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The Next Wave of Generic Litigation: Biologics

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December 2014

What is a Biologic or Biological Product?

- Biological Product
  - Biological products are therapies used to treat diseases and health conditions.
  - Include a wide variety of products including vaccines, blood and blood components, gene therapies, tissues, and proteins (except any chemically synthesized polypeptide).
  - Unlike most prescription drugs made through chemical processes, biological products generally are made from human and/or animal materials.
  - *See* 42 USC §262(i)(1)

What is a Biosimilar?

- Biosimilar as defined by 42 USC §262(i)(2) :
  - The biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and
  - There are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.
- A biosimilar is essentially an officially approved subsequent version of an innovator biopharmaceutical product made by a different sponsor following patent and exclusivity expiry on the innovator product.

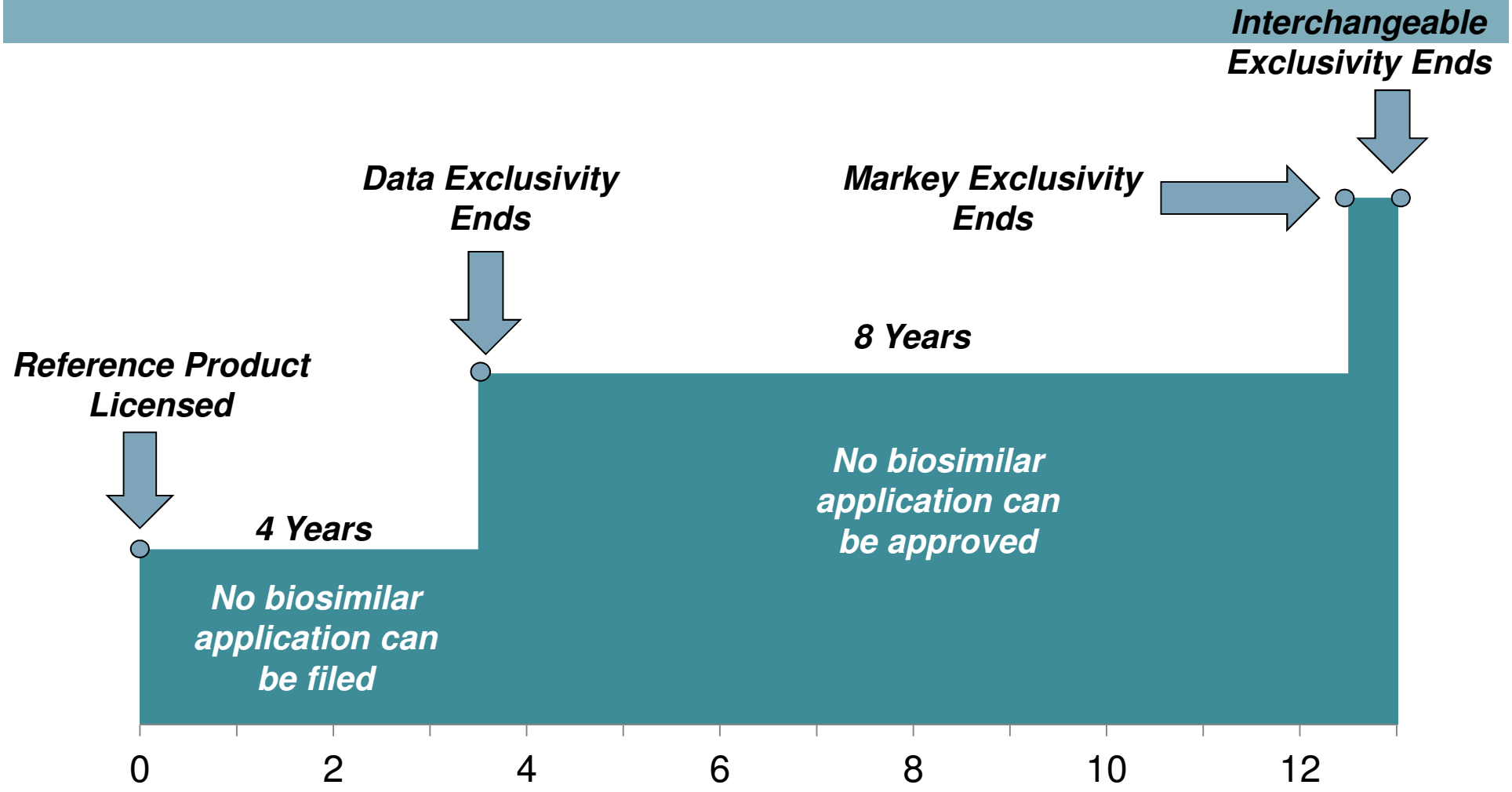
"The Biosimilars Act"

- Biologics Price Competition & Innovation Act of 2009 (BPCIA or "The Biosimilars Act")
  - Part of the Patient Protection and Affordable Care Act ("Obamacare") that was signed into law on March 23, 2010.
- Amended the Public Health Service Act by adding:
  - § 351(k) – licensure requirements for follow-on biologics ("FOB") as either:
    - Biosimilar
    - Interchangeable
  - § 351(l) – framework for patent infringement disputes

Biosimilar vs. Interchangeable

- Biosimilar
  - A biosimilar product is not identical to an innovator product
  - **No clinically meaningful differences** between the biosimilar and the approved biological product in terms of the safety, purity, and potency
  - Instead it must be "highly similar"
    - it must have the identical amino acid sequence and must be highly similar in higher order structures, physicochemical properties, post-translational processing attributes, purity and impurities, and biological and immunochemical functions.
- Interchangeable
  - Interchangeable biologics must produce the **same clinical result** in any given patient, and without negative effects, in terms of safety or efficacy
  - Interchangeable biologics may be substituted without the intervention of the healthcare provider

Data Exclusivity



Data Exclusivity

- The Reference Product Sponsor ("RPS") —the innovator—is entitled to certain data exclusivities:
  - No § 351(k) application can be **filed** until **4 years** after the date the reference product was first licensed by FDA
  - No § 351(k) application can be **approved** until **12 years** after the date the reference product was first licensed by FDA
- Pediatric Exclusivity – Each data exclusivity can be extended for six months

Exclusivity for First FOB

- The first § 351(k) applicant to obtain FDA approval as "interchangeable" receives marketing exclusivity.
  - Subsequent applications for interchangeable product cannot be approved for **one year**.
  - Does not prevent approval of biosimilar products based on the same reference product.
- Interchangeable exclusivity can be shortened or forfeited.
- No market exclusivity for "biosimilar" products.

Pre-Litigation Timeline

Mandatory Disclosure

§ 351(k) application accepted for review

20 days

RPS provided with:

- Complete § 351(k) application
- Information regarding manufacture of FOB

Pre-Litigation Timeline

Confidentiality

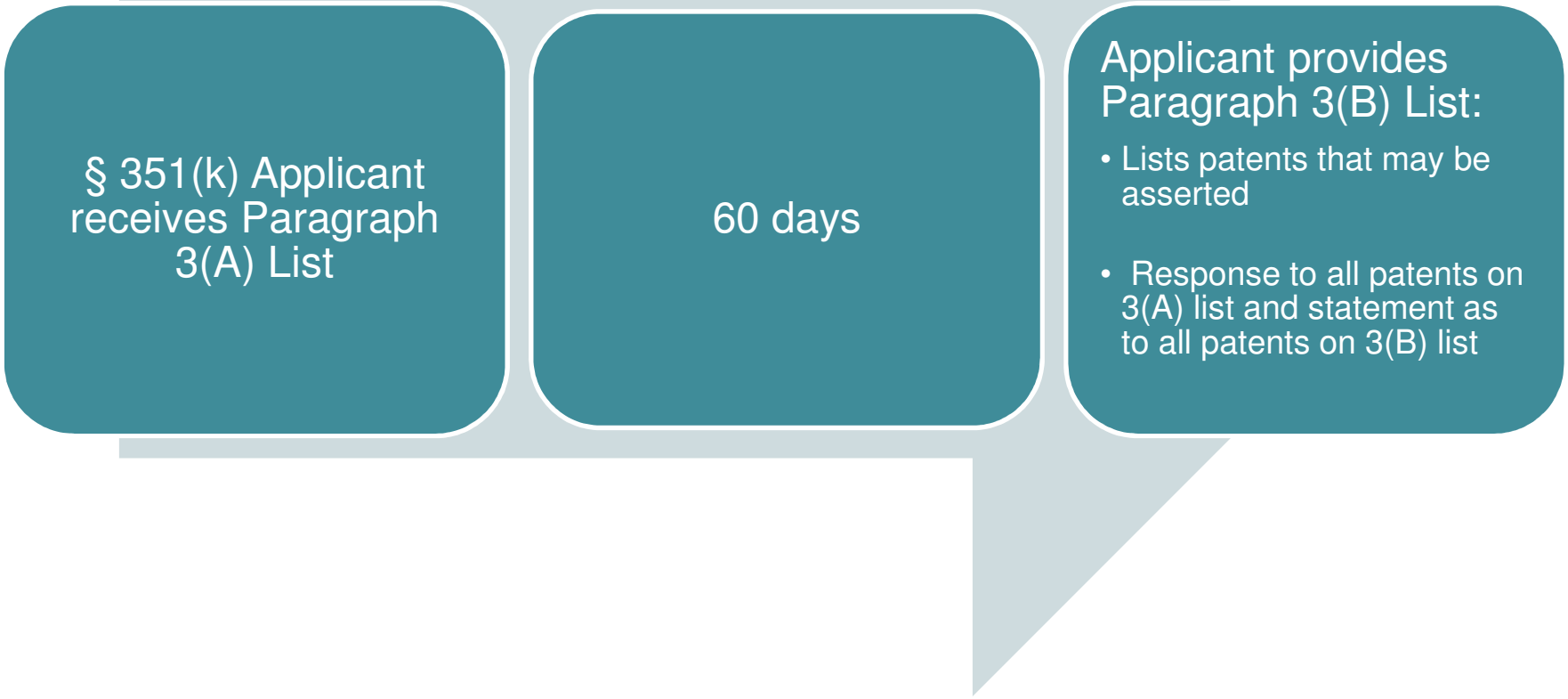
- Information provided to RPS may only be used to determine whether an infringement action can be brought.
- Provided to:
  - Outside Counsel
  - One in-house counsel
- No automatic to disclosure to in-house employees or experts

Pre-Litigation Timeline

Paragraph 3 List

Pre-Litigation Timeline

351(k) Applicant Response



Pre-Litigation Timeline

351(k) Applicant Response

- Patent challenges must include a detailed statement that explains the basis of the contention of why each claim is:
  - Invalid;
  - Unenforceable; or
  - Would not be infringed by the commercial marketing of the FOB.
- Statement of intent must indicate that the applicant does not intend to begin commercial marketing until patent expiry.

Pre-Litigation Timeline

Paragraph 3 List

Pre-Litigation Timeline

Mandatory Negotiation

- Following the exchange of the 3(A) and 3(B) Lists:
  - Parties must engage in good faith negotiation regarding patents to be included in infringement action.
  - Negotiations last maximum of **15 days**
  - If agreement is reached, RPS must bring suit on agreed upon patent list within **30 days**.
  - If no agreement reached, parties exchange Paragraph 5 lists with proposed patents-in-suit, which all must be included in lawsuit

Lawsuit Filed

- The RPS must bring suit within 30 days either
  - Agreement on list of patents is reached; or
  - Exchange of Paragraph 5 Lists.
- Failure to timely file suit will limit remedies available to the RPS.
  - Reasonable royalty only available.
- Must notify FDA of lawsuit

Differences from Hatch-Waxman Litigation

Hatch-Waxman

- Shorter Exclusivities
- Covered patents listed in the Orange Book
- Automatic 30-month stay if Reference Product Sponsor files suit within 45 days of receiving notice of Paragraph IV certification against patent previously listed in the Orange Book.

Biosimilars Act

- Longer Exclusivities
- No Orange Book listing.
- RPS identifies Orange Book-type patents after reviewing copy of § 351(k) application.
- Step-wise procedure for determining patents-in-suit.
- Mandatory Negotiations
- Patents-in-suit determined by bother parties

Strategy for RPS

Portfolio Management

- Develop Patent Portfolio
  - Organize patent portfolio to identify patents applicable to specific biosimilar application
  - Obtain claims that cover design-arounds and/or alternative manufacturing processes
  - Ensure you obtain claims for modifications/improvements/alternate processes/etc.

Strategy for RPS

Portfolio Management

- Consider the potential use of AIA procedures to strengthen portfolio
  - Ex Parte Reexamination
  - Reissue (no prohibition re deceptive intent)
  - Supplemental Examination
  - Continuations
  - New Filings
  - Interferences/Derivation

Strategy for RPS

Litigation Strategy

- Review licensed patents applicable to specific biosimilar applicant
  - Consider licensing/acquiring third-party patents that could be asserted against applicant
- Identify patents that may be appropriate to license to applicant
- Evaluate risk associated with identifying patents during Paragraph 3 List exchanges

Strategy for Applicant

Pre-Litigation Strategy

- Proactively identify RPS' patents
  - Monitor RPS' patent portfolio for pending applications that could issue
  - Identify public licensing deals
- Develop invalidity positions early
  - Search for prior art
  - Consult with experts on invalidity issues
- Develop non-infringement positions early
  - May require testing or expert analysis depending on claims
  - Rely upon the "safe harbor" exemption of 271(e)(1)?

Strategy for Applicant

Post AIA Patent Challenges

- Patents
  - Ex Parte Reexamination
  - Inter Partes Review (IPR)
  - Post-Grant Review (PGR)
  - Interference/Derivations
- Patent Applications
  - 3rd party submissions to PTO
  - Interference/Derivation Proceedings
  - Protest §1.291

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Questions?