DESIGN AND ANALYSIS OF BIOSIMILAR STUDIES

3-part Course instruted by

Shein-Chung Chow, PhD

at the 1st
Annual Biosimilars Forum
Budapest, Hungary | October 6-7, 2016

1

Lecture 1:

Assessing Biosimilarity: Issues and Recent Development

2

Lecture 2 (*soon*):

Assessing Interchangeability: Issues, Designs and Statistical Methods

3

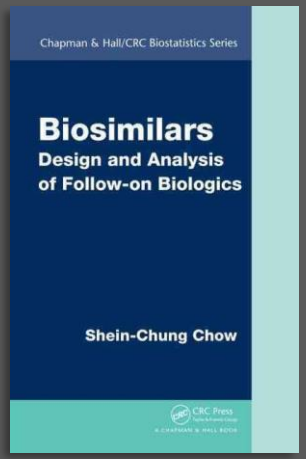
Lecture 3 (*soon*):

Analytical Similarity Assessment in Biosimilar Studies

DESIGN AND ANALYSIS OF BIOSIMILAR STUDIES

Annual Biosimilars Forum

This presentation material includes the 1st lecture (entitled **Assessing Biosimilarity: Issues and Recent Development**) of the scientific course presented by ***Professor Shein-Chung Chow*** at the **1st Biosimilars Forum** in Budapest. The second and third parts of the course will be available to download separately soon, courtesy of Annual Biosimilars Forum event series at the Forum's official website: www.biosimsforum.com



The materials of the course are developed based on

- the book entitled "**Biosimilars: Design and Analysis of Follow-on Biologics**" by *Chow SC* published in 2013 by Chapman and Hall/CRCPress, Taylor & Francis, New York,
- and the 3rd edition of the book entitled "**Design and Analysis of Bioavailability and Bioequivalence Studies**" by *Chow SC* and *Liu JP* published in 2008 by Chapman and Hall/CRC Press, Taylor & Francis, New York.

THE FIRST ANNUAL BIOSIMILARS FORUM
Budapest, Hungary, October 6-7, 2016

Design and Analysis of Biosimilar Studies

Lecture 1: Assessing Biosimilarity: Issues and Recent Development

Lecture 2: Assessing Interchangeability: Issues, Designs and Statistical Methods

Lecture 3: Analytical Similarity Assessment in Biosimilar Studies

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Instructor

Shein-Chung Chow, PhD

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Special Government Employee, United States Food and Drug Administration
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Editor-in-Chief, Journal Biopharmaceutical Statistics and Drug Designing
Editor-in-Chief, Biostatistics Book Series, Chapman and Hall/CRC Press
More than 30 years of experience in pharmaceutical/clinical development
Author or co-author of over 280 methodology papers and 24 books
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Design and Analysis of Biosimilar Studies

Lecture 1
Assessing Biosimilarity: Issues and Recent Development

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Department of Biostatistics and Bioinformatics
Duke University School of Medicine
Durham, North Carolina, USA

October 6, 2016

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Outline

- Expanding biosimilar opportunity
- Fundamental differences
  - Generics versus biosimilars
- Regulatory requirements
  - EU EMA, US FDA, and WHO
- Definition of biosimilarity
- Scientific factors for assessing biosimilarity
- Development of biosimilarity index
- Remarks

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Terminology

- Biosimilars
  - by EU EMA
- Follow-on biologics
  - by US FDA
- Subsequent entered biologics (SEB)
  - by Health Canada
- Similar biotherapeutic product (SBP)
  - by WHO
- Biological/biotechnology-derived products (BDP)
  - as indicated in EMA, FDA, and ICH guidances
- Biogenerics
  - by general population

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What are biosimilars?

- A biosimilar product is a similar biological product such as protein product, vaccine, or blood product whose active drug substance is made of a living cell or derived from a living organism
- Biosimilars are not generic drugs but similar biologic drug products
- Similar is in the sense that it is similar to an innovator drug product in terms of safety, purity, and potency

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"A biosimilar is a biopharmaceutical that contains a version of the active substance of an already authorized biopharmaceutical"

"Similarity to the reference medicinal product in terms of quality characteristics, biological activity, safety, and efficacy needs to be established"[1]

"Biosimilarity means the biologic product is highly similar to the reference product notwithstanding minor differences in clinically inactive components"

"There are no clinically meaningful differences between the biologic product and the reference product in terms of the safety, purity and potency of the product"[2]

Expanding biosimilar opportunity

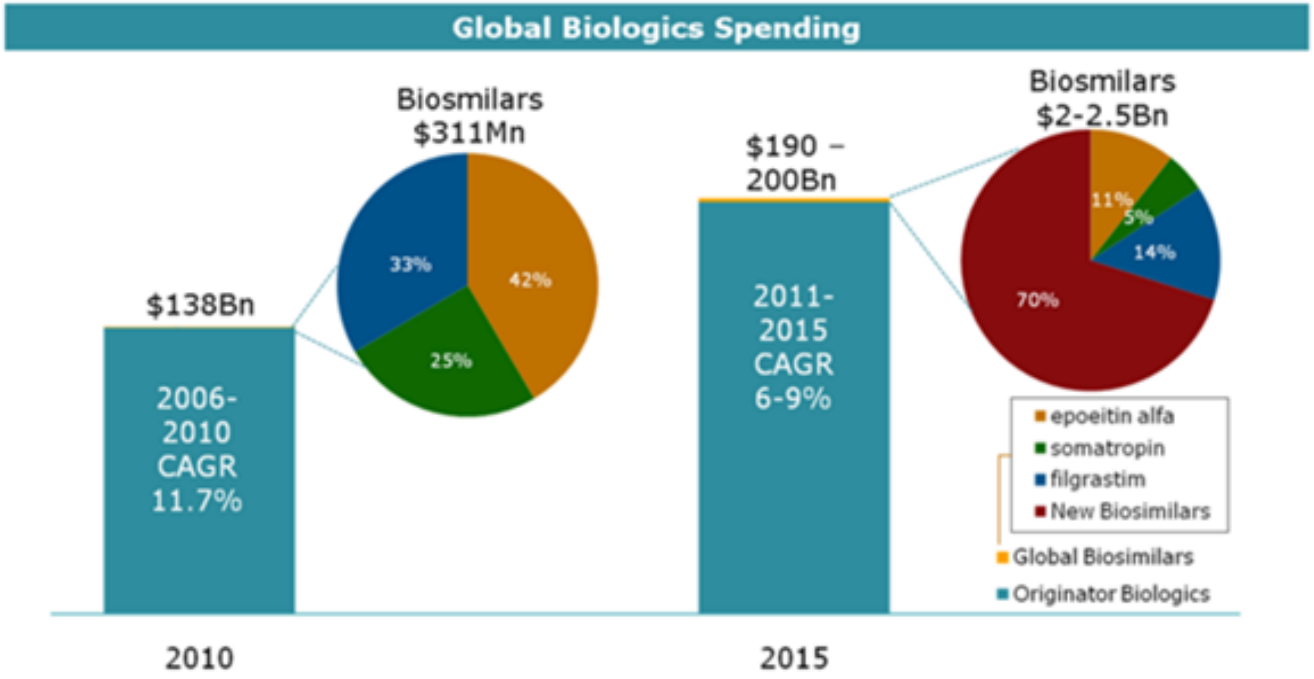
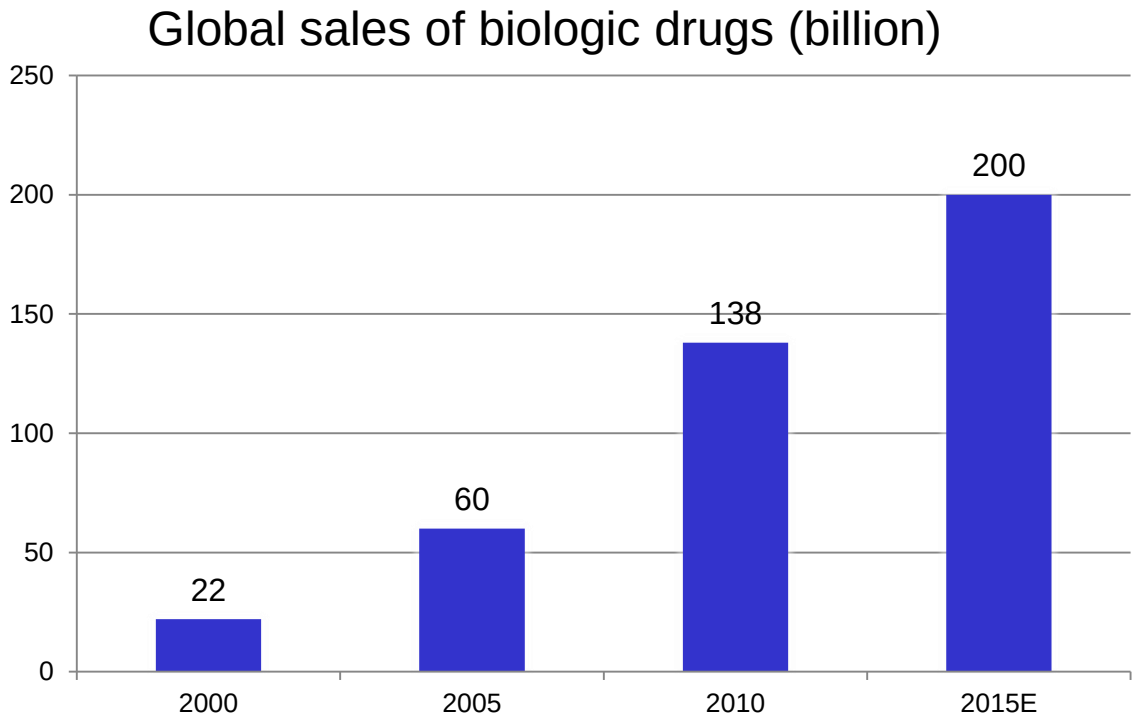


Figure 8.1. Global biologics spending (in billion dollars)

Source: IMS Institute for Healthcare Informatics, MIDAS, December 2010.

Expanding biosimilar opportunity

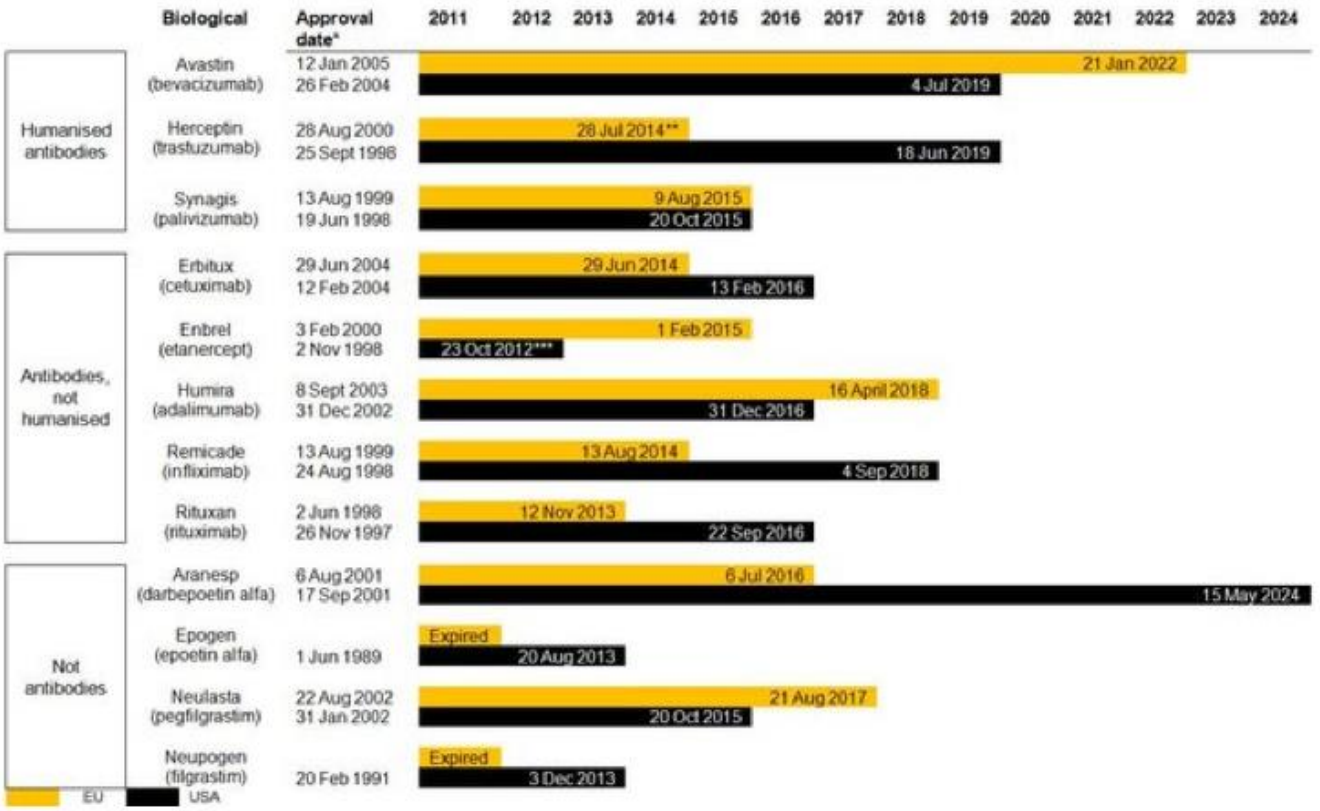


Source: IMS; Lehman Brothers Phama Pipelines

Table 1. Pharmas biggest biological blockbusters

Brand name	Primary indication(s)	Peak year (to date)	Peak year sales ($m)
Humira	Autoimmune diseases	2012	9265
Enbrel	Autoimmune diseases	2011	7830
Rituxan	Autoimmune diseases	2011	6798
Remicade	Autoimmune diseases	2011	6782
Avastin	Colon, lung, renal cancer	2010	6216
Herceptin	HER-2 + breast cancer	2011	5947
Lantus	Diabetes	2011	5452

Figure 1 Biological drug products and their patent protection in EU and USA



* EU provides 10 years of data exclusivity, US BPCI Act provides 12 years exclusivity

** In the UK. Other major EU markets follow on 28 August 2015.

*** Aqueous formulation patent runs until 2023, but dry powder biosimilar possible.

Source: Bernstein Research

Current regulatory submissions in EU and US

Recent events in the USA will play a pivotal role:

4 approved biosimilar;

3 additional known biosimilar filings under the new 351(k) pathway (pending review)

Fundamental differences – generics versus biosimilars

- **Generic drugs**
  - Made by chemical synthesis
  - Defined structure
  - Easy to characterize
  - Relatively stable
  - Usually taken orally and often prescribed by a general practitioner
- **Biosimilars**
  - Made by living cells
  - Heterogeneous structure
    Mixtures of related molecules
  - Difficult to characterize
  - Variable; sensitive to conditions
  - Usually injected and prescribed by specialists
  - Immunogenicity

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Generics vs. biosimilars

- **Generics**
  - Small molecule (chemical) drug products
  - Drug products with identical active ingredient(s)
  - Conduct of bioequivalence (BE) trials is required
  - Regulatory approval pathway is well established
- **Biosimilars**
  - Large molecule biological drug products
  - Generic versions of original biological products
  - It is not generic drug but similar biological products
  - Regulatory approval pathway in US is still not well established

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Past experience for assessing bioequivalence for generics

- Fundamental Bioequivalence Assumption
- Criteria for bioequivalence
- Study design
- Sample size calculation
- Statistical methods
- Drug interchangeability
- Regulatory review/approval

Key question

Can standard methods for assessment of bioequivalence be directly applied for assessment of biosimilarity of follow-on biologics?

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Key question

Can standard methods for assessment of bioequivalence be directly applied for assessment of biosimilarity of follow-on biologics?

NO – due to fundamental differences between generic drugs and biosimilars

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Comparison
In vivo BE and biosimilarity testing

In vivo BE testing

- Drug absorption
- Variability 20-30%
- BE criterion (80%, 125%)
- Confidence interval approach
- Crossover design
- Fundamental BE Assumption
- BE trial is required

Biosimilarity testing

- Drug safety/efficacy
- Variability 40-50%
- (70%, 143%)? SABE?
- Confidence interval approach or biosimilarity index?
- Parallel or crossover design?
- Fundamental Biosimilarity Assumption?
- How many studies are required?

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Fundamental Biosimilarity Assumption – proposal

When a follow-on biologic product is claimed to be biosimilar to an innovator product in some well-defined study endpoints, it is assumed that they will reach similar therapeutic effect or they are therapeutically equivalent .

Proposed by SSAB on October 21, 2009

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What is SSAB?

- SSAB is a Statistical Scientific Advisory Board on Biosimilars, which consists of the following members
  - Shein-Chung Chow,PhD, Duke University School of Medicine
  - Laszlo Endrenyi, PhD, University of Toronto
  - Peter Lachenbruch, PhD, Oregon State University
  - France Mentre, PhD, Paris University
  - Yangfeng Wu, MD, PhD, Peking University
- Established in 2009
  - Submitted a communication package to the FDA in 2010
  - Conducted seminars and workshops at FDA

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Regulatory requirements of biosimilars

World Health Organization (WHO)

European Union

European Medicines Agency (EMA)

The United States of America

Food and Drug Administration (FDA)

Asian Pacific Region

China (March 2015), South Korea, Taiwan, Singapore, Japan, India, etc

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Development of regulatory approval pathway in US

- *Biologics Price Competition and Innovation* (BPCI) Act
  - Passed by US Congress in 2009
  - Written into law on March 23, 2010
- Regulatory requirements/guidances
  - FDA Public Hearing (November 2-3, 2010)
  - Various User Fees Stakeholders' meetings within the FDA between November 2-3, 2010 and December 16, 2011
  - FDA Public Meeting (December 16, 2011)
  - Three FDA draft guidances (February 9, 2012)
  - FDA Public Hearing (May 11, 2012)
  - One FDA draft guidance (May, 2014)

FDA regulatory requirements

- Biologic products that are licensed under a BLA, i.e., US Public Health Service (PHS) Act
  - The robustness of the manufacturing process
  - The degree to which structural similarity could be assessed
  - The extent to which mechanism of action was understood
  - The existence of valid, mechanistically related pharmacodynamic assays
  - Comparative pharmacokinetics
  - Comparative immunogenicity
  - The amount of clinical data available
  - The extent of experience with the original product

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Definition of biosimilarity

A biosimilar product:

Is highly similar to the reference product notwithstanding minor differences in clinically inactive components

There are no clinically meaningful differences in terms of safety, purity and potency.

- US BPCI Act, 2009

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Key questions raised at FDA Public Hearings

- How similar is similar?

  How similar is considered highly similar?
  - Degree of similarity
- What are the criteria for biosimilarity?
  - One-size-fits-all criterion?
  - Should disaggregated criterion?
    - e.g., average for general similarity; then similarity in variability for highly similarity

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Key questions raised at FDA Public Hearings

- Can we establish non-inferiority instead of bioequivalence (biosimilarity)?
  - Selection of non-inferiority margin
- How many biosimilar studies are required?
  - Safety, purity, and potency
- Can standard methods for assessment of bioequivalence of generic drugs be applied?
  - Concern in large variability in biosimilars
  - Standard methods for BE assessment focus on average bioavailability

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Criteria for biosimilarity

- Several criteria available in the literature and/or regulatory guidances for bioequivalence
  - Criteria for ABE, PBE, and IBE
  - Similarity factor for dissolution profile comparison
  - Determination of non-inferiority margin in active control trials
- One-size-fits-all criterion?
  - Shouldn't it be adjusted for variability and/or therapeutic index?
- Degree of similarity?
  - Definition of highly similar
  - The use of disaggregated criteria?

Possible biosimilarity measures

- Absolute change ($\mu_T - \mu_R$)
- Percent change (μ_T / μ_R)
- Relative change in absolute change
- Relative change in percent change
- Responder analysis, i.e., define a responder based on
  - Absolute change
  - Percent change
  - Relative change based on absolute change
  - Relative change based on percent change

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Possible criteria for biosimilarity

- Average versus variability
  - Comparing means, variances or CVs
- Moment-based versus probability-based
- Aggregated versus disaggregated
- Scaled versus non-scaled
  - Adjust for intra-subject variability and/or therapeutic index
- Weighted versus un-weighted
  - Different weights for variance components
- Fixed versus flexible
  - Adjust for intra-subject variability and/or therapeutic index

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Criteria for biosimilarity - proposal

- Average versus variability
  - Sensitive to small change/variation; Highly variable
- Moment-based versus probability-based
  - Can take variability into consideration; More stringent
- Aggregated versus disaggregated
  - Can address the degree of similarity
- Fixed versus flexible
  - Adjust for the variability and/or therapeutic index of the reference product

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Criteria for biosimilarity - proposal

[1] Chow SC and Liu JP (2010). Statistical assessment of biosimilar products. JBS, 20(1), 10-30.

[2] Chow SC et al. (2010). A comparison of moment-based and probability-based criteria for assessment of follow-on biologics. JBS, 20(1), 31-45.

[3] Hsieh TC et al. (2010). Statistical test for evaluation of biosimilarity in variability of follow-on biologics. JBS, 20(1), 75-89.

[4] SSAB white paper on the assessment of biosimilarity of follow-on biologics

JBS=Journal of Biopharmaceutical Statistics

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Non-inferiority vs. equivalence

- Can testing for non-inferiority serve the purpose of testing for similarity?
- Is the non-inferiority margin the same as biosimilarity limit?
- Does the non-inferiority test have to be two-sided?
  - One side of a two-sided test is equivalent to a one-sided test with different alpha
- Does the non-inferiority test have to be symmetric?

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Non-inferiority vs. equivalence

- What is the relationship between non-inferiority and equivalence (similarity)?
  - Non-inferiority = similarity?
- How to determine non-inferiority margin?
  - Non-inferiority margin = similarity limit?
- What is the impact on sample size requirement?
  - Sample size reduction when switches from testing for similarity to testing for non-inferiority

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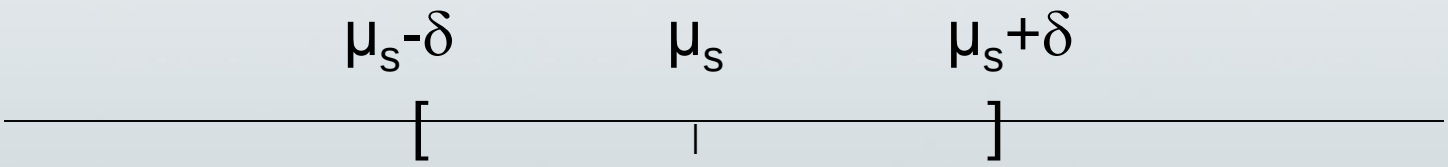
Relationship among non-inferiority, superiority, and equivalence



Inferiority →|← **Equivalence** →|← **Superiority**

|← **Non-inferiority**

Non-superiority →|

One-sided Equivalence

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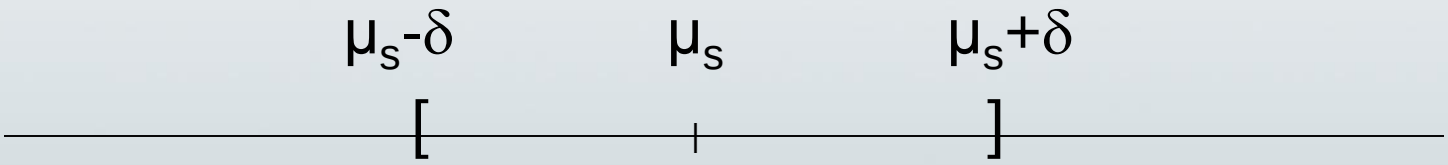
Relationship among non-inferiority, superiority, and equivalence



Inferiority $\rightarrow|\leftarrow$ **Equivalence** $\rightarrow|\leftarrow$ **Superiority**

H_0: $\mu_T-\mu_s \leq -\delta$	H_0: $\lvert\mu_T-\mu_s\rvert \geq \delta$	H_0: $\mu_T-\mu_s \leq \delta$
H_a: $\mu_T-\mu_s > -\delta$	H_a: $\lvert\mu_T-\mu_s\rvert < \delta$	H_a: $\mu_T-\mu_s > \delta$

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Non-inferiority vs. equivalence

- Non-inferiority is one-sided equivalence
- Non-inferiority = equivalence + superiority
  - Superiority may be tested after the non-inferiority has been established
- Non-inferiority ≠ equivalence
  - Non-inferiority ≠ similarity
- Equivalence = non-inferiority + non-superiority
- Non-inferiority margin = equivalence limit
- Sample size calculation
  - Non-inferiority ≠ equivalence (similarity)

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Clinical strategy for non-inferiority

- Since non-inferiority is considered one-sided equivalence, we may consider establishing *non-inferiority* first. Then test for *non-superiority*.
- Utilizing the concept of *asymmetric* equivalence limits
  - Dealing with α_1 and α_2 rather than $\alpha_1 = \alpha_2$
  - Enable us to adopt flexible biosimilarity criteria
- Scientific/academic perspectives
  - Selection of non-inferiority margin
  - The choice of α_1 and α_2 for controlling α

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Remarks

- Equivalence limit
  - Current equivalence limit for small molecule products is fixed (one-size-fits-all criterion) for all drug products
- Non-inferiority margin
  - Non-inferiority margin is not fixed (flexible)
  - Should consult with the 2010 FDA draft guidance
- Non-inferiority margin should reflect the lower equivalence limit
- Sample size requirements for testing non-inferiority and equivalence (similarity) are different

Statistical methods for assessing biosimilarity

- Should be able to take variability into consideration
- Should be robust with respect to the criteria for biosimilarity used
- Should be about to address the degree of similarity
- Should be able to be applied to various study design

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Development of biosimilarity index – proposal

- A biosimilarity index is derived based on reproducibility probability
  - Can address the question that “how similar is similar?”
  - Can address the practical issue of drug interchangeability
- Reference

  Shao J and Chow SC (2002). Reproducibility probability in clinical trials. *Statistics in Medicine*, 21, 1727-1742.

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Biosimilarity index - proposal

- Step 1: Assess average biosimilarity based on bioequivalence criterion
  - (80%, 125%) based on log-transformed data
- Step 2: Calculate the reproducibility based on the observed ratio and variability
- Step 3: Claim biosimilarity if the 95% confidence lower bound of the reproducibility is larger than a pre-specified number p_0

Biosimilarity index - proposal

- p_0 can be obtained by comparing the reference (R) to itself
  - First, we obtain p_{RR} (reproducibility probability when comparing R and itself)
  - p_0 can be selected as 80% of p_{RR}.
  - In practice, we would expect that p_{RR} is high, say 90%
  - In this case, $p_0 = 80\% \times 90\% = 72\%$.
  - To address “highly similar”, we may consider choosimg 90% of p_{RR}

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Advantages

- Takes variability into consideration
- Compares to a standard set by reference itself
- Robust against any criteria used
- Can be applied under different study designs
- Can assess the degree of similarity with appropriate choice of level of reproducibility

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Remarks

- The proposed biosimilar index follows the well-established criterion for assessment of bioequivalence
- Reflect the sensitivity of heterogeneity in variation
- It is able to address “how similar is similar?” and the issue of interchangeability

Study design

- Crossover Design
  - The design of choice for bioequivalence
- Parallel Design
  - Suitable design for biosimilars with relatively long half-lives
  - Does not provide independent estimates for intra-subject variability
- Hybrid parallel + crossover design

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Possible study designs

- Useful study designs
  - Replicated crossover design
  - Parallel design with replicates
  - Balaam's design (TT, RR, TR, RT)
  - Two-sequence dual design (TRT, RTR)
  - Two-sequence four period design (TRTR, RTRT)
  - Modified Balaam's design (TT, RR, TRT, RTR)
  - Extra-reference design (TRR, RTR)
  - Specific design (RRRR, RTRT)

Possible study designs

- Hybrid Parallel-Crossover design
  - Hybrid parallel plus 2x2 crossover design
  - Hybrid parallel plus 2x3 dual crossover design
  - Hybrid parallel plus replicated 2x2 crossover design
  - Complete N-of-1 randomized design
- Potential use of adaptive designs
  - Two-stage seamless design (PK + Clinical)
  - Bayesian adaptive design

How many biosimilar studies are required?

- Biosimilarity requires that there are no clinically meaningful differences in terms of safety, purity and potency.
  - Safety (e.g., PK/PD, safety/tolerability, and/or Immunogenicity studies)
  - Purity (e.g., critical quality attributes during manufacturing process, stability, etc.)
  - Potency (e.g., efficacy study).
- Study endpoints selection depend upon the type of biosimilar studies are conducted.

US FDA draft guidances

- On February 9, 2012, FDA circulated three draft guidances for comments.
  - Scientific Considerations in Demonstrating Biosimilarity to a Reference Product
  - Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product
  - Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation (BPCI) Act of 2009
  - These draft guidance were finalized in 2015

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US FDA draft guidances

- Scientific Considerations in Demonstrating Biosimilarity to a Reference Product
  - This guidance is intended to assist sponsors in demonstrating that a proposed therapeutic protein product is biosimilar to a reference product for purpose of the submission of a marketing application under section 351(k) for the Public Health Service Act

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US FDA draft guidances

- Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product
  - This guidance describes the FDA's current thinking on factors to consider when demonstrating that a proposed protein product is highly similar to a reference product licensed under section 351(a) of the PHS Act for purpose of submitting a marketing application under section 351(k) of the PHS Act.

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US FDA draft guidances

- Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation (BPCI) Act of 2009
  - This guidance provides answers to common questions from sponsors interested in developing proposed biosimilar products, biologics license application (BLA) holders, and other interested parties regarding FDA's interpretation of the Biologics Price Competition and Innovation (BPCI) Act of 2009.

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Clinical pharmacology guidance

- ***Guidance for Industry Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product***
- This guidance document is being distributed for comment purposes only.
- Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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Review of FDA guidances

- Reference standards
  - Single versus multiple references
- Asymmetric two-sided test for biosimilarity
  - One side is for testing non-inferiority
  - The other side is for testing non-superiority
- Stepwise approach
  - Starts with analytical similarity assessment
- Totality-of-the-evidence
  - Biosimilarity across different functional areas

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Reference standards

- U.S.-licensed reference product and other comparators
- Single reference product is less problematic
- Different reference products may be problematic
  - Reference from U.S.-licensed reference product versus reference from non-U.S.-licensed reference product
- What if the two reference products are not biosimilar under similar study design?

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Reference standards

- Reference products could be different
  - Different batches from the same manufacturing process
  - Different sites (locations) of the same manufacturer
  - Different countries such as EU and US
- Which product should be used as the reference product for assessing biosimilarity?

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Reference standards

- If there are two different reference products say R1 and R2, which one should be used as the reference?
  - R1 or R2 with scientific justification
  - Max (R1, R2)
  - Average of R1 and R2
  - Have to show biosimilarity with R1 and R2, respectively

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Reference standards

- Kang and Chow (2013) proposed the use of a 3-arm design for addressing this issue
  - After the conduct of the study, data can be analyzed by comparing the test product with either the average of R1 and R2 or the max(R1, R2)
  - The observed difference between R1 and R2 could be used to (i) verify the criteria for biosimilarity, and (ii) serve as reference standard for future studies
  - One of the controversial issues is that what if we fail to meet the biosimilarity criteria when comparing with R1 but meet the criterion when comparing with R2.

Asymmetric test for non-inferiority

- Non-inferiority is one-sided equivalence
- Non-inferiority = equivalence + superiority
- Test for biosimilarity
  - First, test for non-inferiority with α_1
  - Then, test for non-superiority with α_2
  - Controlling α with appropriate choices of α_1 and α_2
- Sample size calculation
  - Non-inferiority ≠ equivalence (similarity)

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Stepwise approach

- US FDA recommends the stepwise approach to provide evidence of biosimilarity
- Stepwise approach for obtaining totality-of-the-evidence
  - Starts with critical quality attributes in manufacturing process
  - PK/PD assessment
  - Clinical trials
- Remarks
  - Adjustment for stepwise error rate?
  - The order of the stepwise testing procedure may have an impact on the final test results

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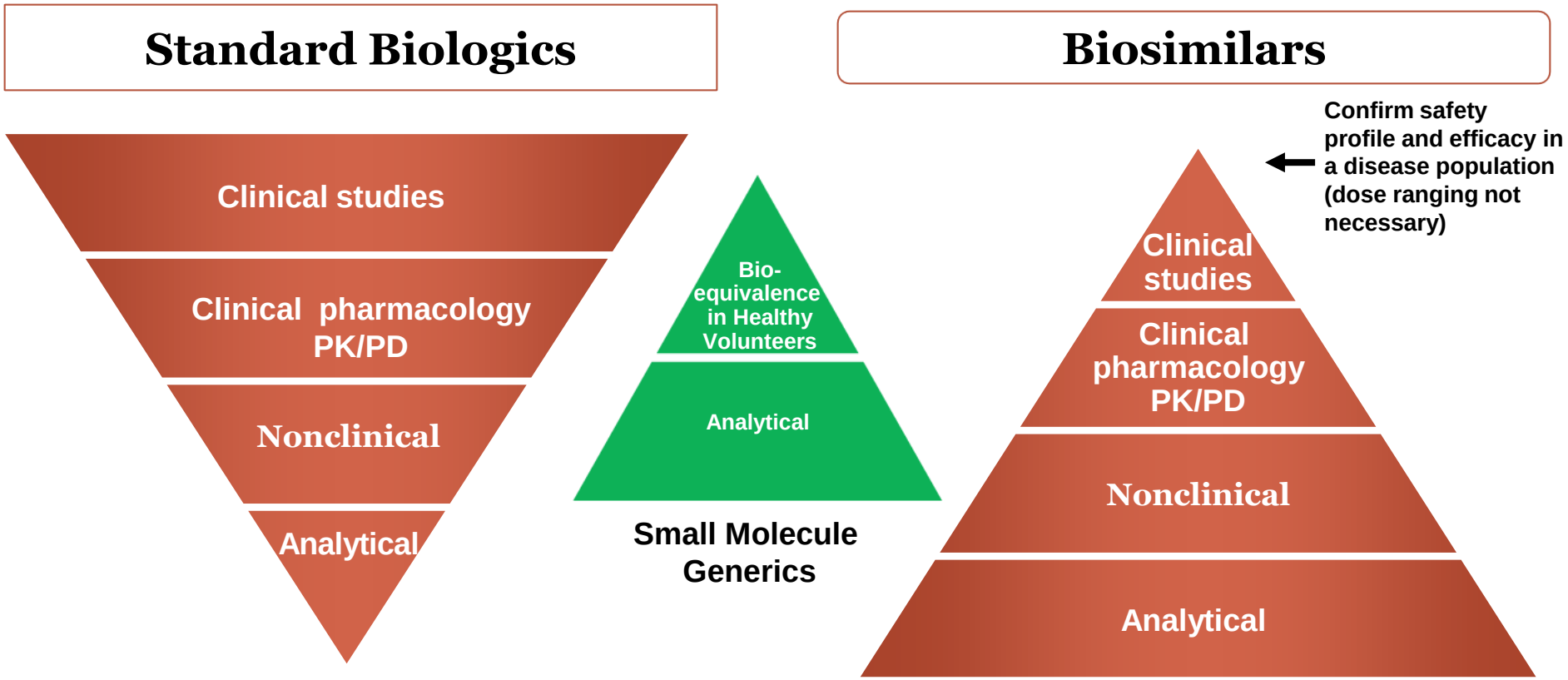
US FDA stepwise approach



Totality-of-the-evidence

- Local biosimilarity versus global biosimilarity
- Degree of biosimilarity may vary from domain to domain
- Each domain may carry different weights
- FDA seems to suggest a scoring system for measurement of totality-of-the-evidence
- Biosimilarity index proposed by Chow et al (2011) may be useful
  - Will achieve the totality-of-the-evidence under different study designs and/or biosimilarity criteria

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Recent development

- Special issues
  - Journal of Biopharmaceutical Statistics (2010)
  - Statistics in Medicine (2012)
  - Journal of Generics and Biosimilar Initiatives (GaBI) (2013)
  - Journal of Biopharmaceutical Statistics (2014)
  - Journal of Pharmaceutical Analysis (2015)
  - Journal of Biopharmaceutical Statistics (2017)
- Books
  - Biosimilars: Design and Analysis of Follow-on Biologics
    Chow SC (2013). Chapman and Hall/CRC Press, NY
  - *Development of Biosimilar Products*
    Endrenyi L et al. (2017). Book manuscript submitted.

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DESIGN AND ANALYSIS OF BIOSIMILAR STUDIES

Annual Biosimilars Forum

The 2nd Lecture of the course will be available soon to download separately signed-up users, courtesy of Annual Biosimilars Forum event series at the Forum's official website: www.biosimsforum.com.

1

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Lecture 3 (coming soon):

Analytical Similarity Assessment in Biosimilar Studies

The event series will continue in 2017

Join us on 5-6 October, 2017 in Budapest for our 2nd Annual Biosimilars Forum regarding hot topics related to the drug development of Bio- and Nanosimilars with a strong scientific FOCUS ON Statistical and Regulatory perspectives. Visit:

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The Annual Biosimilars Forum event series was founded in 2016 by two prestigious Central European scientific societies, the Viennese Section of the IBS and the Hungarian Society for Clinical Biostatistics in cooperation with the Accelsiors CRO Ltd., aimed at increasing effectiveness of clinical research and in order to provide even more effective support in sharing of recent scientific and practical knowledge for biosimilar drug development professionals.

Join us on 5-6 of October, 2017 at Budapest for the 2nd Biosimilars Forum and meet world's prominent biosimilar development experts!

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ABOUT THE ORGANIZERS

The **Viennese Section of the International Biometric Society** is part of the ROeS, the Austrian Swiss Region of the International Biometric Society (IBS). WBS is an independent, non-profit organization which provides a professional forum for discussions of how to apply statistical methods in biological and medical science.

The **Hungarian Society for Clinical Biostatistics** is a national group of International Society for Clinical Biostatistics (ISCB), and it was founded to stimulate research into the principles and methodology used in the design and analysis of clinical research and to increase the relevance of statistical theory to the real world of clinical medicine.

Accelsiors Ltd. – as a scientific driven CRO – has been a committed supporter of biosimilar drug development, many of their professionals were involved into biosimilar drug development from the early beginnings, guided and managed the first biosimilar drug development projects and professionally supporting clinical trials as well as registration in this innovative field and being active in the clinical research arena in the past two decades.