Registration Patents and Exclusivity for 505(b)(2)

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Objectives

- To develop 505(b)(2) submission strategies that are consistent with legal and regulatory requirements and have the potential to provide exclusivity protection and maximize patent protection
- To determine that no patents listed in the Orange Book will be infringed
- To determine if the 505(b)(2) submission is eligible for 1 or more types of exclusivity
- To determine potential barriers to 505(b)(2) approach

Methods

Step 1: Research existing patents

Review patents listed in Orange Book and exclusivity periods

Step 2: Research patents

Review Paragraph IV Certifications submitted to FDA

Step 3: Determine type of data to be submitted:

Bioequivalence and bioavailability data comparing new dosage form to reference listed drug

Toxicology and other preclinical data

Clinical studies to support approval of a new indication

Clinical studies to demonstrate safety and efficacy of an NCE not approved in the US

Clinical studies in pediatric patients

Step 4: Determine any potential applicable exclusivity

New Chemical Entity exclusivity (NCE or significant change)

Patent exclusivity (and restoration under Waxman-Hatch)

Orphan Drug exclusivity

Pediatric exclusivity

Evaluation

- New regulations that went into effect on June18, 2003, apply to patent submissions and listing requirements made on or after August 18, 2003. A Paragraph IV patent certification must certify one of the following:
  - Patent information has not been filed
  - The patent has expired
  - The patent will expire on a specific date
  - The patent is invalid or will not be infringed
- Clinical Data
  - No exclusivity for bioavailability or bioequivalence data alone
  - 5 years exclusivity for an NCE that requires clinical studies conducted by the applicant for approval
  - 3 years exclusivity for a significant change to an approved entity, such as a new indication that requires clinical studies conducted by the applicant for approval
  - 7 years exclusivity for an orphan drug
  - 6 months exclusivity added to existing exclusivity for conducting and submitting pediatric studies in response to a written request
- Barriers to 505(b)(2) Strategies
  - Unexpired patents for reference listed drug for which non-infringement can not be certified
  - Unexpired exclusivities:
    - Patent
    - NCE or significant change
    - Orphan drug
    - Pediatric

Results - Example

Orange Book Search

- Patents and Exclusivity for Zantac:

Paragraph IV Certifications as of September 1, 2004 submitted for Zantac (ranitidine):

Drug Name	Dosage Form	Dosage Strength	RLD
Ranitidine	injection	25 mg/mL, 2 mL and 6 mL and 40 mL vials	Zantac
Ranitidine	tablets	75 mg, 150 mg and 300 mg	Zantac
Ranitidine	capsules	150 mg and 300 mg	Zantac
Ranitidine	oral solution	15 mg/mL	Zantac

Conclusions

Carefully developed 505(b)(2) submission strategies may provide market protections through various exclusivities available for a new sponsor or for innovator of a marketed NCE.

- 505(b)(2) applications are subject to marketing protections of other applicants
  - During the period that the 5 year (NCE) or 3 year (new clinical trials) exclusivity is in effect, FDA may not accept or approve certain applications that rely on the protected product for approval.
  - The only exception is a 505(b)(2) application that contains a Paragraph IV certification can be submitted to FDA after 4 years but not approved until the exclusivity expires.
  - A 505(b)(2)application can not be approved during pediatric or orphan drug exclusivity periods of the protected product.
- Applications submitted under 505(b)(2) may also be protected by exclusivities
  - Patent exclusivity may restore up to five years of patent life for a new product based on the regulatory review period (testing phase and approval phase).
  - Orphan Drug exclusivity is available for a drug that treats a rare disease affecting fewer than 200,000 patients in the US.
  - Pediatric exclusivity can add 6 months to other existing exclusivities.