# Biosimilars

## Hot Topic: Considerations for Clinical Trial Design

## What are the Key Considerations for Clinical Evaluation of Biosimilars?

- The primary goal of a biosimilar clinical trial is to demonstrate similarity between the biosimilar and reference product in terms of efficacy, safety and immunogenicity[1,2]

### Equivalence Studies are Recommended to Demonstrate Biosimilarity

| Equivalence Study | Superiority Study | Noninferiority Study |
|---|---|---|
| Intended to demonstrate: (based on a prespecified margin)[1–4] | Intended to demonstrate:[3,4] | Intended to demonstrate:[3,4] |
| Proposed product has **similar effect** to comparator therapy | Proposed product provides **superior effect** than comparator therapy | Proposed product is **no less effective** than the comparator therapy |
| Used for biosimilars[1–4] | Usually used for new agents vs standard of care[3] | |

**Equivalence studies are designed to identify any clinically-meaningful differences between the biosimilar and reference product, should they exist[1,2]**

AMGEN BIOSIMILARS

# What are the Key Clinical Trial Design Considerations?

### Indication

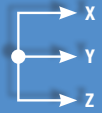
- The most common indication of the reference biologic may not be the most sensitive indication[1]
- Consider indication with highest placebo-adjusted response rate[5]

### Patient population

- Most sensitive population recommended. Consider:[4–6]
  - **Patient homogeneity**
  - **Comorbidities**
  - **Concomitant medications/medication history**
  - **Severity of disease**
- Immunocompetency may influence accuracy of assessing immunogenic risk[5]

### Treatment regimen

- Consider route of administration[2,4]
- Consider monotherapy versus combination therapy with standard of care[5]




### Endpoints

- Clinically relevant, readily assessable, and sensitive to detect differences: may differ from pivotal studies of reference biologic[1,2,4,5]
- Prespecified, scientifically justified margins[1]
- Continuous endpoints may be more sensitive than categorical ones[5]


### Study duration

- Length of study should be sufficient to allow detection of any clinically meaningful differences in efficacy, safety and immunogenicity[1,2,4]

### Comparator study design

- Should allow comparative assessment of efficacy, safety and immunogenicity[1,2,5]
- May be designed to address considerations for switching treatment[5]

**Clinical studies aim to confirm that there are no clinically-meaningful differences between the biosimilar and the reference product, not to independently determine the efficacy and safety of the biosimilar[1,2]**


### References

1. EMA. Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues, 2015. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/01/WC500180219.pdf; 2. 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; 3. Isakov L, et al. Am J Ther 2016;0:1-8 P; 4. Alten R, Cronstein BN. Semin Arthritis Rheum 2015;S2–S8; 5. Lai Z, et al. RMD Open 2016;2:e000154; 6. EMA. Guideline on similar biological medicinal products containing monoclonal antibodies – non-clinical and clinical issues, 2012. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500128686.pdf. All links accessed December 2017.


AMGEN BIOSIMILARS

USA-BIO-061161