

Biosimilars Legislation: An Overview

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Agenda

- **Introduction**
 - Current Framework
 - ANDA Pathway
 - Generic Concepts Do Not Apply to Biosimilars
 - 110th Congress Proposals
 - 111th Congress Proposals
- Major Issues
- Critique of Waxman Bill
- What Happens Next?

Introduction: Current Framework

- **Drugs**
 - Food, Drug, and Cosmetic Act (FDCA)
 - New drug application (NDA)
 - Abbreviated application processes (ANDA)
- **Biologics**
 - Public Health Service Act (PHSA)
 - Biologics license application (BLA)
 - No abbreviated approval pathway

Introduction: ANDA Pathway

- Approval requirements
 - Sameness
 - Bioequivalence
- Underlying presumption:
 - **IF** Sameness and bioequivalence
 - **THEN** Safety/efficacy of generic drug
 - =
 - Safety/efficacy of innovator drug

Introduction: Generic Drug Concepts Do Not Apply to Biosimilars

- Sameness

- Drugs

- Simple & small → sameness generally straightforward for most small molecules

- Biologics

- Large, complex, & 3D → sameness is difficult, if not impossible
 - Tiny changes in manufacturing can mean big changes in the behavior of the product (Eprex®)
 - Biologics and manufacturing processes are unique
 - Analytical methods used for drugs are not sufficient for biologics

Introduction: Generic Drug Concepts Do Not Apply to Biosimilars (cont'd)

- Bioequivalence

- Drugs

- Testing is required for orally ingested products because they may be absorbed into the bloodstream at different rates or in different amounts

- Biologics

- Route of administration is usually via injection directly into bloodstream
 - Two injected products are generally bioequivalent
 - But they may behave differently once in the body

Introduction: 110th Congress Proposals

- **Waxman** (February 2007)
 - Access to Life-Saving Medicine Act (H.R. 1038 / S.623)
- **Inslee** (April 2007)
 - Patient Protection and Innovative Biologic Medicines Act of 2007 (H.R. 1956)
- **Gregg** (May 2007)
 - Affordable Biologics for Consumers Act (S. 1505)
- **Kennedy/Clinton** (June 2007)
 - Biologics Price Competition and Innovation Act of 2007 (S.1695)
- **Eshoo** (March 2008)
 - Pathways for Biosimilars Act (H.R. 5629)

Introduction: 111th Congress Proposals

- Waxman (March 11, 2009)
 - Favored by generic industry
 - Access to Life-Saving Medicine Act
 - H.R. 1427 / S. 726
- Eshoo (March 17, 2009)
 - Favored by innovators
 - Pathways for Biosimilars Act
 - H.R. 1548
- Kennedy (not yet introduced)
 - Potential compromise position

Agenda

- Introduction
- **Major Issues**
 - Data Required for Approval
 - Biosimilarity Standard
 - Interchangeability Standard
 - Innovator Exclusivity
 - Exclusivity for Interchangeables
 - Patent Framework
- Critique of Waxman Bill
- What Happens Next?

Major Issues: Data Required for Approval

- Waxman
 - No clinical studies required
- Eshoo:
 - Requires at least one clinical study
 - FDA can waive this requirement only if it has previously issued guidance
- Kennedy
 - Requires at least one clinical study
 - FDA can waive this requirement at its discretion

Major Issues: Biosimilarity Standard

- Waxman
 - “No clinically meaningful difference...would be expected in terms of the safety, purity, and potency if treatment were to be initiated with the [biosimilar] instead of the reference product”
- Eshoo
 - FDA must issue product-class specific guidance
- Kennedy
 - Applicant must demonstrate a “lack of clinically meaningful differences”

Major Issues: Interchangeability Standard

- Waxman
 - “[T]he patient can be switched one or more times between the reference product and the [biosimilar] without an expected increase in the risk of adverse events...compared to the expected risks from continuing to use the reference product without such switching”
- Eshoo
 - “Same clinical result”
 - Risk of switching cannot be greater than the risk of using the pioneer product without switching
 - FDA guidance
- Kennedy
 - Similar to Eshoo, but no requirement for FDA guidance

Major Issues: Innovator Exclusivity

	Waxman	Eshoo	Kennedy
New Product	5 years	12 years	12 years
New Indication	3 – 6 months	2 years	N/A
Submission of Biosimilar Application	Any time after approval of reference product	4 years after approval of reference product	4 years after approval of reference product

Major Issues: Exclusivity for Interchangeables

- Eshoo: 24 months after 1st commercial marketing
- Waxman & Kennedy:

Exclusivity runs until the <u>earlier of</u>:	Kennedy	Waxman
Days after first commercial marketing	365	180
Months after final court decision on all patents in suit or the dismissal of such an action	18	12
Months after approval if patent litigation is still ongoing	42	36
Months after approval if applicant has not been sued	18	12

Major Issues: Patent Framework

- Waxman
 - Applicant controls much of the process
- Eshoo
 - Innovator and applicant both have some control over process
 - More similar to Hatch-Waxman framework for drugs
- Kennedy
 - Complicated process involving mandatory negotiations
 - Parties must attempt to agree on patents appropriate for litigation

Other Major Issues

- Deadlines for FDA action on applications
- Naming of biosimilars
- Labeling of interchangeable products
- Availability of legal remedies

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 - Exclusivity
 - Patent Framework
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Waxman Exclusivity

- An innovator product is eligible for exclusivity only if
 - “No major substance of the product, nor any highly similar major substance, has [previously] been approved [and] the application submitted for [the innovator] product is approved after the date of enactment . . . [and] could not and did not rely on any clinical safety, purity, or potency study in any other application . . . or any clinical safety or effectiveness study in any application approved under section 505 of the [FDCA].”

Waxman Patent Framework

- Limited information about the application is provided to the innovator:
 - “At any time, including at the initial stages of development, an applicant or prospective applicant . . . **may send a written request for patent information** to the holder of the approved application for the reference product. The holder of the approved application for the reference product shall . . .”

Waxman Patent Framework (cont'd)

- Innovator must provide information about tangentially related patents, including
 - “a list of all those patents . . . [it] believes in good faith relates to the reference product, including patents that claim the approved biological product, any formulation of such product, any method of using such product, any component of such product, or any method or process that can be used to manufacture such product or component, **regardless of whether that method or process is used to manufacture the reference product.**”

Waxman Patent Framework (cont'd)

- Innovator's failure to disclose results in draconian penalties
 - “The owner or licensee of a patent that should have been disclosed in response to a request for patent information made by [a biosimilar] applicant, but that was not timely disclosed . . . **may not bring an action under [35 U.S.C. § 271] for infringement of that patent.**”

Waxman Patent Framework (cont'd)

- All control over litigation timing is given to biosimilar applicant
 - “**At any time** after submitting an application . . . the applicant may provide a notice of the application with respect to any one or more patents identified by the [innovator] . . . An applicant may submit additional notices at any time. . . .”

Waxman Patent Framework (cont'd)

- All control over the patents to be litigated is given to the biosimilar applicant
 - “Within 45 days after the date on which the [innovator] receives a notice under subparagraph (B), the [innovator] may bring an action for infringement **only with respect to the patent or patents included in the notice.**”

Waxman Patent Framework (cont'd)

- Biosimilar applicant can control location of patent litigation
 - “In any action for patent infringement brought by the [innovator] pursuant to section 351(k)(18)(C) of the Public Health Service Act, **the defendant may move to transfer the action** to any other district in which jurisdiction is proper . . . When ruling on any [such] motion . . . **the greatest weight shall be given to the following factors**: (A) The interest in identifying a district court in which the case will be adjudicated expeditiously [and] (B) The strong public interest in obtaining prompt judicial resolution of patent disputes so that the [biosimilar] may be brought to market as expeditiously as possible. . . .”

Waxman Patent Framework (cont'd)

- Draconian penalties limit remedies to royalties (instead of injunction)
 - “In an action for infringement of a patent [for which the innovator brought suit after expiration of the 45-day period, or was brought within the 45-day period and dismissed without prejudice] . . . **the sole and exclusive remedy** that may be granted by a court, upon a finding that the [biosimilar applicant] infringed the patent, or that any person induced or contributed to infringement of the patent, **shall be a reasonable royalty**.”

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Where It Stands Now

- **Waxman proposal**
 - 9 co-sponsors
- **Eshoo proposal**
 - 64 co-sponsors
 - Backed by New Democrat Coalition
- **Kennedy proposal**
 - Expected to be the key Senate bill, but support appears fractured with loss of Hillary Clinton
 - Lost support of Sen. Brown and Sen. Schumer, seeking support of Sen. Dodd

Obama Administration

- Projects \$6.35 billion from biosimilars in 2009-2010 to pay for health reform
- Calculations are based on a 7 year exclusivity period
 - Not clear if this now represents the new standard around which a biosimilars bill must be negotiated

Connection to Health Reform

- Insider viewpoints
 - Kennedy: bill is a way to pay for both health reform and for the national service bill
 - Hatch: inclusion of the bill with health reform is key to its passage
 - Dean: biosimilars legislation is a critical aspect of health reform
- Industry viewpoints
 - Biosimilars
 - Quick timetable for health reform may mean little time for compromise, possibly resulting in passage of a Kennedy-like bill with long exclusivity periods
 - Shorter exclusivity periods mean greater health care savings
 - Innovators
 - Longer exclusivity provides for greater R&D job growth and incentives for innovation

What Happens Next?

- Waxman's health counsel Ann Witt:
 - Waxman's current main priorities are health reform and climate change, not biosimilars
 - "Finding time to get this bill through is challenging"
 - Wild card is whether bill gets tied up in health reform
- Likely structure if a bill is passed:
 - House
 - Any compromise bill is expected to be more in line with Waxman's bill than Eshoo's due to greater expected cost savings associated (shorter exclusivity period)
 - Senate
 - Unclear; still awaiting introduction of Kennedy bill

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