

Video Webcast:

**Snapshot of Critical Issues and
Challenges in the New Biosimilars Framework**



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Implementation of the Biosimilars Framework

- FDA Organization
 - Biosimilar applications will be reviewed by the Division responsible for review and approval of the reference product
 - Biosimilars Review Committee (BRC) “will serve in an advisory capacity to the OND review divisions as they consider sponsor requests for advice about how to develop a biosimilar product and as they review biosimilar BLAs”
 - Will include experts from many disciplines and offices across CDER, representatives from CBER, and representatives from the Office of Chief Counsel
 - John Jenkins, Director of Office of New Drugs, will chair the BRC.
 - New Position – Associate Director for Biosimilars (Leah Christl, Acting)

Guidance Documents

- FDA may issue general or specific guidance, after opportunity for public comment
 - The issuance or non-issuance of such guidance does not preclude approval of a biosimilar
 - FDA must establish a process through which the public can provide FDA with input regarding priorities for issuing guidance
- **Class-specific guidance must include:**
 - A description of the criteria that FDA will use to determine whether a biological product is highly similar to a reference product in such product class, and
 - The criteria, if available, that FDA will use to determine whether a biological product is interchangeable with the reference product.
 - FDA 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, does not allow approval of a biosimilar product. FDA may, however, issue a subsequent guidance document to modify or reverse that prior position.

What is Biosimilarity?

“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.”

Interchangeability

- “...the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.”
- “....can be expected to produce the *same clinical result as the reference product in any given patient*; and...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.*”

Data Requirements

- Data Requirements
 - Analytical studies demonstrating that the biosimilar product is highly similar to the reference product notwithstanding minor differences in clinically inactive components
 - Animal studies, including an assessment of toxicity
 - Clinical study or studies, including but not limited to the assessment of immunogenicity and pharmacokinetics or pharmacodynamics, sufficient to demonstrate safety, purity, and potency in one 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 biosimilar product

- FDA may determine that certain application requirements are unnecessary and may waive the requirement to include such information

“BioBetter”?

- Could the new biosimilars process be used to develop a “biobetter” product, or will the full BLA route be the preferred pathway? Or a hybrid?

Post-Biosimilars Licensure

- REMS
 - “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).”

- Study and/or clinical trial requirements

Biosimilars: Innovator Exclusivities

- 12 years data exclusivity where no biosimilar may be approved - first 4 years where no biosimilar application may be submitted
- Potential orphan exclusivity for longer of 7 years from designation or 12 year data exclusivity
- Additional 6 months for pediatric studies

“Evergreening”

“FIRST LICENSURE.— [12-year exclusivity and 4-year biosimilar application delay] 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.”

Interchangeable Product Exclusivity

- Only products deemed interchangeable (as opposed to biosimilar) are eligible for exclusivity
- FDA may not approve a second interchangeable product until the earlier of:
 - 1 year after commercial marketing of first interchangeable product
 - 18 months after final court decision or dismissal in patent suit under patent notice provisions
 - 42 months after approval of first interchangeable if sued for patent infringement under patent notice provisions and still ongoing after 42 months
 - 18 months after approval of first interchangeable if not sued under patent notice provisions

Confidential Information

- Biosimilar applicant provides application information to:
 - One or more outside attorneys
 - One in-house attorney
 - Patent owner representative if they retained right to assert

- “provided that . . . they do not engage, formally or informally, in patent prosecution relevant or related to the referenced product”

- Others, including scientific consultants, require written agreement

Patent Procedures

- No Orange Book Listing
- Encompasses method of manufacture claims
- Complex and fast-moving interactions between referenced product holder and biosimilar applicant

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