Summary of Biologics Price Competition and Innovation Act (2010)

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Biosimilar Definitions

- **Biosimilarity**
  - Means “highly similar” to the Pioneer product notwithstanding minor differences in clinically inactive components; and where there are no clinically meaningful differences between the biological product and the Pioneer in terms of safety, purity and potency.

- **Interchangeable**
  - Means a biological product found to be Biosimilar; that can be expected to produce the same clinical result as the Pioneer in any given patient; and if the product is administered more than once to an individual the risk in terms of safety or diminished efficacy of alternating or switching between use of the product and the Pioneer is no greater than the risk of using the Pioneer without such alteration or switch.

  - A Biosimilar found to be interchangeable may be substituted for the Pioneer without the intervention of “the health care provider who prescribed the reference product.”
Basic Regulatory Structure

Drugs v. Biologics

- Pioneer, generic and pediatric exclusivities available
- Generic 505(b)(2) “paper” NDA; ANDA
- Orange Book listing of patents; certification by generic applicant
- Automatic 30 month stay
- Same
- Biosimilar License Application (“Biosimilar”); Biosimilar Interchangeable License Application (“Biogeneric”)
- Private exchange of patent information
- No automatic stay
Pioneer Exclusivities

Drugs v. Biologics

• 5 year marketing exclusivity available for new active moiety

• 3 year marketing exclusivity (with clinicals) for new indication, dosage, etc.

• 12 year marketing exclusivity for new biological structures – but if application is filed by same sponsor or manufacturer of the Pioneer product (or a licensor, predecessor in interest or a related party), the changed biological structure must also result in a (1) change in indications, route of administration, dosing schedule, dosing form, delivery system, delivery device or strength or (2) change in safety, purity or potency

• no follow on exclusivity for same biological structure
Pioneer Exclusiveties

Drugs v. Biologics

- ANDA, can be filed after 4 years with Par IV certification
- pediatric exclusivity* adds 6 months to all exclusivities and OB listed patents
- Biosimilar application can be filed after 4 years
- pediatric exclusivity* adds 6 months to 12 year exclusivity; 6 months to 4 year filing restriction; and 6 months to biologic 7 year Orphan Drug exclusivity

* Note: FDA must accept pediatric studies ≥ 9 months before expiration of exclusivity or no extension
Generic Exclusivity

Drugs v. Biologics

• ANDA – first to file and to certify under Paragraph IV (challenging Orange Book patents) receives 6 months of generic exclusivity; can be forfeited under various conditions

• Biogeneric license - first to obtain an “interchangeable” license receives exclusivity against any subsequent interchangeable license application for any condition of use in Pioneer product until: (1) one year after commercial marketing by first licensee; or (2) 18 months after court decision (appellate court, if appealed) on all patents or dismissal of action against first licensee; or (3) 42 months after first licensee approval if litigation is still pending, or 18 months after first licensee approval if no suit is filed (i.e., where 1st licensee fails to market)
Biosimilar Application Requirements

• Biosimilar License Application

  ▪ Showing of “Biosimilar” based on data from (1) analytical studies showing “highly similar” to Pioneer (different inactives allowed); (2) animal studies (including toxicity); and (3) clinical studies to demonstrate safety, purity and potency in one or more conditions of use.

  ▪ Has same mechanism of action for conditions of use on label (if known), route of administration, dosage and strength of Pioneer product.

  ▪ Production facility must meet standards designed to assure product continues to be safe, pure and potent.
• Biogeneric license
  
  ▪ Must be “Biosimilar” to Pioneer.

  ▪ Must also show that (1) Biosimilar can be expected to produce same clinical results as Pioneer in any given patient; and (2) any risk in terms of safety or diminished efficacy from switching between Pioneer and Biosimilar is no greater than using Pioneer without switching.
Patent Procedures for Biosimilars

• Biosimilar applicant required to provide Pioneer with confidential access to Biosimilar application including manufacturing process within 20 days of FDA “acceptance for review”

• Within 60 days of confidential access Pioneer required to provide Biosimilar applicant with list of patents that could reasonably be asserted; and a designation of patents available for license (“initial Pioneer list”)
• Within 60 days of receiving Pioneer patent list, Biosimilar applicant
  ▪ May provide a list of patents that Biosimilar applicant believes could reasonably be asserted by Pioneer (“initial Biosimilar list”).
  ▪ Shall provide the Pioneer with a claim by claim analysis for each patent listed by the Pioneer or the Biosimilar applicant, of the factual and legal basis as to why patent is invalid, unenforceable or will not be infringed or a statement that Biosimilar applicant does not intend to begin marketing its product before such patent expires.
  ▪ Shall provide Pioneer with a “response” regarding each patent designated by Pioneer as being available for licensing.
Within 60 days of receipt of patent list and claim by claim statement by Biosimilar applicant, Pioneer is required to provide a claim by claim rebuttal on infringement, validity and enforceability for each patent addressed in Biosimilar applicant’s statement.

After receipt of Pioneer rebuttal, the parties are required to engage in good faith negotiations for up to 15 days to try to arrive at list of patents subject to an infringement action ("negotiated list").
Patent Procedures for Biosimilars (cont.)

• If no resolution of patents after 15 days, patent exchange procedures are triggered
  ▪ Biosimilar applicant initially notifies Pioneer of the number of patents it will exchange.
  ▪ Within 5 days of receiving Biosimilar applicant’s number, the parties are required to simultaneously exchange lists of patents that each believes should be subject to an infringement action.
  ▪ The number of patents listed by Pioneer cannot be greater than the number notified by Biosimilar applicant unless Biosimilar applicant lists zero patents in which case Pioneer may list one patent.
  ▪ Pioneer must then bring an infringement action within 30 days for each patent on both lists (“exchanged lists”).
• If favorable resolution within the 15 days, Pioneer must bring an infringement action within 30 days for each patent on “negotiated list”
  
  ▪ FDA to be notified of infringement action by Biosimilar applicant within 30 days.
  
  ▪ FDA to publish notice of complaint in Federal Register.
Patent Procedures for Biosimilars (cont.)

• Newly issued/licensed patents”
  - Defined as patent issued/licensed after date of “initial Pioneer list.”
  - Within 30 days of issued/licensed patent, Pioneer must supplement its initial list.
  - Within 30 days of receiving supplement, Biosimilar applicant must provide statement on claim by claim basis as to non-infringement, invalidity or unenforceability on newly issued/licensed patent.
  - Newly issued/licensed patents do not become part of the negotiated/exchanged patent procedures but are subject to Preliminary Injunction procedures.
• Biosimilar Notice of Commercial Marketing and Preliminary Injunction Procedures
  
  ▪ Biosimilar applicant must provide Pioneer with 180 day notice of intent to market.

  ▪ Pioneer may seek preliminary injunction (PI) on any patents on the “initial Pioneer list” or “initial Biosimilar list” that are not also included on the “negotiated list” or the “exchanged lists” (this is the “PI patent list”).

  ▪ Both parties required to reasonably expedite discovery in any infringement action seeking PI.
Limitation on DJ Actions

- If Biosimilar applicant provides confidential access to application, no DJ can be brought by either party before the 180 days notice of commercial marketing is received; DJ can only be brought on “PI patent list.”

- If Biosimilar applicant fails to provide (1) claim by claim statement on initial pioneer list (or newly issued patent) within 60 day (or 30 day) time frame; (2) notice of number of to be exchanged patents; (3) notice of complaint to FDA; (4) or 180 day notice prior to marketing, Pioneer can bring DJ on any patent on “initial Pioneer list” and on any newly issued patent.

- If Biosimilar applicant fails to provide access to confidential information Pioneer can bring DJ or any patent that claims biological product or use of product (but not manufacture of product).
• What happens if Pioneer leaves a patent off its initial patent list?
  ▪ Unless Biosimilar applicant includes the patent on its initial list, Pioneer cannot sue on it prior to launch.
  ▪ Exception to this rule is where Biosimilar applicant fails to provide confidential access.

• Can a Pioneer be forced to license its patents?
  ▪ If a Pioneer fails to bring an infringement action within 30 days of (1) a negotiated patent resolution, or (2) following exchange of patent lists where there is no resolution; or
  ▪ If a Pioneer brings an infringement action within 30 days but the suit is dismissed without prejudice or the suit is not prosecuted in good faith.
FAQs (cont.)

• What are the tradeoffs when negotiating/exchanging patent lists?
  ▪ Patents on negotiated list or on exchanged lists (if negotiation fails) can be litigated immediately.
  ▪ Patents on initial Pioneer list but not on negotiated or exchanged lists cannot be litigated until the 180 day marketing notice is received from Biosimilar applicant.

• What happens if a newly issued/licensed patent is not notified to Biosimilar applicant within 30 days?
  ▪ Patent cannot be litigated prior to Biosimilar launch.
Summary of Patent Litigation Timeline

- Confidential access not provided to Biosimilar application
  - DJ can be brought at any time on composition or use (but not manufacturing) patents.
- Confidential access provided to Biosimilar application
  - Within 215/220 days of FDA receipt of Biosimilar - infringement can be brought on all patents on negotiated/exchanged lists.
  - Within 180 days prior to launch – infringement suit or DJ can be brought on all patents on initial lists (but not also on the negotiated or exchanged lists) and on all newly issued/licensed patents properly noticed by Pioneer.
- Biosimilar applicant fails to comply with certain specified requirements
  - DJ can be brought on any patent on initial lists or on newly issued/licensed patents.
- After launch – suit can be brought on any patent
For more information, visit www.fr.com/biologics

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