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# Biosimilars -- Patent Process

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H. R. 3590

One Hundred Eleventh Congress  
of the  
United States of America

AT THE SECOND SESSION

*Began and held at the City of Washington on Tuesday,  
the fifth day of January, two thousand and ten*

An Act

Entitled The Patient Protection and Affordable Care Act.

*Be it enacted by the Senate and House of Representatives of  
the United States of America in Congress assembled,*

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the “Patient Protection and Affordable Care Act”.

(b) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

Sec. 1. Short title; table of contents.

TITLE I—QUALITY, AFFORDABLE HEALTH CARE FOR ALL AMERICANS

Subtitle A—Immediate Improvements in Health Care Coverage for All Americans

Sec. 1001. Amendments to the Public Health Service Act.

“PART A—INDIVIDUAL AND GROUP MARKET REFORMS

“SUBPART II—IMPROVING COVERAGE

“Sec. 2711. No lifetime or annual limits.

“Sec. 2712. Prohibition on rescissions.

“Sec. 2713. Coverage of preventive health services.

“Sec. 2714. Extension of dependent coverage.

“Sec. 2715. Development and utilization of uniform documents and standardized definitions

“Sec. 2716. Prohibition of discrimination based on

“Sec. 2717. Ensuring the quality of care.

“Sec. 2718. Bringing down the cost of health care

“Sec. 2719. Appeals process.

## ACA and BPCIA

- Signed into law March 23, 2010
- Title VII, Subtitle A of ACA, § 7001-7003
- Amends PHSA (42 USC 262) to create approval process and related provisions for biosimilar and interchangeable biological products

### **TITLE VII—IMPROVING ACCESS TO INNOVATIVE MEDICAL THERAPIES**

#### **Subtitle A—Biologics Price Competition and Innovation**

# ACA & Biologics – Key Points

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- ▶ Enables DHHS Secretary through FDA to issue guidance regarding standards, criteria and process using public comment.
  - ▶ Very general; leaves implementation up to the FDA
  - ▶ Says nothing about naming procedures.
- ▶ Creates a chiefly private process for resolution of patent disputes, including disclosure provisions.
  - ▶ Informational back and forth re: patent status follows leading up to any litigation.
  - ▶ Vast departure from Hatch-Waxman provisions for ANDAs.
  - ▶ NO Orange Book listings to guide the process.
- ▶ Exclusivity:
  - ▶ 12 years of data exclusivity for pioneer biologics; 4 years data exclusivity.
  - ▶ 1 year data exclusivity for first interchangeable product.
  - ▶ Additional 6 months for pediatric studies.

# ACA & Biologics

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- ▶ ACA creates an approval pathway for submission of a BLA for a “biosimilar” and/or “interchangeable” biologic.

## Definitions:

- ▶ **Biosimilarity** means that “the biological product is **highly similar** to the reference product notwithstanding minor difference in clinically inactive components” and there are “no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, potency.”
- ▶ **Interchangeability** means that biosimilarity is fulfilled, and the biological product “**may be substituted** for the reference product without the intervention of the health care provider who prescribed the reference product.”

# ACA & Biologics

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- ▶ **Biosimilarity** BLA application content must include analytical studies, animal studies, and clinical study or studies:
  - ▶ Must have same mechanism(s) of action for condition(s) of use that have been previously approved for the reference product;
  - ▶ Must have same route of administration, dosage form, and strength;
  - ▶ Facility assures safe, pure, potent product;
- ▶ **Interchangeability** BLA application content must include above re: biosimilar *plus*:
  - ▶ A showing of the expectation to provide the same clinical result as reference product in any given patient; AND
  - ▶ A showing that where “administered more than once to an individual, the risk in terms of safety of diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alteration or switch.”

# “Interchangeable” Products

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- ▶ Benefit for “interchangeability”?
  - ▶ The interchangeable product “may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.” [link to state laws]
  - ▶ A biosimilar product cannot be switched for RP without doctor intervention
- ▶ FDA has **not yet issued** guidance on Interchangeability
  - ▶ “At this time it would be difficult as a scientific matter for a prospective biosimilar applicant to establish interchangeability in an original 351(k) application .... **FDA is continuing to consider the type of information sufficient to enable FDA to determine that a biological product is interchangeable with the reference product.**”

# FDA Biosimilar Activities

- ▶ Biosimilar Implementation Committee, co-chaired by CDER and CBER Directors
- ▶ OND installed an Acting Associate Director for Biosimilars
- ▶ Biosimilars Review Committee created within CDER to advise OND
- ▶ Solicitation of public comment and public meetings on variety of issues.
- ▶ Purple Book created, September 2014
- ▶ First product, Zarxio, approved in March 2015; market entry Sept. 2015.
- ▶ Final Guidance Documents, April 2015 (drafts – 2013):
  - ▶ *Q & A Regarding Implementation of BPCIA Biosimilar Product Development*
  - ▶ *Scientific Considerations in Demonstrating Biosimilarity to a Reference Product*
  - ▶ *Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product*
- ▶ Draft Guidance Document - *Nonproprietary Naming for Biological Products* (August 2015).

# Patent Information Exchange

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Not later than 20 days after the Secretary notifies the ... applicant that the application has been accepted for review, the ... applicant—

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

*Public Health Service Act §351(l)(2) (42 U.S.C. 262(l)(2))*



# Patent Information Exchange

- ▶ After receipt, RP sponsor must within 60 days provide the applicant with a list of all patents “reasonably believe[d] to be infringed” and identify which patents it would be prepared to license to the applicant. *§351(l)(1); (l)(3)(A)(i) & (ii)*.
- ▶ Various exchanges and actions over 60 day increments, culminating in good faith negotiations between the two parties and, if the parties cannot come to agreement, the filing of a patent infringement action. *§351(l)(4)-(6); §351(l)(6)(B)*.
- ▶ Requires that the applicant provide the RP sponsor with at least 180 day notice prior to first commercial marketing. *§351(l)(8)(A)*.
- ▶ RP may then seek a preliminary injunction preventing the biosimilar applicant from manufacturing or selling the biosimilar product until specific patent disputes are resolved. *§351(l)(8)(B)*.

# Legal Challenges: Amgen v. Sandoz

- ▶ Amgen filed suit in Oct. 2014, alleging unfair competition and conversion under CA law, and patent infringement linked to Zarxio, a biosimilar version of Neupogen.
- ▶ Amgen challenged Sandoz refusal to follow process after July 7 FDA acceptance of application. September 2014 letter informed Amgen that Sandoz decided not to disclose the application, proposing an alternative exchange of info.
- ▶ Federal Circuit panel found for Sandoz that patent exchange process in statute is optional, not mandatory. Cited the availability of immediate suit for infringement and preliminary injunction to delay release of biosimilar.
- ▶ Also held that the 180 notice can only begin *after* the FDA has approved the biosimilar. Sandoz delayed release of Zarxio until September 2015 following FDA's March 2015 approval.

# Legal Challenges: Amgen v. Apotex

*Raises issue left by Amgen v. Sandoz: what is effect on notice requirement if commercial marketing if biosimilar applicant participates in the “patent dance”?*

- ▶ Amgen filed complaint in August 2015 regarding biosimilar version of Neulasta (pegfilgrastim) seeking a declaratory judgment that notice is ineffective.
- ▶ Apotex followed patent exchange process in statute. As a result, the parties have agreed to the inclusion of two U.S. patents in legal action. However, Apotex declined to provide Amgen the exact date of expected market, claiming it was not mandatory.
- ▶ Complaint alleges that Apotex provided Amgen with a “Notice of Commercial Marketing pursuant to 42 U.S.C. § 262(l)(8)(A)” stating an intent to launch “immediately upon receiving FDA approval.” Apotex noted that the product “has not yet been licensed by FDA.”

# Additional Questions Going Forward

- ▶ *What does FDA's draft naming guidance mean for biosimilar products? Does it upset international norms?*
- ▶ *What is the impact of Zarxio's market entry, and pricing? What will cost savings look like with biosimilar products?*
- ▶ *Will cases affect new products the same way as old products? (NCE v. 12 years exclusivity)*
- ▶ *Will Congress respond to provide legislative fix, if needed?*
- ▶ *How do international accords, such as the Trans-Pacific Partnership, influence biosimilars competition?*
  - ▶ *E.g., effective market protection "of at least 8 years from the date of first marketing approval..." TPP, Article QQ.E.20.*