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INTELLECTUAL PROPERTY LAW

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U.S. Biosimilars
Red Flags for Patent Attorneys

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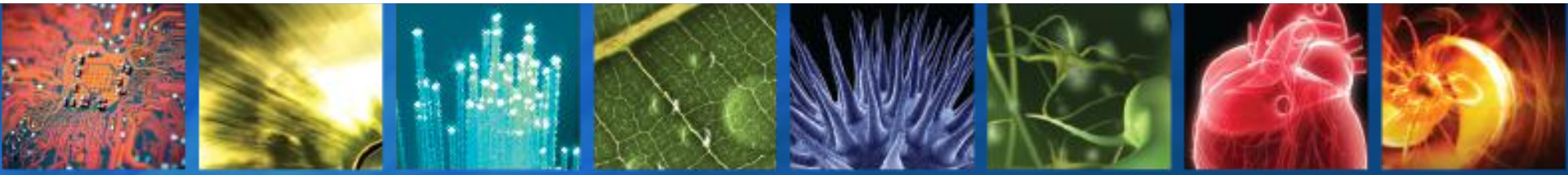

Biologics Price Competition and Innovation Act ("the Biosimilars Act")

- Signed into law March 23, 2010, as part of the Patient Protection and Affordable Care Act of 2009; amends § 351 of the Public Health Services Act.

- Codified at 42 U.S.C. § 262.

- Creates an abbreviated approval pathway for generic 'biological products' that are demonstrated to be *highly similar* (i.e., biosimilar) to or *interchangeable* with an FDA-licensed reference biological product.

What are Biological Products?

- Biological products are therapies used to treat diseases and health conditions. They 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, e.g.*, 42 USC § 262(i)(1) (emphasis added).
- "Protein" – any alpha amino acid polymer with a specific defined sequence that is greater than 40 amino acids in size. *See* FDA Draft Guidance, "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product" at 22.
- "Chemically synthesized polypeptide" – any alpha amino acid polymer that

  (1) is made entirely by chemical synthesis; and

  (2) is less than 100 amino acids in size. *See id*.

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How do you demonstrate biosimilarity? Interchangeability?

Biosimilarity - The Statute

A biosimilar is a biological product that is ***highly similar*** to an already approved biological product, notwithstanding minor differences in clinically inactive components, and for which there are ***no clinically meaningful differences*** between the biosimilar and the approved biological product ***in terms of the safety, purity, and potency***. *See* 42 USC § 262(i)(2) and (3) (emphasis added).

The FDA

- Current Draft Guidance Documents
  - Scientific Considerations in Demonstrating Biosimilarity to a Reference Product
  - Quality Considerations in Demonstrating Biosimilarity to a Reference Product
  - Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009
- Additional FDA Guidance expected in 2013
  - Submission of Clinical Pharmacology Data as Evidence of Biosimilarity for Biologics and Protein Products
- The FDA has not yet provided a guidance document regarding the standard for demonstrating interchangeability

Biosimilarity - What has the FDA told us?

The FDA will consider the "***totality of evidence*** provided by a sponsor to support a demonstration of biosimilarity, and recommends that sponsors use a ***stepwise approach*** in their development of biosimilar products." *See* FDA Draft Guidance, "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product" (emphasis added)

Biosimilarity - What has the FDA told us?

- The FDA expects that a showing of biosimilarity will be based on:
  - Analytical studies
  - Animal studies; and
  - A clinical study or studies. *See* FDA Draft Guidance, "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product"

- The type and amount of testing will be "determined on a product-specific basis." *Id.*

- As a whole, the guidance documents focus on extensive characterization of both the proposed biosimilar product and the reference product.

Biosimilarity

- What does this mean for patent attorneys?
- What types of tests, instruments, studies will be used to demonstrate biosimilarity?
- What kind of patent protection is in place?
  - 271(e) Safe Harbor
  - Need for testing post-approval
- When can the biosimilar application be filed with the FDA?
- What happens once the biosimilar application is filed with the FDA?

The Biosimilar Application

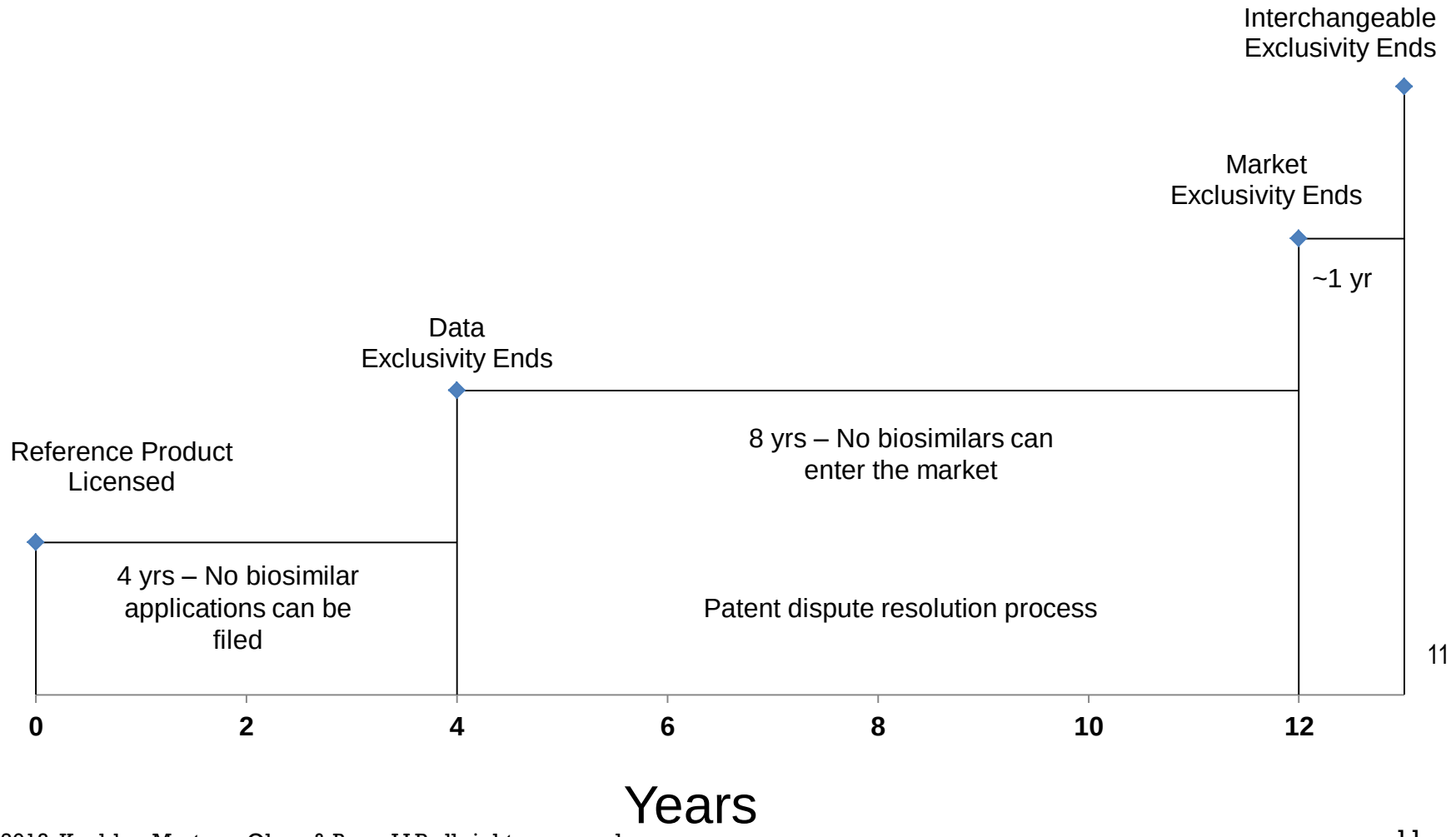
- An application submitted for biosimilar approval may not be submitted until four years after "the date on which the reference product was first licensed…." 42 USC § 262(k)(7)(B).

- An application submitted for biosimilar approval may not be approved until twelve years after "the date on which the reference product was first licensed…." 42 USC § 262(k)(7)(A).

- The filing of a biosimilar application triggers a complex exchange of information between the applicant and the reference product sponsor (RPS) prior to the filing of a lawsuit. 42 USC § 262(l).

- The filing of a biosimilar application constitutes an artificial act of patent infringement that confers jurisdiction on the federal courts. 35 U.S.C. § 271(e)(2)(C).

Exclusivity Timeline

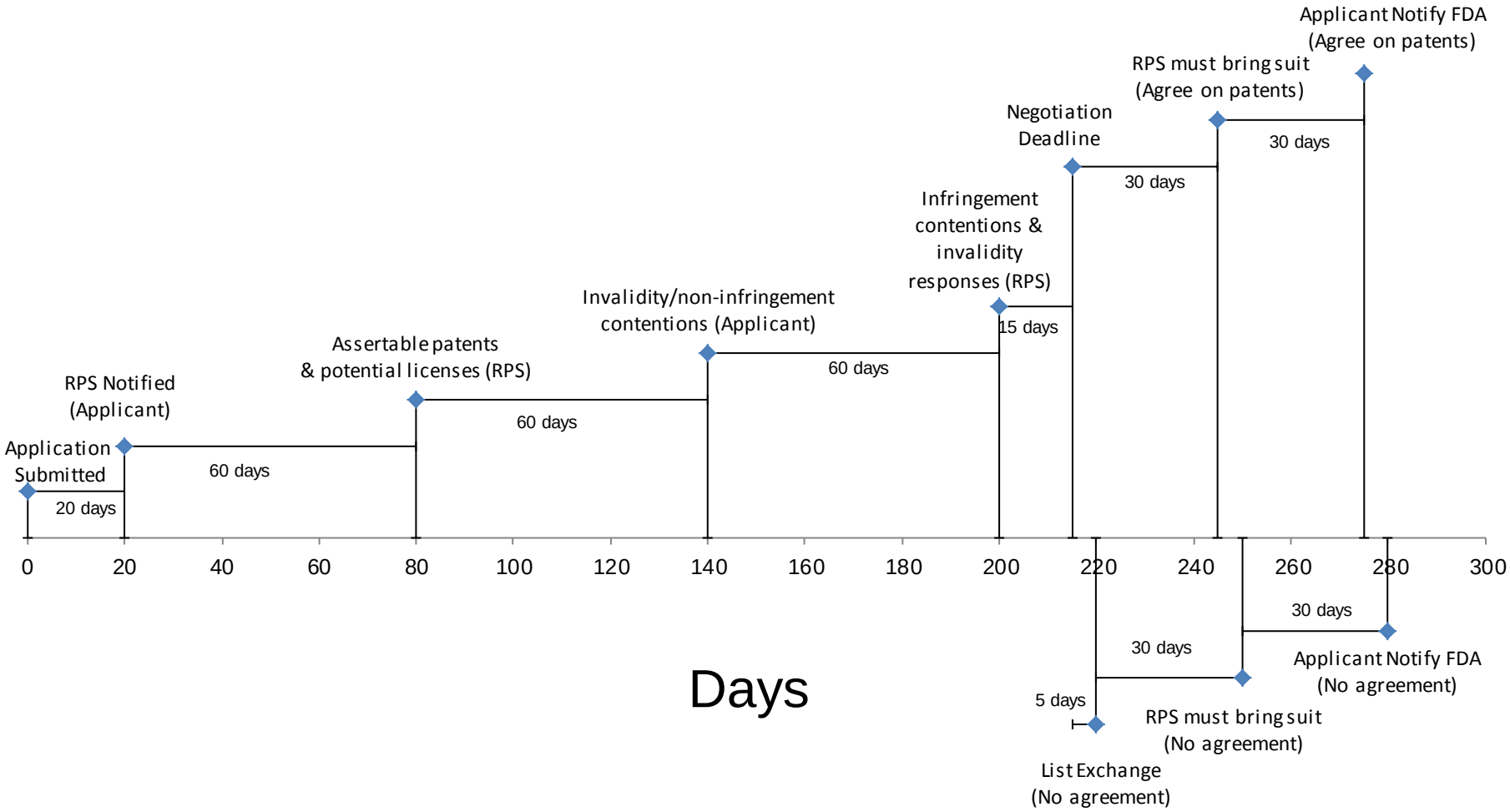


Patent Litigation under the Biosimilars Act

Which patents will be litigated?

- The listing and sharing of patent information is conducted by the Reference Product Sponsor (RPS) and the Applicant through a series of prescribed confidential exchanges prior to the filing of a lawsuit. 42 USC § 262(l).

Patent Exchange Timeline



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Preparing in Advance for the Patent Exchange

Pre-Litigation Strategies for Reference Product Sponsor

- Organize patent portfolio to identify patents applicable to specific biosimilar application
- Obtain claims that cover design-arounds and alternative manufacturing processes
- Consider licensing additional third-party patents that could be asserted against applicant
- Review existing licenses and determine standing and ability to enforce
- Evaluate risk associated with identifying patents (i.e., research tools or platform technology)
- Identify patents that may be appropriate to license to applicant
- Monitor applicant's compliance with disclosure rules to assess whether an injunction may be available

Pre-Litigation Strategies for Applicant

- Proactively identify RPS' patents
  - Monitor any publicly announced licensing deals
- Develop non-infringement positions early
  - May require testing or expert analysis depending on claims
- Develop invalidity positions early
  - Search for prior art
  - Consult with experts on invalidity issues
- Monitor RPS' patent portfolio for pending applications that could issue
- Comply with exchange deadlines in order to avoid DJ action

Portfolio Review by Reference Product Sponsor

- Do you have claims to design-arounds? Methods of manufacture?
- Make sure you have coverage not just for your product/process but also for modifications/improvements/alternate processes/etc.
- Consider dividing claims into one or more cases to allow the ability to assert only one of the patents in a given litigation
- Assess whether to assert any “platform technology” patents
- Consider licensing/acquiring additional patents
- Consider standing issues
  - Especially true for licensed and acquired patents
- Consider the potential use of AIA procedures to strengthen portfolio (e.g., supplemental examination)

Portfolio Review by Biosimilar Applicant

- Review of Applicant's patent portfolio
  - While not involved in the patent exchange, are there patents that can be used offensively against the RPS? Against other future biosimilars?
  - Are there claims that can be obtained to use offensively?
  - Are there patents that can be licensed? Acquired? Obtained?
- Patents on platform technologies or research tools
  - How are these patents being used by the Applicant?
  - Can the Applicant rely upon the "safe harbor" exemption of 271(e)(1)?

Evaluation of Litigation Risk by Reference Product Sponsor

- Consider strength of all patents in portfolio
  - Perhaps some would be better served in the second phase of litigation
- Consider use of platform technology or research tool patents for future litigation against other biosimilar applicants for different products

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Licensing and Enforcement Considerations

Licensing Issues for Reference Product Sponsor

- Third party ownership issues
  - RPS' patent portfolio often involves patents licensed from third parties
- Review existing license agreements
  - Evaluate standing issues
  - Review provisions relating to enforcement and joinder of licensor
- Consider whether any provisions should be updated
  - Shortened notice period for infringement
  - Consent to joinder
  - Confidentiality issues
  - Rights to sublicense
  - Acceptable terms for sublicense

Issues to be Addressed in License Agreements

- Standing
- Timing – consider provisions requiring prompt action once a biosimilar application is filed
  - *e.g.*, if a University is involved, can they move quickly to provide information? Approve involvement in lawsuits? etc.
- Confidentiality and access to the biosimilar application
  - Prosecution bar issues
- Consider provisions to require Licensor to maintain/update a list of all relevant licensed patents
- Notification – consider provisions requiring RPS/Licensee to provide prompt notice to Licensor of the filing of a biosimilar application
  - Include additional notice procedures tied to deadlines in the patent exchange procedure

Issues to be Addressed in License Agreements

- Control of litigation and patent exchange
  - Timing is key – pre-litigation timing deadlines are short, consider provisions requiring action within a specified timeframe
  - Strategy Choices
    - Who has control? Input?
    - Decision as to which patents to include during the patent exchange process
    - Choice of counsel
    - Willingness to be a party to the litigation

Enforcement Considerations

- Prepare EARLY – given the short time frames for the pre-litigation exchange, you must be prepared ahead of time

- Strategies for timing of litigation
  - Which patents should be included in the first wave of litigation v. the potential second wave of litigation?

- Compliance with the pre-litigation procedures
  - Compliance impacts available remedies

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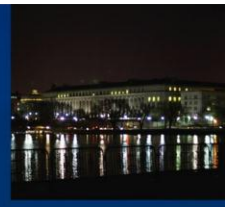
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