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Fordham IP Conference 2015 -- Program 8A: Biosimilars

What Took You So Long? Biosimilars Come to The U.S.

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The Public Count of Biosimilars and Biosimilar Applications

(as of April 8, 2015, that is …)

- **One** FDA-approved biosimilar:
  - Sandoz's Zarxio®, approved March 6, 2015
  - Reference product: Amgen's Neupogen® (filgrastim)
- **Four** other publicly announced biosimilar application filings:
  - Apotex: referencing Amgen's Neulasta® (pegfilgrastim)
  - Apotex: referencing Amgen's Neupogen® (filgrastim)
  - Celltrion: referencing Janssen Biotech's Remicade® (infliximab)
  - Hospira: referencing Amgen's Epogen® and Janssen Biotech's Procrit® (epoetin alfa)

The Biologics Price Competition and Innovation Act of 2009

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42 U.S. Code § 262 - Regulation of biological products

Enacted as part of the Affordable Care Act, because it was "the sense of the Senate that a biosimilars pathway balancing innovation and consumer interests should be established."

BPCIA, Pub. L. No. 111-148, § 7001(b), 124 Stat. at 804

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(k) Licensure of biological products as biosimilar or interchangeable

A subsection (k) applicant submits a Biologics License Application

One reference product per BLA

FDA can approve as biosimilar or as interchangeable

Exclusivity for first interchangeable biosimilar (from 1 year to 42 months based on various factors)

No BLA may be filed within 4 years of licensure of reference product

No BLA may be approved within 12 years of licensure of reference product

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42 U.S. Code § 262 - Regulation of biological products

(*l*) Patents

(1) Confidential access to subsection (k) application and information

- Applies unless otherwise agreed to by the Applicant and RPS.
- Confidential access to outside counsel and one in-house attorney for RPS, with a prosecution bar
- May be used exclusively to determine patent applicability
- Information remains confidential into litigation
- If no lawsuit filed, RPS must destroy or return the information

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(*l*) Patents

"(2) Subsection (k) application information

Not later than 20 days after the Secretary notifies the subsection (k) applicant that the application has been accepted for review, the subsection (k) applicant—

(A) shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application; and

(B) may provide to the reference product sponsor additional information requested by or on behalf of the reference product sponsor."

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(*l*) Patents

(3) List and description of patents

- Within 60 days after receiving the BLA and manufacturing information, the RPS "shall provide" the Applicant a list of all patents for which the RPS believes a claim of infringement could reasonably be asserted, and identify those patents the RPS would be prepared to license to the Applicant. 42 U.S.C. § 262(*l*)(3)(A).
- Within 60 days thereafter, the Applicant "may provide" its own list of additional patents that could be infringed, and "shall provide" for each listed patent either a statement that it will remain off the market until the patent expires or, on a claim-by-claim basis, a detailed statement of its factual and legal basis for believing that the patent is invalid, unenforceable, or not infringed, as well as a response to the RPS's identification of patents it would be prepared to license. 42 U.S.C. § 262(*l*)(3)(B).
- Within 60 days thereafter, the RPS "shall provide," for the disputed patents, a reciprocal detailed statement with its position that each patent will be infringed and is valid and enforceable. 42 U.S.C. § 262(*l*)(3)(C).

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(*l*) Patents

(4) Patent resolution negotiations

- Good-faith negotiation to identify which listed patents shall be the subject of an infringement action under subsection 262(*l*)(6).
- If no agreement within 15 days, subsection 262(*l*)(5) applies.

(5) Patent resolution if no agreement

- Applicant identifies the number of patents that it believes should be the subject of a patent infringement lawsuit.
- Parties within 5 days exchange lists of those patents.
- RPS may name no more than the number from Applicant.
- If Applicant's number is zero, RPS may name one.

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(6) Immediate patent infringement action

- Within 30 days of arriving at a patent list, by agreement or under subsection 262(*l*)(5), the RPS "shall bring an action for patent infringement" as to each listed patent.
- The Applicant shall provide a copy of the Complaint to FDA within 30 days of service.
- FDA must publish the Complaint in the Federal Register.

(7) Newly issued or licensed patents

- Patents that issue or become exclusively licensed by the RPS after the subsection 262(*l*)(3)(A) list was provided to the Applicant are deemed added to the list.

The Biologics Price Competition and Innovation Act of 2009

35 U.S. Code § 271 – Patent infringement

271(e)(2) It shall be an act of infringement to submit

- (C)(i) with respect to a patent that is identified in the list of patents described in section 351(l)(3) of the Public Health Service Act (including as provided under section 351(l)(7) of such Act), an application seeking approval of a biological product, or
- (ii) if the applicant for the application fails to provide the application and information required under section 351(l)(2)(A) of such Act, an application seeking approval of a biological product for a patent that could be identified pursuant to section 351(l)(3)(A)(i) of such Act,

if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug, veterinary biological product, or biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

The Biologics Price Competition and Innovation Act of 2009

35 U.S. Code § 271 – Patent infringement

271(e)(4) For an act of infringement described in paragraph (2) --

(A) – the court "shall order" effective date of approval to be not earlier than patent expiry;

(B) – injunctive relief "may be granted" to prevent commercial manufacture, use, sale, offer for sale, or importation into the United States

(C) – damages "may be awarded only if" there has been commercial manufacture, use, sale, offer for sale, or importation into the United States

(D) – the court "shall order a permanent injunction" prohibiting infringement until patent expiry if the suit is brought under 262(*l*)(6) and the product has not yet been approved because of the 12-year exclusivity provision in 262(k)(6)

"The remedies prescribed by subparagraphs (A), (B), (C), and (D) are the only remedies which may be granted by a court for an act of infringement described in paragraph (2), except that a court may award attorney fees under section 285."

The Biologics Price Competition and Innovation Act of 2009

35 U.S. Code § 271 – Patent infringement

271(e)(6) --

- If the RPS does not bring the 262(*l*)(6) action within 30 days on a patent listed in the 262(*l*)(4) or 262(*l*)(5) list, then:

  "the sole and exclusive remedy that may be granted by a court, upon a finding that the making, using, offering to sell, selling, or importation into the United States of the biological product that is the subject of the action infringed the patent, shall be a reasonable royalty."

- If the RPS does not timely list a patent under 262*(l)*(3), including as updated under 262*(l)*(7), "that should have been included," it "may not bring an action under this section for infringement of the patent with respect to the biological product."

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42 U.S. Code § 262 - Regulation of biological products

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"(8) Notice of commercial marketing and preliminary injunction

(A) Notice of commercial marketing
The subsection (k) applicant shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k).

(B) Preliminary injunction
After receiving the notice under subparagraph (A) and before such date of the first commercial marketing of such biological product, the reference product sponsor may seek a preliminary injunction prohibiting the subsection (k) applicant from engaging in the commercial manufacture or sale of such biological product until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent that is—

(i) included in the list provided by the reference product sponsor under paragraph (3)(A) or in the list provided by the subsection (k) applicant under paragraph (3)(B); and

(ii) not included, as applicable, on—

(I) the list of patents described in paragraph (4); or
(II) the lists of patents described in paragraph (5)(B).

(C) Reasonable cooperation
If the reference product sponsor has sought a preliminary injunction under subparagraph (B), the reference product sponsor and the subsection (k) applicant shall reasonably cooperate to expedite such further discovery as is needed in connection with the preliminary injunction motion."

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"(9) Limitation on declaratory judgment action

(A) Subsection (k) application provided
If a subsection (k) applicant provides the application and information required under paragraph (2)(A), neither the reference product sponsor nor the subsection (k) applicant may, prior to the date notice is received under paragraph (8)(A), bring any action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent that is described in clauses (i) and (ii) of paragraph (8)(B).

(B) Subsequent failure to act by subsection (k) applicant
If a subsection (k) applicant fails to complete an action required of the subsection (k) applicant under paragraph (3)(B)(ii), paragraph (5), paragraph (6)(C)(i), paragraph (7), or paragraph (8)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent included in the list described in paragraph (3)(A), including as provided under paragraph (7).

(C) Subsection (k) application not provided
If a subsection (k) applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product."

The Current Crop of Lawsuits

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- Celltrion v. Janssen Biotech, District of Massachusetts
- Celltrion v. Kennedy Trust for Rheumatology Research, SDNY
- Hospira v. Jannsen Biotech, SDNY
- Sandoz v. Amgen, N.D. California and Federal Circuit
- Amgen v. Sandoz, N.D. California and Federal Circuit (currently on appeal)
- Janssen Biotech v. Celltrion, District of Massachusetts

Where Are We Headed?