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Biosimilars Webinar

July 23, 2013

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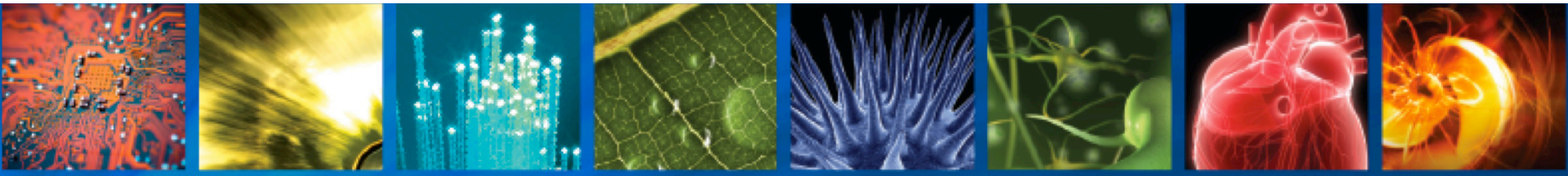

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Biosimilars Overview

Biologics Price Competition and Innovation Act ("BPCIA")

- Signed into law March 23, 2010, as part of the Patient Protection and Affordable Care Act of 2009; amends §351 of Public Health Services Act.
- Codified at 42 U.S.C.§262.
- Creates an abbreviated approval pathway for '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 *See* FDA Draft Guidance.
- "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 *See* FDA Draft Guidance.

Biosimilarity and Interchangeability

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, e.g.*, 42 USC §262(i)(2) and (3) (emphasis added).

An "interchangeable" product:

–Must demonstrate ***biosimilarity*** to the referenced product

–expected to produce the ***same clinical result*** as the reference product in any given patient

–The risk of safety or diminished efficacy of alternating or switching between the biological product and the reference product is not greater than the risk of using the reference product without the switch. *See e.g.*, 42 USC §262(k)(4)

The Pre-Litigation Exchange

- 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).

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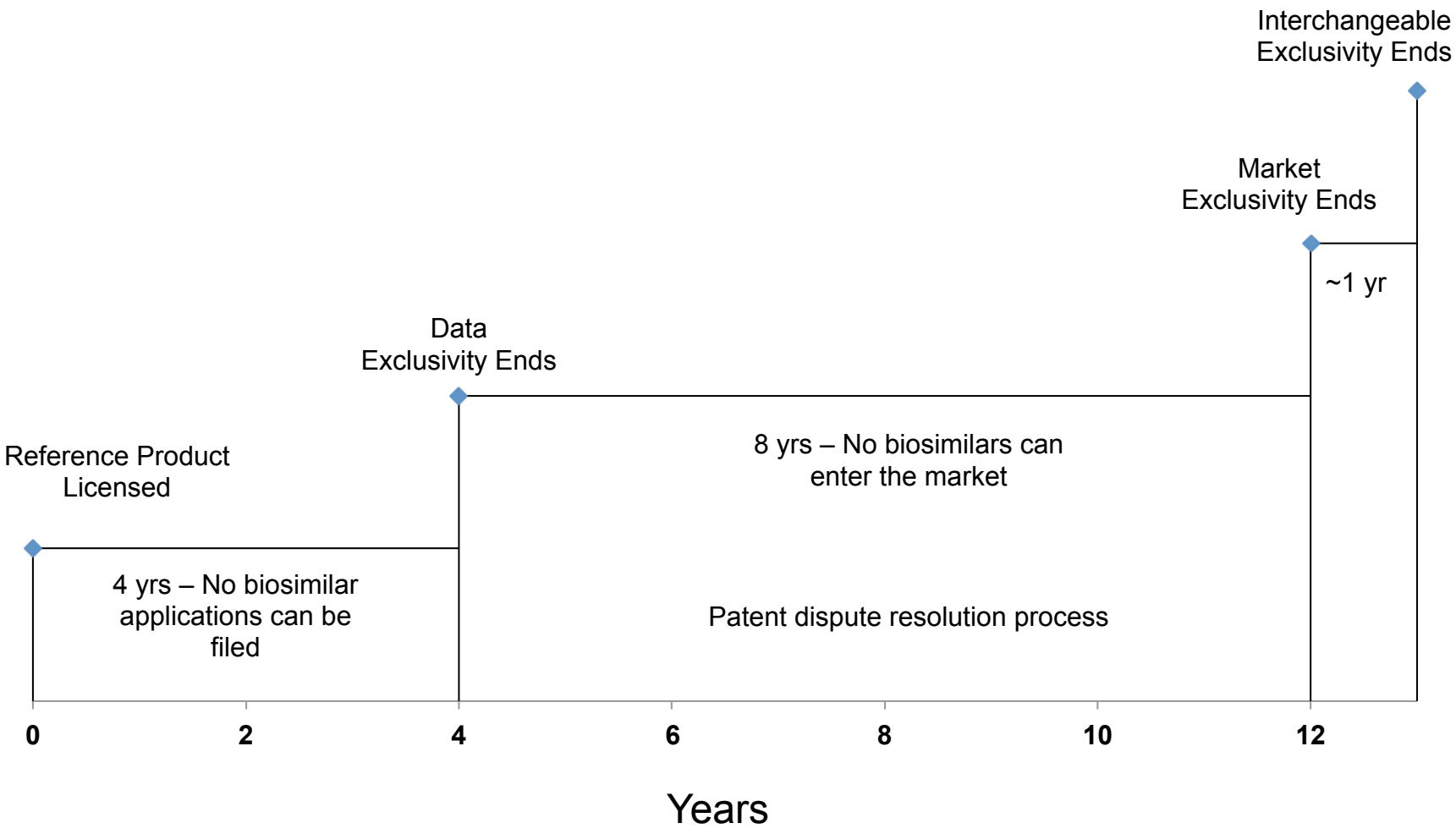
Pre-Litigation Patent Exchange

Exclusivity Timeline



Biosimilar Exclusivity

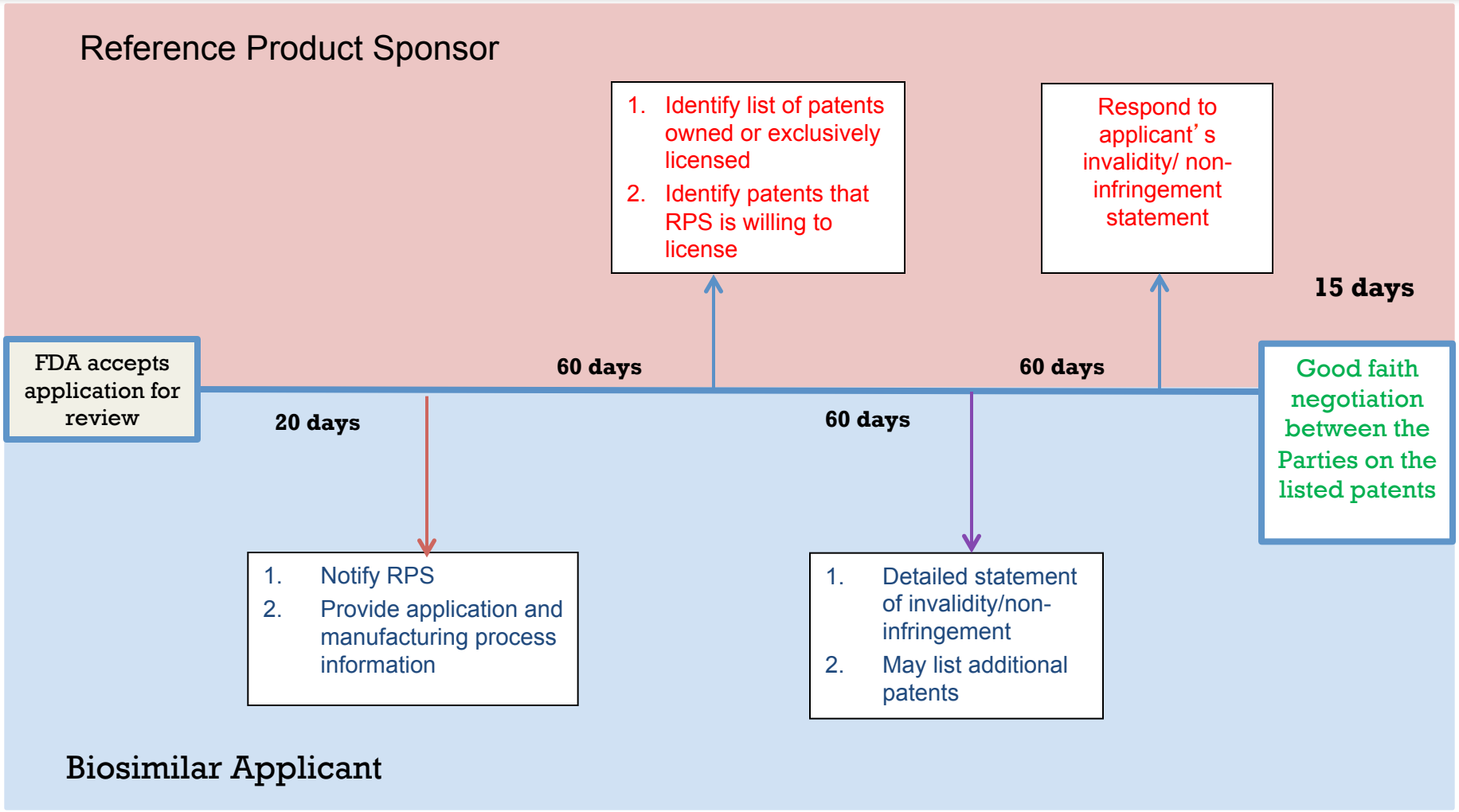
- If a product is determined to be "interchangeable" the applicant receives a period of market exclusivity. 42 USC §262(k)(6).

- There is no market exclusivity period for products determined to be "biosimilar."

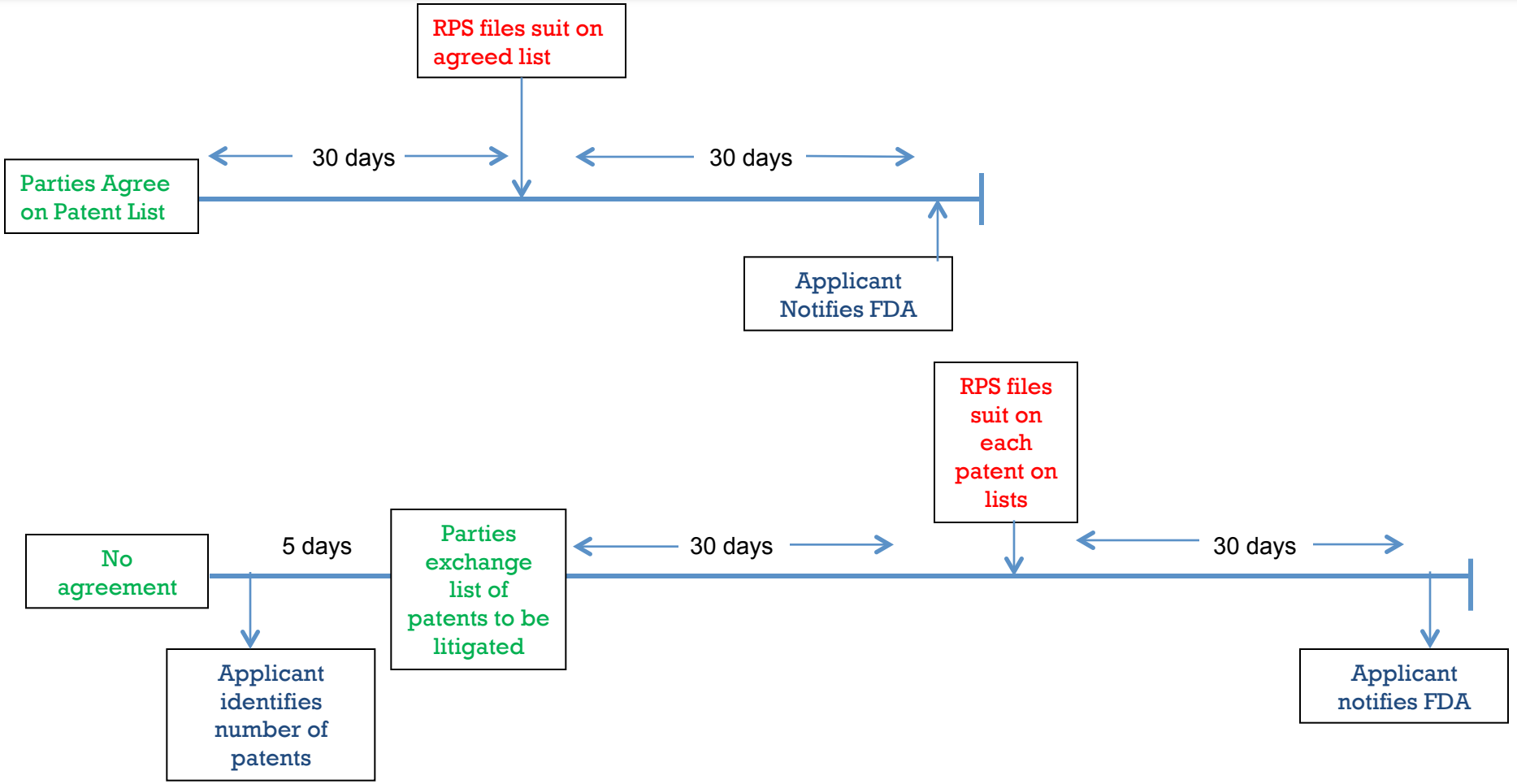
Summary of Pre-Litigation Exchange

- Phase 1: Disclosure
  - Biosimilar Applicant discloses application
  - RPS discloses patents to be asserted and potentially licensed
  - Biosimilar Applicant can identify additional RPS patents
- Phase 2: Contentions
  - Applicant provides non-infringement and invalidity positions
  - RPS provides infringement contentions and invalidity response
- Phase 3: Negotiation
  - Parties identify patents to be asserted in initial wave of litigation

Timeline for Pre-Litigation Exchange



Timeline for Initiation of Litigation



FDA Actions

- 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
  - Formal Meetings between the FDA and the Biosimilar Biological Product Sponsors or Applicants
- Additional FDA Guidance expected
  - Hopefully we will see Guidance on what will be required to prove interchangeability

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Preparing in Advance for the Patent Exchange: The Reference Product Sponsor's Perspective

Reference Product Sponsor – Portfolio Review

- Organize patent portfolio to identify patents applicable to specific biosimilar application
- 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
  - Assess whether to assert any "platform technology" patents

Issues to be Addressed in License Agreements

- 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.
- 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
- Rights to Sublicense – including acceptable terms
- Standing and Joinder

Issues to be Addressed in License Agreements

- Confidentiality and access to the biosimilar application
  - Prosecution bar issues
- Control of litigation and patent exchange
  - 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
- Consider provisions to require Licensor to maintain/update a list of all relevant licensed patents

Reference Product Sponsor – Claim Strategies

- Obtain claims that cover design-arounds and alternative manufacturing processes
  - 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
  - Consider the potential use of AIA procedures to strengthen portfolio (e.g., supplemental examination)

Post-AIA Portfolio Strategies for the RPS

- Ex Parte Reexamination
- Reissue (no prohibition re deceptive intent)
- **Supplemental Examination**

- **Continuations**
- New Filings

- Interferences/Derivation

Supplemental Examination

- Submitted by Patentee
  - Information believed to be relevant to patent
    - "any ground" of patentability
      - 101 to 112
  - If relevant → ex parte reexamination
  - 12 "items" (documents/issues)
- "Removes" item for inequitable conduct (if timely completed)
- Applies to all enforceable patents
- Costs: 16,500 (LE: 4,400; 12,100; page fees)
- SNQ (substantial likelihood that it is important for patentability)
- Timing—3 months for initial decision

Continuations

- Possible Estoppel aspects from IPR/PGR
  - Prioritized Examination
- Consider patents with a single very focused claim
- Pre-AIA, AIA, Hybrid priority options

Opportunities Involving AIA Options

- Prioritized Examination and continuations
  - Avoid estoppel of IPR/PGR
  - Choose when patent issues?
  - Focused claim sets to avoid proceedings
- Supp. Exam early to close open items
  - Inequitable conduct
  - 112/101
- Settlement options if in PGR/IPR/Derivation
  - Unrelated patents/leverage

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Preparing in Advance for the Patent Exchange: The Applicant's Perspective

Pre-Litigation Strategies for Applicant

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

Post-AIA Strategies for Challenging Patents

- Patents
  - *Ex Parte* Reexamination
  - *Inter Partes* Review (IPR)
  - Post-Grant Review (PGR)
  - Interference/Derivations

- Applications
  - 3rd party submissions
  - Interference/Derivation
  - Protest §1.291

Various Benefits and Risks (Reexam/IPR/PGR/Court)

- Cost
- Control
- Speed
- Grounds
- Success rate
  - To commence
  - Claim interpretation
  - Invalidity standard
  - Ultimate result
- Amendments
- Discovery
- Reviewer
- Estoppel
- Stay of Litigation (or other)
- Anonymity

Ex Parte Reexamination

- Cost: Least expensive option (for an issued patent)
- Success rate:
  - 12% of petitions → unpatentable
  - 65% of petitions → claim amendments
  - 23% of petitions → no change
  - No further involvement for 3rd party in proceedings
- Speed: no required timing, but generally
  - About 1 year if patent is in litigation
  - About 2.5 years if patent is not in litigation
  - If appealed to PTAB, 1-2 more years (only Patent Owner can appeal)
- Discovery: none
- Estoppel: none (no settlement possible)

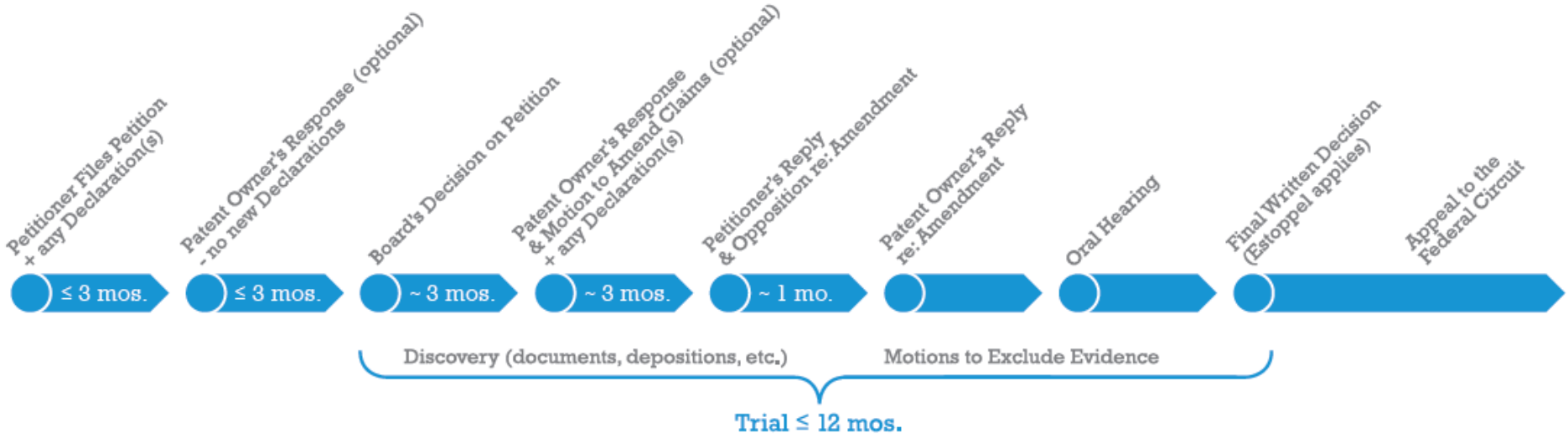
IPR/PGR

- More 3rd party control, higher costs
- Speed:
  - No more than 18 months from petition (ext. 6 months for good cause)
  - Rehearing request available, but no PO appeal to PTAB (just to Fed. Cir)
- Success rate:
  - No IPR/PGR proceeding is yet complete
  - More than 90% of Petitions lead to initiation of trial
  - Challenger is active participant throughout process, including oral hearing

IPR/PGR (continued)

- Discovery:
  - Declarations, depositions of declarants, limited deposition of third parties, very focused document discovery
- Estoppel:
  - Petitioner estopped on a claim-by-claim basis for issues raised or reasonably could have been raised
  - Patentee estopped from pursuing canceled claims or claims patentably indistinct from canceled claim in a continuation application
  - If parties settle (and no Final Written Decision), then no estoppel

IPR/PGR Timeline



Re-examination v. IPR/PGR

	Re-examination	IPR/PGR
Decision Maker	3 Examiners (SPE/QAS)	3 Patent Attorney Judges
Technical Training	Yes	Yes
Challenger Participates	Little to none	Equal to patentee; Hearing; Oppose proposed amendments
Discovery	None	Limited
Type of Evidence	Limited	Only Limited in IPR
Invalidity Standard	Preponderance	Preponderance
Claim Construction	Broadest Reasonable	Broadest Reasonable
Speed	"Slow" (unless in litigation)	Fast
Claim Amendments	Yes	Yes
Anonymous	Yes	No

Reexam v. IPR v. PGR

	Reexamination	IPR	PGR
Eligible	Any patent	Any patent	First-to-File patents only
Timing	Any point	-After PGR eligibility expires -Within 1 year of lawsuit -Petitioner cannot first file DJ of invalidity	-Within 9 months of issue -Petitioner cannot first file DJ of invalidity
Grounds	-102/103 -OTDP	-102/103 -OTDP? (probably not)	-All grounds under §282 (except BM) -OTDP? (probably not)
Estoppel	None	102, 103 OTDP? (probably not)	-All grounds under §282 (except BM) (OTDP? (probably not))
Evidence	-Patents and printed publications	-Patents and printed publications	-Any evidence
To Commence	Substantial New Question	Reasonable likelihood that challenger will prevail on 1 claim (50/50)	More likely than not claim is invalid (greater than 50%); or novel/unsettled legal question
Stay of Litigation?	Discretionary (Fresenius v. Baxter)	Discretionary (more likely)	Discretionary (more likely?)
Cost	12k (LE/SE/ME)	23k (600/claim)	30k (800/claim)

District Court v. IPR/PGR

	District Court	IPR/PGR
Decision Maker	Judge or Jury	3 Patent Attorney Judges
Technical Training	No	Yes
Discovery	Broad	Limited (IPR; PGR is slightly broader)
Evidence	Broad	Limited (IPR; PGR is slightly broader)
Invalidity Standard	Clear and Convincing	Preponderance
Claim Construction	Skilled Artisan w/ PH	Broadest Reasonable
Speed	Slow	Fast
Cost	$$$	$$
Estoppel	Yes – but different	Yes – but different
Claim Amendments	No	Yes

Opportunities Involving Post Grant Options

- Anonymous/OTDP
  - Ex Parte Reexamination
- Goal is to amend claims to block other competitors
  - IPR/PGR
- Patentee estoppel (more effective earlier)
  - IPR/PGR
- Prepare & Share vs. File
- Avoid/minimize petitioner estoppel (settlement or timing)

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Enforcement Considerations

Enforcement Considerations - Reference Product Sponsor

- Consider strength of all patents in portfolio in determining which patents to assert
- Strategies for timing of litigation
  - Which patents should be included in the first wave of litigation v. the potential second or third waves of litigation?
- Consider use of platform technology or research tool patents for future litigation against other biosimilar applicants for different products
- Claim Strategies for pending applications
- Preliminary Injunction Considerations
- Role of the Third Party Patent Owner/Licensor

Enforcement Considerations - Biosimilar Applicant

- Whether to submit under BPCIA or as a regular BLA
- Timing of application filing
- Pursue Post-Grant challenges?
- Strategies in view of other competitors
- Prepare for potential third wave of litigation
- Consider use 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?

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Additional Information

Additional Information

- Presentation Slides – available upon request
- Sheila Swaroop and Carol Pitzel Cruz, "Patent Licensing Considerations for Biologics under the BPCIA," Journal of Commercial Biotechnology Vol. 19, No. 3 (July 2013) – available upon request
- Appendix A – BPCIA Pre-Litigation Exchange Summary

Disclaimer

- This presentation and our discussion constitute an educational and informational presentation and should not be construed as individualized legal advice or representation.
- The presentation of these materials does not establish an attorney-client relationship. Representation can be initiated only upon completion of our standard new client/new matter process, including completion of a conflicts check, execution of an engagement agreement and payment of any applicable retainer.
- Any discussions are based solely upon non-confidential information you may provide. It is our understanding that you will not provide us with any confidential information and will not do so until representation is initiated.

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Questions

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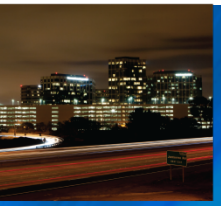
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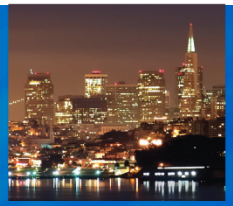
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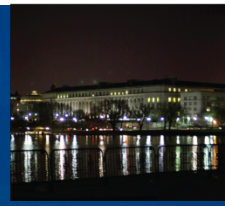
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Appendix A

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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. 42 USC §262(l).

Disclosure of the Application to the RPS

- No later than 20 days after an Applicant is notified that their biosimilar application has been accepted for review, the Applicant:
  - *Shall* provide the RPS with a) a copy of the application and b) a description of the process(es) used to manufacture the biological product. 42 USC §262 (l)(2)(A).
  - *May* provide the RPS with additional information requested by the RPS. 42 USC §262(l)(2)(B).
- If the Applicant does not provide a copy of their application within 20 days of acceptance the RPS may bring a DJ action.
- Confidential information may only be used to evaluate a claim of infringement. 42 USC §262(l)(1)(D).
  - May not be included in any publicly available complaint or pleading. 42 USC §262(l)(1)(F).
  - If RPS does not file infringement action, RPS must return or destroy confidential information. *Id.*
  - Effect of violation is injunctive relief. 42 USC §262(l)(1)(H).

List and Description of Patents

Not later than 60 days after receipt of the application and other information from the Applicant, the RPS *shall*:

- Provide a list of any patents that could reasonably be asserted by the RPS or a patent owner that has granted an exclusive license to the RPS. 42 USC §262(l)(3)(A)(i).

- Identify those patents on the list that the RPS would be willing to license to the Applicant. 42 USC §262(l)(3)(A)(ii).

- An issued patent that RPS does not list at this juncture cannot be the basis of a preliminary injunction against Biosimilar Applicant. 42 USC §262(l)(8)(B) (the "forfeiture provision").

List and Description by the Biosimilar Applicant

Within 60 days of receiving the RPS' patent list, the Applicant:

- *MAY* provide its own list identifying those patents that it believes could reasonably be asserted by the RPS against the Applicant. 42 USC §262(l)(3)(B)(i)
- *MUST* respond to the RPS' patent list by:
  - Providing invalidity/non-infringement contentions, 42 USC §262(l)(3)(B)(ii)(I); or
  - Providing a statement that the Applicant does not intend to begin commercial marketing of the biological product until an identified patent expires. 42 USC §262(l)(3)(B)(ii)(II)
- *MUST* respond to the RPS regarding the patents offered for license. 42 USC §262(l)(3)(B)(iii)

Contentions by the Reference Product Sponsor

- Not later than 60 days after receipt of the Applicant's invalidity/non-infringement contentions, the RPS *MUST* provide infringement contentions and respond to the applicant's invalidity contentions. 42 USC §262(l)(3)(C)

Patent Resolution Negotiations

- The RPS and Applicant are required to engage in "good faith negotiations" to agree on which, if any, of the patents listed by the RPS (or the Applicant) will be the subject of patent infringement litigation. 42 USC §262(l)(4)(A)
  - The Parties have 15 days to reach an agreement on which patent(s) should be litigated. 42 USC §262(l)(4)(B)
- If the Parties agree on a list of patents that will be litigated, the RPS has 30 days in which to bring an action for patent infringement. 42 USC §262(l)(6)(A)

Failure to Reach Agreement

If no agreement is reached after 15 days of negotiations:

- The Applicant provides the RPS with the number of patents it believes should litigated. 42 USC §262(l)(5)(A).
- Within 5 days, the Parties simultaneously exchange a list of patents each believes should be a part of the infringement action. 42 USC §262(l)(5)(B).
- The RPS must bring a patent infringement action with respect to *each* patent included on the two lists within 30 days. 42 USC §262(l)(6)(B).
  - Failure to timely file suit will limit remedies available to RPS.
    - Reasonable royalty only. 35 USC § 271(e)(6)(B).
  - Litigation does not automatically stay approval process. 35 USC § 271(e)(6).

Post Complaint

- Once a complaint is filed, the Applicant must notify the FDA, which must publish notice of the lawsuit in the federal register.
- There is no automatic regulatory stay of approval of the biosimilar application during the litigation.
- The Applicant must provide notice to the RPS not later than 180 days before the date of first commercial marketing.
  42 USC §262(l)(8)(A).
  - The RPS may seek a preliminary injunction prior to biosimilar market launch.
  - PI limited to patents identified in original RPS/Applicant patent lists but not the subject of the initial litigation.
    42 USC §262(l)(8)(B).

Declaratory Judgment

- If Applicant complies with all requirements, neither party can bring a Declaratory Judgment (DJ) action prior to the 180 day marketing notice. 42 USC §262(l)(9)(A).
- If applicant fails to act on a response, RPS may bring DJ action on any patent listed in the RPS' list, 42 USC §262(l)(9)(B):
  - Failure to exchange list of patents
  - Failure to provide detailed statements on RPS' listed patents
  - Failure to provide notice of commercial marketing
  - Failure to notify FDA of infringement action
- If an applicant does not disclose its application to the RPS, the RPS may bring a DJ action for infringement of "any patent that claims a biological product or a use of the biological product" and seek injunctive relief against the applicant. 42 USC §262(l)(9)(C).
  - Process/manufacturing patents seem to be excluded

Newly Issued or Exclusively Licensed Patents:

- For patents issued or exclusively licensed to RPS after the RPS provides the initial list of patents to the Applicant, the RPS must provide a supplemental list within 30 days of issuance or licensing. 42 USC §262(l)(7).

- Then, within 30 days, Applicant must provide statements on a claim-by-claim basis as to non-infringement, invalidity, and unenforceability. *Id.*

- Newly issued/licensed patents are not subject to the negotiation/ exchange procedure, but can be used for preliminary injunction.