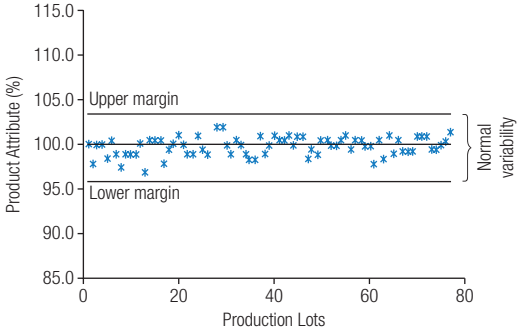
Biosimilars

Hot Topic: Biologic Comparability Testing Versus Demonstration of Biosimilarity

How Are Biologics Monitored to Ensure that Quality is Maintained From Batch-to-Batch?

- Based on time and experience with a product, manufacturers establish acceptable ranges of variation and tightly control key product attributes that are likely to impact biological function[1–3]

Normal Variability in Final Product for a Monoclonal Antibody[2]



How Are Biologics Monitored to Ensure that Quality is Maintained Following a Manufacturing Change?

- Changes to the manufacturing process for biologics often occur post-approval (for example, to improve quality, efficiency and/or reliability of manufacture)[1–3]
- These changes require rigorous risk assessments in accordance with international guidelines to confirm that product attributes remain within the pre-defined ranges of variation with no anticipated impact on quality, safety, or efficacy[1]

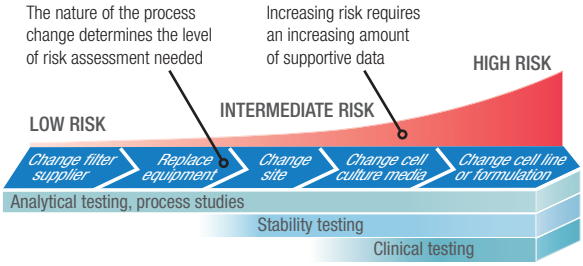


Figure adapted from Lee JF, et al. Curr Med Res Opin 2012;28:1053–1058

Comparability testing is required following manufacturing process changes for approved biologics[1]

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How Does the Development of a Biosimilar Differ From Demonstration of Comparability After a Manufacturing Process Change?

Demonstrate Biosimilarity[4–6]

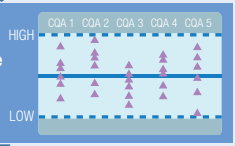
Different manufacturer, new product biosimilar candidate compared with reference product

No access to reference product's history, manufacturing process, established controls or acceptance parameters

Fully characterize reference product

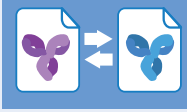
Identify reference product critical quality attributes (CQAs) and establish acceptable ranges of variation

Each data point represents testing from a unique reference lot



Develop and identify cell clone that meets predefined margins, establish cell banks and manufacturing process

Establish biosimilarity



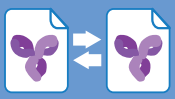
Analytical studies	✓
Non-clinical studies	✓
Comparative clinical PK/PD	✓
Clinical safety, efficacy and immunogenicity evaluation	✓

Demonstrate Comparability[1,4]

Same manufacturer, same product tested before and after change

Extensive knowledge of product history, manufacturing process, established controls and acceptance parameters

Establish comparability



Analytical studies	✓
Non-clinical studies	?*
Comparative clinical PK/PD	?*
Clinical safety, efficacy and immunogenicity evaluation	?*

*May/may not be required depending on risk of process change

Demonstration of biosimilarity is a much more complex process compared with the demonstration of comparability of a biologic before and after a manufacturing process change[3,4]

References

1. ICH. ICH Harmonised tripartite guideline: Comparability of biotechnological/biological products subject to changes in their manufacturing process Q5E. 2004. Available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q5E/Step4/Q5E_Guideline.pdf; 2. Ramanan S, Grampp G. BioDrugs 2014;28:363-72; 3. Declerck P, et al. Pharm Res 2016;33:261-8; 4. FDA. Scientific considerations in demonstrating biosimilarity to a reference product. Guidance for industry, 2015. Available at: https://www.fda.gov/downloads/drugs/guidances/ucm291128.pdf; 5. EMA. Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues, 2014. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/01/WC500180219.pdf; 6. McCamish M & Woollett G. Clin Pharmacol Ther. 2012;91:405-17. All links accessed November 2017.

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