BfArM
Bundesinstitut für Arzneimittel und Medizinprodukte

# Equivalence vs. Non-Inferiority
## Introduction

## BMWP / EMA Workshop on Biosimilar MAbs
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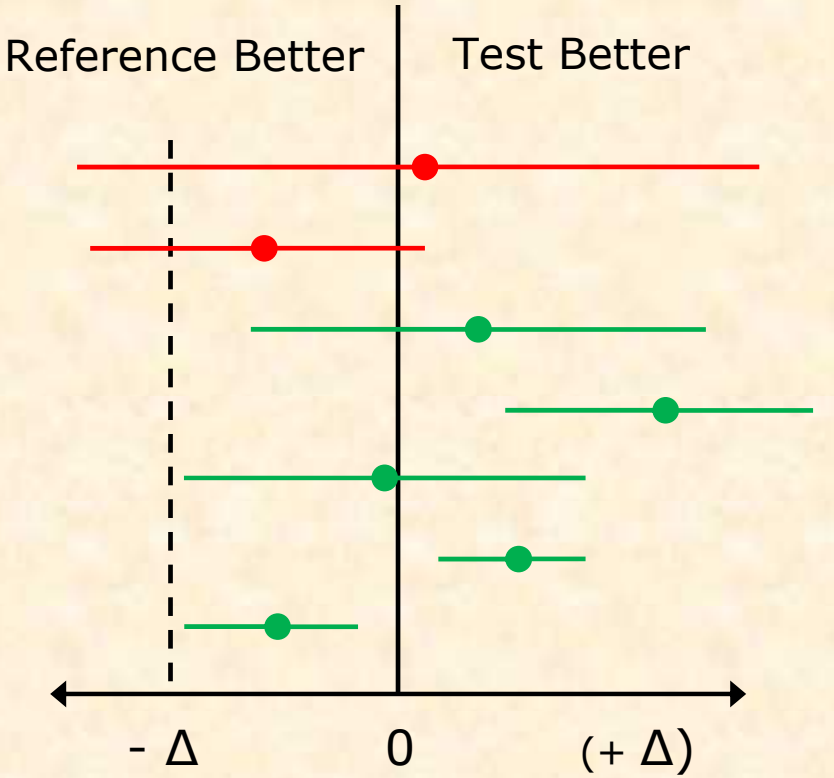
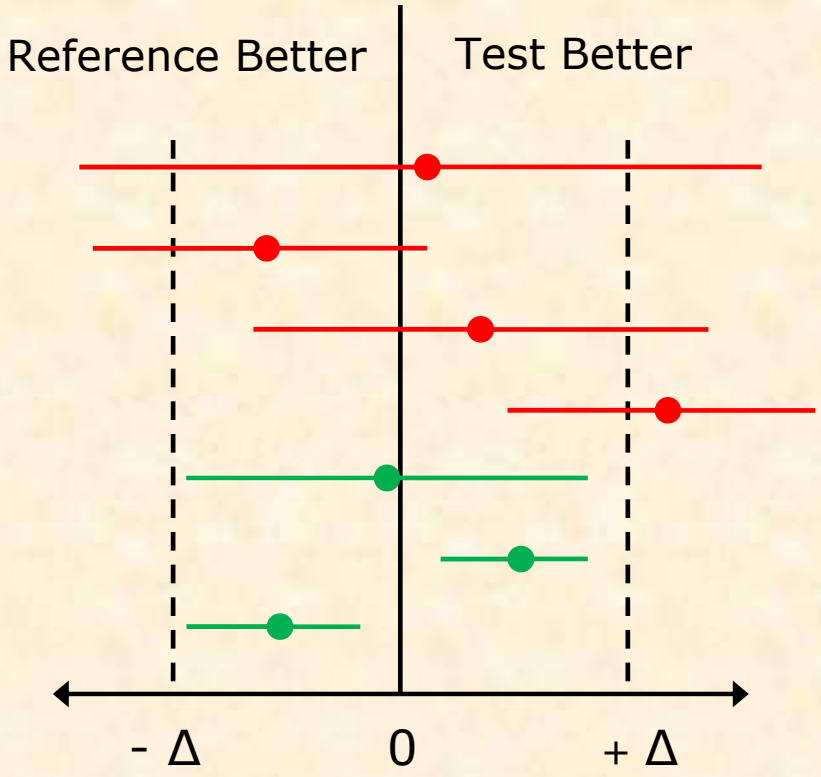
# What's the Difference?

## Non-inferiority Design




Difference in Outcome
Test Treatment minus Reference Treatment

## Equivalence Design




Difference in Outcome
Test Treatment minus Reference Treatment

# What are the Issues?

- Biosimilar intended to be used
  - For the same indication(s)
  - At the same dose(s) and dosing regimens

  approved for the reference product
- Therefore,
  - clinically relevant dissimilarity (in either direction) not acceptable
  - Equivalence trials appear logical requirement

# What are the Issues?

- Non-inferior efficacy
  - At least as efficacious as reference product
  - Formally, superior efficacy acceptable
  - Superior efficacy may result in safety issues, esp. for drugs with narrow therapeutic margin

# What are the Issues?

- However,
  - Are equivalence trials always feasible and necessary?
  - How should we define clinical relevance with regard to the upper equivalence margin?
  - Should it be based on safety considerations?
  - How likely is clinically relevant superiority?
  - Symmetric equivalence margins?