete for substantive review

New Definitions

- **"Commercial Marketing"**
  - Introduction into interstate commerce of an ANDA drug *or an AG*, outside control of the ANDA holder
  - Implications:
    - Marketing an AG by an FTF can trigger the 180-day exclusivity
    - Exports from Indian parent to its US subsidiary?
      - Both should be identified in ANDA
    - Settlements w/brand

Marketing Notice

21 C.F.R. § 314.107(c)(2)

FTF Marketing Notice

- New ANDAs (submitted after Dec. 5, 2016)
- A first-filer must inform FDA within 30 days of beginning marketing
- Penalty: 180-days deemed to begin upon final approval
- Unforeseen Issue?
  - Multiple first filers

FDA Stay of Approval

(a/k/a 30-Month Stay of Approval)

21 C.F.R. § 314.107(b)(3)

FDA Stay of Approval

- **New regulations codify FDA's previous policies**
- **Entry of a Preliminary Injunction (PI) during original stay period extends the stay**
  - PI: *likelihood* of both validity and infringement PI
- **Stay ends upon**
  - Win by ANDA
  - Court order to end stay
  - Lawsuit dismissal without finding on infringement

New NDA Orange Book Requirements

21 C.F.R. §§ 314.53 (b) and (f)

Heightened Use Code Requirements

- **Applies to**
  - New NDAs and 505(b)(2)s
  - New patent listings in old NDAs and 505(b)(2)s
- **Use Code Must Be Specific to the Approved Indication of Use**
  - Broad claim: narrower UC, only to specific approved MOU
  - Coextensive claim: UC only to the specific approved MOU
  - Narrower claim: UC only to the specific approved MOU claimed in the patent (not the broader product insert)
- **MOU**
  - Use Code limit increased to 250 characters
  - Must specifically identify sections of package insert

Updating OB info

- **NDA holder must update w/in 14 days if:**
  - Patent no longer meets requirements for listing
    - E.g., non-appealable finding of invalidity
  - A court orders NDA holder to amend or withdraw patent from OB
  - Patent term is extended by PTO
- **FDA won't remove from OB if implicates 180-days**
- **Generic's remedy: delisting counterclaim**

Challenging OB Information

21 C.F.R. § 314.53(f)(1)

Challenging OB Information 21 C.F.R. § 314.53(f)(1)

- **Anyone can challenge listing of any patent listed for any NDA**
  - Anyone:
    - Does not need to be a generic company or an ANDA/505(b)(2) applicant
  - Any Patent:
    - Does not need to be a P-IV or section viii patent
    - Regardless of date listed
  - Any NDA
    - Regardless of approval date

Challenge Procedure

Drug Substance or Product	Method of Use
• **Challenger Submits Statement of Dispute** – Specific grounds for disagreement with accuracy or relevance • **FDA Forwards (unreviewed) to NDA Holder**	• **Challenger Submits Statement of Dispute** – Specific grounds for disagreement with accuracy or relevance – Limited to narrative description of scope of patent claim, up to 250 characters • **FDA Forwards (unreviewed) to NDA Holder**

Challenge Procedure (cont.)

Drug Substance or Product	Method of Use
• **NDA Holder Must Respond w/in 30 Days (Form 3542) to:** – Confirm correctness of listing, or – Amend or withdraw listing	• **NDA Holder Must Respond w/in 30 Days (Form 3542) to:** – Confirm correctness of Use Code, or – Amend patent information (e.g., UC of up to 250 characters)

Challenge Procedure (cont.)

Drug Substance or Product	Method of Use
• FDA will not change OB listing unless NDA holder amends or withdraws	• Rule Does Not Address Any "Default" FDA Action

Remedy?

- Court order in a validity action
- Counterclaim for delisting or correction
- Standing: not just "Anyone"

Revised Notice Letter Requirements

21 C.F.R. § 314.95

Notice Letter Timing & Content

- **Notice Letter is Invalid if Sent:**
  - Before receipt of Paragraph IV acknowledgment letter, or
  - After P-IV letter, but before 1st working day after new patent is listed in OB (for newly-listed patent)
- **Contents:**
  - Slightly revises or adds some required statements
  - E.g., that the applicant has received the P-IV acknowledgment letter for the ANDA

Sending the Notice Letter

- **Method of Sending**
  - **Old:** USPS registered mail, or advance permission
  - **New:** registered or certified mail OR any "designated delivery service"
  - Designated Delivery Service:
    - Generally available to the public
    - Maintains electronic records
    - Overnight or 2-day delivery services
    - E.g., FedEx, UPS

Thank you!

Questions? pbraier@gbpatent.com

All views expressed are Paul Braier's, and are not necessarily the views of Greenblum & Bernstein, P.L.C.