BIOSIMILARS AND THE BPCI ACT: WHERE ARE WE NOW AND WHERE ARE WE GOING?

Presented by the
American Bar Association
Section of Science and Technology,
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   Ken Burchfiel, Michael Dzwonczyk and William Simmons, Ph.D.
Biosimilars and the BPCI Act: Where Are We Now and Where Are We Going?
Regulatory Issues, Part 1

John Engel, Managing Partner, Engel & Novitt LLP

Thursday, September 19, 2013 | 2:00 PM Eastern
Sponsored by the ABA Section of Science and Technology Law and the ABA Section of Intellectual Property Law

Outline Of Presentation

• Rationale For Adoption Of U.S. Biosimilars Pathway
• Healthcare Reform Law Enabled U.S. Biosimilars Pathway
• Key Regulatory Features Of U.S. Biosimilars Pathway
• Implementation Of U.S. Biosimilars Pathway By FDA
• Key Regulatory Considerations In U.S. Biosimilars Pathway
• Where Does The U.S. Pathway Stand Relative To The European Record
• Additional Reading That Might Be Of Interest
Rationale For Adoption Of U.S. Biosimilars Pathway (1)

- The over 50-year-old provisions of the PHS Act governing biological product licensure are limited:
  - Contain inherently-flexible standards
  - No statutory mandate for pre-clinical or clinical trials
  - Confer substantial discretion on FDA
  - Defers to the Agency’s expert scientists
  - Impose mandate for FDA approval once a biological product is demonstrated to be safe, pure, and potent
  - Enabled the biotech revolution – especially early biotech approvals
  - Licensure of many biological products was based on limited data sets

Rationale For Adoption Of U.S. Biosimilars Pathway (2)

- 42 U.S.C. § 262(a)(2)(C) provides:
  
  (C) The Secretary shall approve a biologics license application -
  (i) on the basis of a demonstration that -
  (I) the biological product that is the subject of the application is safe, pure, and potent; and
  (II) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and
  (ii) if the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c) of this section.

- This is the traditional, 351(a) pathway for a BLA, and it remains available today for all biological products
Rationale For Adoption Of U.S. Biosimilars Pathway (3)

• However, the PHS Act provisions for licensing biological products:
  – Lacked authority for biosimilars in FDA’s legal opinion
  • FDA would not license third-party applications for comparable biologics leveraging published data and prior FDA findings of safety, purity, and potency
  – Lacked Hatch-Waxman-like R&D incentives for biological products
  • PHS Act biologics received patent-term restoration but were ineligible for non-patent exclusivity

Health-Care Reform Law Enabled U.S. Biosimilars Pathway

• Patient Protection & Affordable Care Act (PPACA), Public Law No. 111-148 (March 23, 2010)

• The “Biologics Price Competition and Innovation Act” or BPCI Act, establishes the biosimilars pathway
  – From unamended BPCIA (S.1695, 110th Congress)
  • Adopted by Senate HELP Committee (June 27, 2007) and reported to Senate Floor (November 19, 2008)
  • Incorporated in toto in the Senate-passed health-care reform bill
  • Absence of Conference Committee on PPACA meant no further opportunity to amend the provisions of the BPCI Act
Key Regulatory Features Of U.S. Biosimilars Pathway (1)

- BPCIA grants FDA express authority to review applications for, license, and regulate biosimilars
- Biosimilar is limited to single reference biologic (RB)
  - Must rely on FDA’s prior S&E finding for RB
- Sponsors effectively follow two-step process:
  - Biosimilarity based on specific statutory requirements
    - Analytics, preclinical, and clinical studies, including immunogenicity (any of which FDA can waive)
    - Interchangeability presumably based on switching studies
- Sponsors can pursue a subset of indications

Key Regulatory Features Of U.S. Biosimilars Pathway (2)

- Clinical studies in all uses are not mandated if the biosimilar and RB share the same mechanism of action
  - Facilitates extrapolation of indications consistent with sound science
- Biosimilar applications can proceed without FDA guidance
- Biosimilars must follow standard requirements for biologics approvals
  - User fees, risk-mitigation strategies, etc.
Implementation Of U.S. Biosimilars Pathway By FDA (1)

- Two years after enactment of the BPCI Act, FDA issued three Draft Guidance documents (Feb. 2012):
  - "Quality Consideration in Demonstrating Biosimilarity to a Reference Protein Product" ("Quality Guidelines")
  - "Scientific Consideration in Demonstrating Biosimilarity to a Reference Product" ("Scientific Guidelines")
  - "Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009" ("Biosimilars Q&A")

- These Draft Guidances current establish the core regulatory framework for biosimilars in the U.S.
  - Revisions and further Guidance forthcoming

Implementation Of U.S. Biosimilars Pathway By FDA (2)

- Subsequently, the Biosimilar User Fee Act of 2012 (BsUFA) was enacted as part of the Food and Drug Administration Safety and Innovation Act (FDASIA)
- Based on BsUFA and associated Performance Goals and Procedures, FDA issued another Draft Guidance:
  - Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants (Mar. 2013)
    - Outlines requirements for biosimilar development programs, user fees, and related administrative considerations
**Key Regulatory Considerations In U.S. Biosimilars Pathway (1)**

- FDA has delineated requirements for demonstrating analytical similarity using a “stepwise approach”
  - FDA will conduct “risk-based” review of “totality of evidence” submitted
  - FDA will determine scope and type of testing required on a case-by-case ("product-specific") basis
- FDA expects sponsors to generate “extensive” analytical, physico-chemical, and characterization data utilizing “state-of-the-art” technology
  - If products cannot be adequately characterized, sponsor should confer with FDA on appropriateness of biosimilar pathway for the development program

**Key Regulatory Considerations In U.S. Biosimilars Pathway (2)**

- FDA’s Draft Guidance delineates requirements for demonstrating nonclinical and clinical similarity
  - Following analytical characterization and comparisons, FDA generally expects the stepwise approach to include a comparison of:
    - Animal toxicity
    - Animal pharmacokinetics (PK) and pharmacodynamics (PD)
    - Animal immunogenicity
    - Human PK and PD
    - Human clinical safety and effectiveness
    - Human clinical immunogenicity
Key Regulatory Considerations In U.S. Biosimilars Pathway (3)

- FDA anticipates conveying advice on scope of studies after reviewing structural/functional data
  - Advice conveyed through array of meetings:
    - Biosimilar Initial Advisory meeting: covers feasibility of biosimilar pathway for a given biologic and general advice on the development program’s scope
    - Biosimilar Product Development (BPD) Type 1 meeting: addresses clinical hold, special protocol assessments, important safety issues, or a dispute(s)
    - BPD Type 2 meeting: discuss specific issue(s) to allow FDA to provide targeted advice
    - BPD Type 3 meeting: provide advice based on in-depth data review for ongoing development program
    - BPD Type 4 meeting: review dossier format/content

Key Regulatory Considerations In U.S. Biosimilars Pathway (4)

- FDA’s implementation of BPCI Act, including provision of advice to sponsors and review of applications, is biosimilar user-fee-funded
  - Unlike other user fee programs (e.g., PDUFA), BsUFA “front loads” user fee payments
    - Biosimilar sponsors pay a portion of total user fee at each major stage of development program
      - Regulatory framework may only evolve as quickly as development programs advance with user fees paid
    - Biosimilar sponsors pay the same total user fee as a traditional BLA for an originator biological product
  - As of 1Q2013, FDA had received 51 meeting requests on 12 different biological products, had held 38 initial meetings, and had received 15 INDs
Where Does The U.S. Pathway Stand Relative To The European Record?

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Further Reading That Might Be Of Interest


Thank You! Questions?

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Biosimilars and the BPCI Act: Where Are We Now and Where Are We Going? Regulatory Issues, Part 2

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Thursday, September 19, 2013 | 2:00 PM Eastern
Sponsored by the ABA Section of Science and Technology Law and the ABA Section of Intellectual Property Law

Agenda

• Use of data comparing biosimilar with comparator product not licensed in the United States
• Considerations for biosimilars of complex products
• Interchangeability and state substitution laws
• Naming
• Exclusivity
**Use of Non-US Comparator Products**

- **Issue:** Can applicant rely on studies that compare the biosimilar to a non-US-licensed product?
- **Statutory language:**
  - Defines “reference product” as “the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k)”
  - States that application may include additional supportive information, “including publicly-available information with respect to the reference product or another biological product”

**Draft Guidance on Non-US Comparators**

- In general, applicant needs to provide data directly comparing the biosimilar with the US-licensed reference product (US RP)
- Analytical studies and at least one human pharmacokinetic (and, if appropriate, at least one pharmacodynamic) study must involve US RP
- But may use non-US comparator data “in certain circumstances” to support biosimilarity
- For “certain complex biological products, a modified approach may be needed”
Draft Guidance: Non-US Products

- Applicant may use data from animal or clinical studies comparing proposed biosimilar with non-US-licensed comparator, if applicant:
  - Scientifically justifies relevance of data to the biosimilarity assessment; and
  - Establish acceptable “bridge” to US RP (likely including clinical PK/PD study with US RP)

Complex Products: BPCIA Provision on Guidance

- Statute permits, but does not require, product-class specific guidance
- Guidance may state that current science and experience do not allow approval of biosimilars in a product class (other than recombinant proteins)
- Any product-class guidance must describe:
  - FDA’s criteria for determining whether biosimilars are “highly similar” to reference products in the class; and
  - The criteria (“if available”) that FDA will use to make interchangeability decisions
FDA Approach to Complex Biologics

• FDA officials have stated that the agency does not plan to issue product class guidance at this time
• Draft Guidance focuses on therapeutic proteins
• Also states: “If the reference product cannot be adequately characterized with state-of-the-art technology, the sponsor should consult FDA for guidance on whether an application for such a protein product is appropriate for submission under section 351(k) of the PHS Act”

Interchangeability : BPCIA

• Application must establish
  – Biosimilar can be expected to produce the same clinical result as RP in any given patient
  – If product is administered more than once to an individual, risk of alternating or switching between products is not greater than risk of using RP alone
• “Interchangeable” product may be substituted for the RP without the intervention of the prescriber
Draft Guidance on Interchangeability

• “Higher standard” than biosimilarity
• “Difficult” to establish in original biosimilar application given the “sequential nature” of the assessment
• Clinical switching study needed (Sherman)
• “Unlikely” that clinical comparisons with a non-US-comparator would support a determination of interchangeability with US RP

Substitution: State Laws

• Biosimilar substitution bills introduced, but not yet signed into law, in 12 states
  – Arizona, Arkansas, California, Colorado, Delaware, Illinois, Maryland, Massachusetts, Mississippi, Pennsylvania, Texas, Washington
• Biosimilar substitution laws signed into law in 6 states
  – Florida, Indiana, North Dakota, Oregon, Utah, Virginia
Example: Florida Conditions for Biosimilar Substitution

• FDA has determined product to be interchangeable with prescribed biological product;
• Prescribing physician does not express preference against biosimilar substitution in writing, verbally, or electronically;
• Pharmacist notifies “person presenting the prescription of the substitution”;
• Pharmacist notifies prescriber of the substitution within 10 business days of dispensing the biosimilar; and
• Pharmacist retains written or electronic record of the substitution for at least 2 years

Developments on Naming

• World Health Organization (WHO) International Nonproprietary Names (INN)
  – WHO current policy for glycosylated biosimilars: same INN as RP, but further qualified by a Greek letter suffix
  – WHO is actively considering how to adopt a globally harmonized approach to naming biosimilars (e.g., a distinct prefix to INN)
• Moves toward unique names in various regions, e.g., Japan, Australia
Naming: FDA Statements

- October 2010 Federal Register notice
  - FDA “must be able to distinguish between a reference product, … a biosimilar product, and an interchangeable product”
  - Sought comments on distinct prefix or suffix
- 2011 article in New England Journal of Medicine: “Tracking adverse events associated with the use of reference and biosimilar products will be difficult if the specific product or manufacturer cannot be readily identified”
- Approach in recent BLA approvals (e.g., tbo-filgrastim)

Exclusivity

- A biosimilar application may not be:
  - Submitted until 4 years after first licensure of RP
  - Effective until 12 years after first licensure of RP
- “First licensure” excludes date of approval of:
  - Supplements;
  - Certain nonstructural modifications (e.g., new dosage form) from same company or “related entity”; and
  - Structural modifications that do not result in changes in safety, purity, or potency from same company or “related entity”
Pediatric Exclusivity

- If conditions for pediatric exclusivity are met, RP gets an additional 6 months of exclusivity:
  - 4 years + 6 months until biosimilar application may be submitted
  - 12 years + 6 months until approval of biosimilar application may be effective
  - 7 years + 6 months for orphan drug exclusivity

Exclusivity: Draft Guidance

- Requests for exclusivity should be submitted with the BLA
- Applicant should describe how proposed product meets the statutory requirements and submit “adequate data and information” to support the request
- No substantive interpretation of first licensure provision
Questions?

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STRATEGIC USE OF USPTO PATENT TRIALS IN BIOSIMILARS LITIGATION

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Patent Lists

| ¶(3)(A) | RPS list of infringed patents |
| ¶(3)(B) | Optional applicant list of additional infringed patents |
| ¶(4)(A) | Agreed list |
| ¶(5)(A) | If no agreed list, applicant decides number of patents |
| ¶(5)(B) | Exchange of short lists |
| ¶(6)   | RPS sues on patents included in list |
Sponsor listing strategy

List all patents that could be asserted
- Any unlisted patent will be barred

- Decide which patents to assert in first stage litigation (30 days after negotiation) (¶ 6)
  - Basis for permanent injunction and damages

- Decide which patents to assert in second stage litigation (within 180 days of commercial marketing)
  - Relief is limited to a reasonable royalty

35 USC 271(e)(6)(A),(B)

Patent Lists

Lists Determine Scope of Relief

- If parties fail to agree on the initial list (¶ (4)), the number of patents listed by applicant under ¶ (5)(B)(i) limits the initial scope of the infringement action – it can be ONE patent - ¶ (5)(B)(ii)

- No preliminary injunction for a listed patent - ¶ (8)(B)

- If the applicant excludes a patent from its final ¶ (5)(B) list, a preliminary injunction is available as well as a permanent injunction and damages – ¶ 8(B)
Applicant decides scope of suit

- Applicant learns of all potentially infringed patents
- Applicant elects to:
  - Include all patents proposed by sponsor and risk immediate suit on all patents
    - Eliminate preliminary injunction
    - Resolve patent disputes before FDA approval
  - Exclude some or all patents proposed by sponsor and postpone suit on excluded patents until 180 days before commercial marketing
    - Risk preliminary injunction in later actions

42 USC 262(l)(8)

Applicant listing strategy 1

- Agree to sponsor's list of all patents and be sued immediately on some or all of them
- Add patents to sponsor's list and invite immediate suit on them as well
- Potentially limit damages to a reasonable royalty on listed patents if sponsor does not sue immediately
  - 35 USC 271(e)(6)(B)
- Avoid preliminary injunction on listed patents
- Preserve ability to launch at risk before final Federal Circuit judgment
Applicant listing strategy 2

- Limit sponsor's proposed list to one or a few patents
- Avoid immediate suit on other listed patents
- Risk preliminary and permanent injunction on other listed patents 180 days before commercial marketing
- Postpone trial and market entry

USPTO Patent Trials

New *inter partes* proceedings for challenging patents:
- *Inter partes review*
- *Post-grant review*

- Administrative litigation in USPTO
  - Limited to issues of validity
- Independent of US district court infringement actions
USPTO Patent Trials

Inter partes review:
• based only on published prior art
  – Lack of novelty or obviousness
• must be filed within 1 year of patent infringement litigation commencement
• final USPTO validity decision within 1 year
• direct appeal to Federal Circuit

2-Track Patent Litigation
USPTO patent trials provide:
• A parallel path in patent litigation--
  – Validity issues decided in USPTO
  – Infringement issues decided in court
    • limiting scope of discovery
    • limiting litigation expenses
  – Stay of court action is likely
    • limiting litigation expenses
Parallel Patent Strategy

• Early validity decision in USPTO and immediate appeal to Federal Circuit
• Reduced costs of district court discovery, summary judgment motions and trial
• Applicant's advantages:
  – Expert judges
  – Favorable burden of proof
  – Avoidance of preliminary injunction
• Sponsor's advantages: none

Settlement

• Terminates USPTO review
  – without trial
  – no estoppel
• Leverage
  – credible threat of invalidation
• Terms
  – discretion of parties
  – confidential
2-Track Patent Litigation

1 YEAR

DISTRICT COURT INFRINGEMENT ACTION

STAY OF DISTRICT COURT ACTION

USPTO PATENT TRIAL INITIATED

MOTIONS AND USPTO DECISION

APPEAL

FEDERAL CIRCUIT DECISION

2 YEARS

PRETRIAL DISCOVERY AND MOTIONS

1 YEAR

DISTRICT COURT INFRINGEMENT ACTION

PRETRIAL DISCOVERY AND MOTIONS

TRIAL OF VALIDITY AND INFRINGEMENT

DECISION BY JUDGE

2 YEARS

DENIAL OF PRELIMINARY INJUNCTION

USPTO PATENT TRIAL INITIATED

MOTIONS AND USPTO DECISION

APPEAL

FEDERAL CIRCUIT DECISION
2-Track Patent Litigation

1 YEAR | 2 YEARS | 3 YEARS

DISTRICT COURT INFRINGEMENT ACTION
PRETRIAL DISCOVERY AND MOTIONS
TRIAL OF VALIDITY AND INFRINGEMENT
DECISION BY JUDGE

VALID
LIMITED DISCOVERY
TRIAL OF INFRINGEMENT/DAMAGES ONLY

INVALID
NO TRIAL
NO DAMAGES

MOTIONS AND USPTO DECISION
SETTLEMENT
TRIAL/NO TRIAL
EARLY MARKET ENTRY?

USPTO Patent Trial Costs

Inter Partes Review
Post-Grant Review

Trial
Petition
PTO Fees
Patent Litigation Costs

Litigation Costs 2011

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Patent Owner's Disadvantage

Based on inter partes reexamination:
- 90% of petitions will be granted
- Claims will be canceled or amended in over 80% of proceedings
- Initiation of a proceeding will immediately affect patent valuation

Invalidity Defenses

![Invalidity Defenses Chart]

- Red: All claims invalid
- Yellow: Claims amended
- Blue: All claims valid

Federal Court HWA (?) vs. Inter partes Reexamination
**Inter partes Reexamination Results 1999-2012**

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<th>Number of cases decided</th>
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**Inter Partes Review**

- PTO final decision in 1 year - certainty
- Limited costs
- Favorable odds for requester
- Full participation by requester
  - Limited discovery
  - Expert testimony and cross-examination
  - All proceedings are *inter partes* before APJ
- Estoppel consequences
Estoppel

- Defendant may not raise in district court (or in a later USPTO proceeding):
  - Any defense that was actually raised, or that reasonably could have been raised in inter partes review or post-grant review
  - Estoppel from *inter partes* review is limited to prior art defenses
- If you can't win in the USPTO with a favorable burden of proof, why would you win in district court?

Applicant listing strategy 1

- Agree to sponsor's list of all patents and be sued immediately on some or all of them
- Challenge core patents in concurrent USPTO trials
  - Leverage settlement
  - Move to stay action if *inter partes* review is instituted
- Avoid preliminary injunction on listed patents
  - Preserve ability to launch at risk before final Federal Circuit judgment
Applicant listing strategy 2

- Limit sponsor's proposed list to one or a few patents
- Avoid immediate suit on other listed patents
  - Postpone trial on other patents until 180 days before commercial marketing
  - Risk preliminary injunction on other patents and delay in market entry after approval
- Challenge core patents in concurrent USPTO trials
  - Avoid preliminary injunction if IPR is instituted
  - Move to stay action if IPR is instituted

This presentation is for educational purposes only, and does not provide legal advice or comment on the application of US law or USPTO regulations to any specific patent or application.

The views expressed herein are not necessarily those of Sughrue Mion, PLLC or any of its clients.
Thanks!

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PREPARING FOR BIOSIMILAR PATENT DISPUTES

MANAGING BIOLOGIC PATENTS IN THE NEW ERA OF US POST GRANT PROCEEDINGS

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Overview

• Section 351(k) –
  – Definitions for Biosimilarity and Interchangeability
  – Required content of biosimilar application
  – Interchangeability standards and exclusivity
  – Exclusivity for Reference Product
  – General Rules

• Section 351(l) – Patent Rules
  42 USC § 262(l) Patents:
  (1) Confidential Access to Applications
  (2) Application Information
  (3) List and Description of Patents
  (4) Patent Resolution Negotiations
  (5) Patent Resolution If No Agreement
  (6) Immediate Patent Infringement Action
  (7) Newly Issued or Licensed Patents
  (8) Notice of Commercial Marketing and PIs
  (9) Limitation on DJ Actions

Pre-Litigation Procedure

• No Orange Book listing
• Notice of acceptance of application by the biosimilar applicant(s)
• Complete disclosure of the biosimilar application to the reference product sponsor
• Exchange of lists of patents where a claim of patent infringement could reasonably be asserted by the reference product sponsor
• Exchange of infringement claims and defenses
• Dispute resolution negotiations before an infringement suit can be filed.
Initial Disclosures by Subsection K Applicant

- Notification and Patent Infringement Action
  - Applicant must notify, within 20 days, of FDA's acceptance of the application to the reference product sponsor, providing “confidential access” \((E)\) to the application and, optionally, other information (e.g., describing manufacturing processes)
  - Provided to in-house and designated outside counsel; as well as to a designated representative of the owner of any relevant patent exclusively licensed to the reference product sponsor \((B)\) to \((D)\)
  - Purpose: to provide the reference product sponsor with the information needed to ascertain if the biosimilar product would infringe any patents owned or exclusively licensed by the reference product sponsor.

Exchange of Patents Lists

- 60 days later:
  - After receiving the application and any other disclosures, the reference product sponsor must then provide the biosimilar applicant with a list \((3)(A)\) of patents owned or exclusively licensed by the reference product sponsor that it reasonably believes would be infringed if the biosimilar product is made, used, sold, offered for sale, or imported in the U.S. without a license from the reference product sponsor.
  - The reference product sponsor must also identify any patents it is willing to license.
  - There is no remedy available for any unlisted patent.
Exchange of Patent Lists

• 60 Days Later:
  – At a minimum, the applicant must provide the sponsor with a detailed, claim-by-claim statement as to the patents in the sponsor's list that the applicant considers invalid and/or not infringed, OR a statement that the applicant is not going to market before the sponsor's patents expire.
  – The biosimilar applicant then has the opportunity, but no obligation, to provide the sponsor with its own list of patents for which it believes the reference sponsor could assert (e.g., reasonably claim are infringed).

• 60 Days Later:
  – The reference product sponsor must provide a detailed statement why it believes that the patents are valid and infringed.
Number of Patents Litigated

- The parties are required to negotiate to determine the patents to be litigated.
- If no agreement is reached, the biosimilar applicant will identify the number of sponsor patents it believes should be litigated \( ((§)(5)(A)) \)
- Simultaneously, the sponsor will identify the patents it believes should be litigated.
- Importantly, the legislation requires that the number of sponsor patents cannot be greater than the number of patents the applicant identifies. \( ((§)(5)(B)(ii)) \)
- The sponsor must then bring an infringement action within 30 days.

Notice of Commercial Marketing

- The statute requires the biosimilar applicant to provide the reference product sponsor with notice of commercial marketing at least 180 days before the first commercial marketing of the biosimilar. \( ((§)(8)(A)) \)
Reasonable royalties

– If the innovator fails to bring a patent suit within the specified time or if the suit is timely brought but is not prosecuted in good faith or is dismissed without prejudice, the sole relief available to the innovator is reasonable royalties. 35 U.S.C. 271(e)(6)(A),(B)

– The exclusion of injunctive relief for the innovator creates a strong incentive for the innovator to bring a timely suit and to prosecute the litigation in good faith.

Pre-litigation Strategies

• Biosimilar Applicant has the ability to initially limit the number of patents at issue
  – Immediately reduces costs
  – Permits additional time for identifying potential weaknesses in excluded patents
Pre-litigation Strategies

• Continually identify, review and monitor any relevant patent portfolios
• Objectively assess claims well in advance of litigation – there will be little time to do this under the statute

Thank you.
**Biosimilar Patent Litigation §351(i) Provisions**

**F.D.A. Notifies Applicant That Application Has Been Accepted**
- 20 days

**Applicant Notifies RLP Sponsor and Provides a Copy of Its Application Under Confidential Terms**
- 60 days

**RLP Sponsor**
1. Provides Applicant with **List of Patents** that may be infringed and
2. Identifies patents it is **willing to license**
- 60 days

**Applicant**
1. May provide a **List of Patents** that are not infringed or invalid
2. Provides Detailed **Statement of Invalidity or Noninfringement** for each RLPs patent, or states that it will wait until expiration and
3. States patents it is willing to take a license
- 60 days

**Negotiations**
- (15 days)

**Agreement on List**
- 30 days

**Disagreement**

**Agreement on List**
- Applicant notifies RLPs of **number of patents** at issue
- 5 days

**Disagreement**

**Simultaneous Exchange of Patent Lists**
- 30 days

**Agreement on List**
- RLP sponsor files lawsuit on all agreed patents
- 30 days

**Disagreement**
- Applicant notifies FDA of suit and provides complaint
- 30 days

**Disagreement**
- RLP sponsor files lawsuit on patents in both lists
- 30 days

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- **¶(3)(A)**
- **¶(3)(B)**
- **¶(4)(A)**
- **¶(5)(A)**
- **¶(5)(B)**
BIOSIMILAR PATENT LITIGATION PROVISIONS

**NO STAY OF FDA APPROVAL**

- FDA APPROVAL
- 180 DAYS
- COMMERCIALIZATION

**LITIGATION**

- APPLICANT NOTICE TO RLP SPONSOR

**PRELIMINARY INJUNCTION AGAINST COMMERCIAL MARKETING**

- LATER ISSUED OR LICENSED PATENTS
- PATENT(S) IN SUIT ON ¶4(A) or ¶5(B) LIST
- ANY PATENT ON ¶3(A) or ¶3(B) LIST THAT IS NOT ON ¶4(A) or ¶5(B) LIST

**NO REMEDY FOR INFRINGEMENT OF NON-LISTED PATENTS**

**TRIAL**

- APPLICANT WINS
- ACTION DISMISSED WITHOUT PREJUDICE
- RLP SPONSOR WINS

- EXCLUSIVITY AGAINST OTHER APPLICANTS
- REASONABLE ROYALTY IS SOLE REMEDY
- PERMANENT INJUNCTION UNTIL EXPIRATION
## Patent Lists

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BIOLOGICS PRICE COMPETITION AND INNOVATION ACT OF 2009

[42 U.S.C. §262]

[351] Regulation of biological products

(i) “Biological product” defined

In this section:

(1) The term “biological product” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

(2) The term ‘biosimilar’ or ‘biosimilarity’, in reference to a biological product that is the subject of an application under subsection (k), means--

(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and
(B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

(3) The term `interchangeable' or `interchangeability', in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

(4) The term `reference product' means the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k).


**[351](k) LICENSURE OF BIOLOGICAL PRODUCTS AS BIOSIMILAR OR INTERCHANGEABLE**

**[351(k)](1) IN GENERAL-** Any person may submit an application for licensure of a biological product under this subsection.

**[351(k)](2) CONTENT-**

(A) IN GENERAL-

(i) REQUIRED INFORMATION- An application submitted under this subsection shall include information demonstrating that--

(I) the biological product is biosimilar to a reference product based upon data derived from--

(aa) analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;

(bb) animal studies (including the assessment of toxicity); and
(cc) a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate safety, purity, and potency in 1 or more appropriate conditions of use for which the reference product is licensed and intended to be used and for which licensure is sought for the biological product;

(II) the biological product and reference product utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism or mechanisms of action are known for the reference product;

(III) the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product;

(IV) the route of administration, the dosage form, and the strength of the biological product are the same as those of the reference product; and

(V) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

(ii) DETERMINATION BY SECRETARY- The Secretary may determine, in the Secretary's discretion, that an element described in clause (i)(I) is unnecessary in an application submitted under this subsection.

(iii) ADDITIONAL INFORMATION- An application submitted under this subsection--

(I) shall include publicly-available information regarding the Secretary's previous determination that the reference product is safe, pure, and potent; and
(II) may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product.

(B) INTERCHANGEABILITY - An application (or a supplement to an application) submitted under this subsection may include information demonstrating that the biological product meets the standards described in paragraph (4).

[351(k)](3) EVALUATION BY SECRETARY - Upon review of an application (or a supplement to an application) submitted under this subsection, the Secretary shall license the biological product under this subsection if--

(A) the Secretary determines that the information submitted in the application (or the supplement) is sufficient to show that the biological product--

(i) is biosimilar to the reference product; or

(ii) meets the standards described in paragraph (4), and therefore is interchangeable with the reference product; and

(B) the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

[351(k)](4) SAFETY STANDARDS FOR DETERMINING INTERCHANGEABILITY - Upon review of an application submitted under this subsection or any supplement to such application, the Secretary shall determine the biological product to be interchangeable with the reference product if the Secretary determines that the information submitted in the application (or a supplement to such application) is sufficient to show that--

(A) the biological product--

(i) is biosimilar to the reference product; and
(ii) can be expected to produce the same clinical result as the reference product in any given patient; and

(B) for a biological product that 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 biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

(351(k)(5) GENERAL RULES-

(A) ONE REFERENCE PRODUCT PER APPLICATION- A biological product, in an application submitted under this subsection, may not be evaluated against more than 1 reference product.

(B) REVIEW- An application submitted under this subsection shall be reviewed by the division within the Food and Drug Administration that is responsible for the review and approval of the application under which the reference product is licensed.

(C) RISK EVALUATION AND MITIGATION STRATEGIES- The authority of the Secretary with respect to risk evaluation and mitigation strategies under the Federal Food, Drug, and Cosmetic Act shall apply to biological products licensed under this subsection in the same manner as such authority applies to biological products licensed under subsection (a).

(351(k)(6) EXCLUSIVITY FOR FIRST INTERCHANGEABLE BIOLOGICAL PRODUCT- Upon review of an application submitted under this subsection relying on the same reference product for which a prior biological product has received a determination of interchangeability for any condition of use, the Secretary shall not make a determination under paragraph (4) that the second or subsequent biological product is interchangeable for any condition of use until the earlier of--

(A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;
(B) 18 months after--

(i) a final court decision on all patents in suit in an action instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(ii) the dismissal with or without prejudice of an action instituted under subsection (l)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(C)(i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (l)(6) and such litigation is still ongoing within such 42-month period; or

(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (l)(6). For purposes of this paragraph, the term `final court decision' means a final decision of a court from which no appeal (other than a petition to the United States Supreme Court for a writ of certiorari) has been or can be taken.

[351(k)](7) EXCLUSIVITY FOR REFERENCE PRODUCT-

(A) EFFECTIVE DATE OF BIOSIMILAR APPLICATION APPROVAL- Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a).

(B) FILING PERIOD- An application under this subsection may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a).

(C) FIRST LICENSURE- Subparagraphs (A) and (B) shall not apply to a license for or approval of--

(i) a supplement for the biological product that is the reference product; or
(ii) a subsequent application filed by the same sponsor or manufacturer of the biological product that is the reference product (or a licensor, predecessor in interest, or other related entity) for--

(I) a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or

(II) a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

[351(k)](8) GUIDANCE DOCUMENTS-

(A) IN GENERAL- The Secretary may, after opportunity for public comment, issue guidance in accordance, except as provided in subparagraph (B)(i), with section 701(h) of the Federal Food, Drug, and Cosmetic Act with respect to the licensure of a biological product under this subsection. Any such guidance may be general or specific.

(B) PUBLIC COMMENT-

(i) IN GENERAL- The Secretary shall provide the public an opportunity to comment on any proposed guidance issued under subparagraph (A) before issuing final guidance.

(ii) INPUT REGARDING MOST VALUABLE GUIDANCE- The Secretary shall establish a process through which the public may provide the Secretary with input regarding priorities for issuing guidance.

(C) NO REQUIREMENT FOR APPLICATION CONSIDERATION- The issuance (or non-issuance) of guidance under subparagraph (A) shall not preclude the review of, or action on, an application submitted under this subsection.

(D) REQUIREMENT FOR PRODUCT CLASS-SPECIFIC GUIDANCE- If the Secretary issues product class-specific guidance under subparagraph (A), such guidance shall include a description of--
(i) the criteria that the Secretary will use to determine whether a biological product is highly similar to a reference product in such product class; and

(ii) the criteria, if available, that the Secretary will use to determine whether a biological product meets the standards described in paragraph (4).

(E) CERTAIN PRODUCT CLASSES-

(i) GUIDANCE- The Secretary may indicate in a guidance document that the science and experience, as of the date of such guidance, with respect to a product or product class (not including any recombinant protein) does not allow approval of an application for a license as provided under this subsection for such product or product class.

(ii) MODIFICATION OR REVERSAL- The Secretary may issue a subsequent guidance document under subparagraph (A) to modify or reverse a guidance document under clause (i).

(iii) NO EFFECT ON ABILITY TO DENY LICENSE- Clause (i) shall not be construed to require the Secretary to approve a product with respect to which the Secretary has not indicated in a guidance document that the science and experience, as described in clause (i), does not allow approval of such an application.
(A) APPLICATION OF PARAGRAPH- Unless otherwise agreed to by a person that submits an application under subsection (k) (referred to in this subsection as the `subsection (k) applicant') and the sponsor of the application for the reference product (referred to in this subsection as the `reference product sponsor'), the provisions of this paragraph shall apply to the exchange of information described in this subsection.

(B) IN GENERAL-

(i) PROVISION OF CONFIDENTIAL INFORMATION- When a subsection (k) applicant submits an application under subsection (k), such applicant shall provide to the persons described in clause (ii), subject to the terms of this paragraph, confidential access to the information required to be produced pursuant to paragraph (2) and any other information that the subsection (k) applicant determines, in its sole discretion, to be appropriate (referred to in this subsection as the `confidential information').

(ii) RECIPIENTS OF INFORMATION- The persons described in this clause are the following:

(I) OUTSIDE COUNSEL- One or more attorneys designated by the reference product sponsor who are employees of an entity other than the reference product sponsor (referred to in this paragraph as the `outside counsel'), provided that such attorneys do not engage, formally or informally, in patent prosecution relevant or related to the reference product.

(II) IN-HOUSE COUNSEL- One attorney that represents the reference product sponsor who is an employee of the reference product sponsor, provided that such attorney does not engage, formally or informally, in patent prosecution relevant or related to the reference product.

(iii) PATENT OWNER ACCESS- A representative of the owner of a patent exclusively licensed to a reference product sponsor with respect to
the reference product and who has retained a right to assert the patent or participate in litigation concerning the patent may be provided the confidential information, provided that the representative informs the reference product sponsor and the subsection (k) applicant of his or her agreement to be subject to the confidentiality provisions set forth in this paragraph, including those under clause (ii).

(C) LIMITATION ON DISCLOSURE- No person that receives confidential information pursuant to subparagraph (B) shall disclose any confidential information to any other person or entity, including the reference product sponsor employees, outside scientific consultants, or other outside counsel retained by the reference product sponsor, without the prior written consent of the subsection (k) applicant, which shall not be unreasonably withheld.

(D) USE OF CONFIDENTIAL INFORMATION- Confidential information shall be used for the sole and exclusive purpose of determining, with respect to each patent assigned to or exclusively licensed by the reference product sponsor, whether a claim of patent infringement could reasonably be asserted if the subsection (k) applicant engaged in the manufacture, use, offering for sale, sale, or importation into the United States of the biological product that is the subject of the application under subsection (k).

(E) OWNERSHIP OF CONFIDENTIAL INFORMATION- The confidential information disclosed under this paragraph is, and shall remain, the property of the subsection (k) applicant. By providing the confidential information pursuant to this paragraph, the subsection (k) applicant does not provide the reference product sponsor or the outside counsel any interest in or license to use the confidential information, for purposes other than those specified in subparagraph (D).

(F) EFFECT OF INFRINGEMENT ACTION- In the event that the reference product sponsor files a patent infringement suit, the use of confidential information shall continue to be governed by the terms of this paragraph until such time as a court enters a protective order regarding the information. Upon entry of such order, the subsection (k) applicant may redesignate confidential information in accordance with the terms of that order. No confidential information shall be included in any publicly-available complaint or other pleading. In the event that the reference product sponsor does not file an infringement action by the date specified in paragraph (6), the reference product sponsor shall return or destroy all
confidential information received under this paragraph, provided that if the reference product sponsor opts to destroy such information, it will confirm destruction in writing to the subsection (k) applicant.

(G) RULE OF CONSTRUCTION- Nothing in this paragraph shall be construed--

   (i) as an admission by the subsection (k) applicant regarding the validity, enforceability, or infringement of any patent; or

   (ii) as an agreement or admission by the subsection (k) applicant with respect to the competency, relevance, or materiality of any confidential information.

(H) EFFECT OF VIOLATION- The disclosure of any confidential information in violation of this paragraph shall be deemed to cause the subsection (k) applicant to suffer irreparable harm for which there is no adequate legal remedy and the court shall consider immediate injunctive relief to be an appropriate and necessary remedy for any violation or threatened violation of this paragraph.

[351(l)](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.
(A) LIST BY REFERENCE PRODUCT SPONSOR- Not later than 60 days after the receipt of the application and information under paragraph (2), the reference product sponsor shall provide to the subsection (k) applicant--

(i) a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted by the reference product sponsor, or by a patent owner that has granted an exclusive license to the reference product sponsor with respect to the reference product, if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application; and

(ii) an identification of the patents on such list that the reference product sponsor would be prepared to license to the subsection (k) applicant.

(B) LIST AND DESCRIPTION BY SUBSECTION (k) APPLICANT- Not later than 60 days after receipt of the list under subparagraph (A), the subsection (k) applicant--

(i) may provide to the reference product sponsor a list of patents to which the subsection (k) applicant believes a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application;

(ii) shall provide to the reference product sponsor, with respect to each patent listed by the reference product sponsor under subparagraph (A) or listed by the subsection (k) applicant under clause (i)--

(I) a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the opinion of the subsection (k) applicant that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application; or
(II) a statement that the subsection (k) applicant does not intend to begin commercial marketing of the biological product before the date that such patent expires; and

(iii) shall provide to the reference product sponsor a response regarding each patent identified by the reference product sponsor under subparagraph (A)(ii).

(C) DESCRIPTION BY REFERENCE PRODUCT SPONSOR- Not later than 60 days after receipt of the list and statement under subparagraph (B), the reference product sponsor shall provide to the subsection (k) applicant a detailed statement that describes, with respect to each patent described in subparagraph (B)(ii)(I), on a claim by claim basis, the factual and legal basis of the opinion of the reference product sponsor that such patent will be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application and a response to the statement concerning validity and enforceability provided under subparagraph (B)(ii)(I).

(4) PATENT RESOLUTION NEGOTIATIONS-

(A) IN GENERAL- After receipt by the subsection (k) applicant of the statement under paragraph (3)(C), the reference product sponsor and the subsection (k) applicant shall engage in good faith negotiations to agree on which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6).

(B) FAILURE TO REACH AGREEMENT- If, within 15 days of beginning negotiations under subparagraph (A), the subsection (k) applicant and the reference product sponsor fail to agree on a final and complete list of which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6), the provisions of paragraph (5) shall apply to the parties.
[351(0)](5) PATENT RESOLUTION IF NO AGREEMENT-

(A) NUMBER OF PATENTS- The subsection (k) applicant shall notify the reference product sponsor of the number of patents that such applicant will provide to the reference product sponsor under subparagraph (B)(i)(I).

(B) EXCHANGE OF PATENT LISTS-

(i) IN GENERAL- On a date agreed to by the subsection (k) applicant and the reference product sponsor, but in no case later than 5 days after the subsection (k) applicant notifies the reference product sponsor under subparagraph (A), the subsection (k) applicant and the reference product sponsor shall simultaneously exchange--

(I) the list of patents that the subsection (k) applicant believes should be the subject of an action for patent infringement under paragraph (6); and

(II) the list of patents, in accordance with clause (ii), that the reference product sponsor believes should be the subject of an action for patent infringement under paragraph (6).

(ii) NUMBER OF PATENTS LISTED BY REFERENCE PRODUCT SPONSOR-

(I) IN GENERAL- Subject to subclause (II), the number of patents listed by the reference product sponsor under clause (i)(II) may not exceed the number of patents listed by the subsection (k) applicant under clause (i)(I).

(II) EXCEPTION- If a subsection (k) applicant does not list any patent under clause (i)(I), the reference product sponsor may list 1 patent under clause (i)(II).
(A) ACTION IF AGREEMENT ON PATENT LIST- If the subsection (k) applicant and the reference product sponsor agree on patents as described in paragraph (4), not later than 30 days after such agreement, the reference product sponsor shall bring an action for patent infringement with respect to each such patent.

(B) ACTION IF NO AGREEMENT ON PATENT LIST- If the provisions of paragraph (5) apply to the parties as described in paragraph (4)(B), not later than 30 days after the exchange of lists under paragraph (5)(B), the reference product sponsor shall bring an action for patent infringement with respect to each patent that is included on such lists.

(C) NOTIFICATION AND PUBLICATION OF COMPLAINT-

(i) NOTIFICATION TO SECRETARY- Not later than 30 days after a complaint is served to a subsection (k) applicant in an action for patent infringement described under this paragraph, the subsection (k) applicant shall provide the Secretary with notice and a copy of such complaint.

(ii) PUBLICATION BY SECRETARY- The Secretary shall publish in the Federal Register notice of a complaint received under clause (i).

(7) NEWLY ISSUED OR LICENSED PATENTS-

In the case of a patent that--

(A) is issued to, or exclusively licensed by, the reference product sponsor after the date that the reference product sponsor provided the list to the subsection (k) applicant under paragraph (3)(A); and

(B) the reference product sponsor reasonably believes that, due to the issuance of such patent, a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application, not later than 30 days after such issuance or licensing,
the reference product sponsor shall provide to the subsection (k) applicant a supplement to the list provided by the reference product sponsor under paragraph (3)(A) that includes such patent, not later than 30 days after such supplement is provided, the subsection (k) applicant shall provide a statement to the reference product sponsor in accordance with paragraph (3)(B), and such patent shall be subject to paragraph (8).

[351(l)](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.
(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, United States Code, 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, United States Code, 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, United States Code, for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product.
(505B)(n) New Active Ingredient-

(1) NON-INTERCHANGEABLE BIOSIMILAR BIOLOGICAL PRODUCT- A biological product that is biosimilar to a reference product under section 351 of the Public Health Service Act, and that the Secretary has not determined to meet the standards described in subsection (k)(4) of such section for interchangeability with the reference product, shall be considered to have a new active ingredient under this section.

(2) INTERCHANGEABLE BIOSIMILAR BIOLOGICAL PRODUCT- A biological product that is interchangeable with a reference product under section 351 of the Public Health Service Act shall not be considered to have a new active ingredient under this section.

Products Previously Approved Under Section 505-

(1) REQUIREMENT TO FOLLOW SECTION 351- Except as provided in paragraph (2), an application for a biological product shall be submitted under section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act).

(2) EXCEPTION- An application for a biological product may be submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) if--

(A) such biological product is in a product class for which a biological product in such product class is the subject of an application approved under such section 505 not later than the date of enactment of this Act; and

(B) such application--

(i) has been submitted to the Secretary of Health and Human Services (referred to in this subtitle as the `Secretary') before the date of enactment of this Act; or (ii) is submitted to the Secretary not later than the date that is 10 years after the date of enactment of this Act.

(3) LIMITATION- Notwithstanding paragraph (2), an application for a biological product may not be submitted under section 505 of the Federal Food, Drug, and
Cosmetic Act (21 U.S.C. 355) if there is another biological product approved under subsection (a) of section 351 of the Public Health Service Act that could be a reference product with respect to such application (within the meaning of such section 351) if such application were submitted under subsection (k) of such section 351.

(4) DEEMED APPROVED UNDER SECTION 351- An approved application for a biological product under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) shall be deemed to be a license for the biological product under such section 351 on the date that is 10 years after the date of enactment of this Act.

(5) DEFINITIONS- For purposes of this subsection, the term 'biological product' has the meaning given such term under section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act).

Pediatric Studies-

(1) APPLICATION OF CERTAIN PROVISIONS- The provisions of subsections (a), (d), (e), (f), (i), (j), (k), (l), (p), and (q) of section 505A of the Federal Food, Drug, and Cosmetic Act shall apply with respect to the extension of a period under paragraphs (2) and (3) to the same extent and in the same manner as such provisions apply with respect to the extension of a period under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act.

(2) MARKET EXCLUSIVITY FOR NEW BIOLOGICAL PRODUCTS- If, prior to approval of an application that is submitted under subsection (a), the Secretary determines that information relating to the use of a new biological product in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act--

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

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(B) if the biological product is designated under section 526 for a rare disease or condition, the period for such biological product referred to in section 527(a) is deemed to be 7 years and 6 months rather than 7 years.

(3) MARKET EXCLUSIVITY FOR ALREADY-MARKETED BIOLOGICAL PRODUCTS- If the Secretary determines that information relating to the use of a licensed biological product in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under subsection (a) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act--

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526 for a rare disease or condition, the period for such biological product referred to in section 527(a) is deemed to be 7 years and 6 months rather than 7 years.

(4) EXCEPTION- The Secretary shall not extend a period referred to in paragraph (2)(A), (2)(B), (3)(A), or (3)(B) if the determination under section 505A(d)(3) is made later than 9 months prior to the expiration of such period.

Orphan Products- If a reference product, as defined in section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act) has been designated under section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb) for a rare disease or condition, a biological product seeking approval for such disease or condition, a biological product seeking approval for such disease or condition under subsection (k) of such section 351 as biosimilar to, or interchangeable with, such reference product may be licensed by the Secretary only after the expiration for such reference product of the later of--

(1) the 7-year period described in section 527(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360cc(a)); and

(2) the 12-year period described in subsection (k)(7) of such section 351.
§ 271. Infringement of patent

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

(b) Whoever actively induces infringement of a patent shall be liable as an infringer.

(c) Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial noninfringing use, shall be liable as a contributory infringer.

...[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.
For an act of infringement described in paragraph (2)-

(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product, and

(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product, and

(D) the court shall order a permanent injunction prohibiting any infringement of the patent by the biological product involved in the infringement until a date which is not earlier than the date of the expiration of the patent that has been infringed under paragraph (2)(C), provided the patent is the subject of a final court decision, as defined in section 351(k)(6) of the Public Health Service Act, in an action for infringement of the patent under section 351(l)(6) of such Act, and the biological product has not yet been approved because of section 351(k)(7) of such Act.

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.

Subparagraph (B) applies, in lieu of paragraph (4), in the case of a patent--

(i) that is identified, as applicable, in the list of patents described in section 351(l)(4) of the Public Health Service Act or the lists of patents described in section 351(l)(5)(B) of such Act with respect to a biological product; and
(ii) for which an action for infringement of the patent with respect to the biological product--

(I) was brought after the expiration of the 30-day period described in subparagraph (A) or (B), as applicable, of section 351(l)(6) of such Act; or

(II) was brought before the expiration of the 30-day period described in subclause (I), but which was dismissed without prejudice or was not prosecuted to judgment in good faith.

(B) In an action for infringement of a patent described in subparagraph (A), 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.

(C) The owner of a patent that should have been included in the list described in section 351(l)(3)(A) of the Public Health Service Act, including as provided under section 351(l)(7) of such Act for a biological product, but was not timely included in such list, may not bring an action under this section for infringement of the patent with respect to the biological product.