

# **In Vitro Dissolution Profiles Similarity Assessment in Support of Drug Product Quality: What, How, and When**

**MAY 21, 2019**

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Breakout Session Day 1

**2:15 – 3:15 PM: Pharmacy Hall N211**

**3:15-4:15 PM: Pharmacy Hall N314**

# Breakout Sessions C, Day 1

- *WHAT IS THE PROPER “INFERENCE SPACE” FOR DISSOLUTION STUDIES? – ADDRESSING THIS IS KEY TO EXPERIMENTAL DESIGN*
  - Facilitators: Meiyu Shen (FDA), James Reynolds (Abbvie)
  - Scribe: David Lavrich (Merck)/ Ivelisse Colon-Rivera (Vertex)

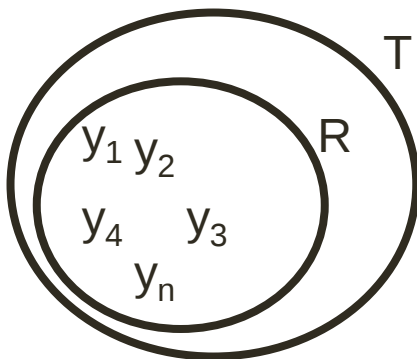
# Session Background

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Target population (T) is the population (process) of interest

Research population (R) is the portion of the target available to study

Sample is the particular observations (measurements) from the research set



Statistical inference is making probability statements about the Target based on the Sample

$$Y = \{y_1, y_2, \dots, y_n\} ; T \sim F\{\mu, \sigma\}$$

$$Y \rightarrow f(Y) \rightarrow T$$

# Question 1

What should our target population be when performing in vitro similarity testing?

## Question 2

What levels of Type I (Probability declaring similar when not similar) and Type II (Probability of declaring not similar when similar) error rates are acceptable?

## Question 3

To what extent can prior information (choice of profile model, estimates of intra-batch variance, expected impact of the difference between test and reference, ...) be incorporated into the similarity decision?

## Question 4

Should preliminary tests of modeling assumptions be required (e.g., tests for normality, variance homogeneity...)?

# Question 5

How much flexibility should there be in

- the choice of batches (number, recent, consecutive)?
- the required number of within batch replicates?
- the number of dissolution time points?

## Question 6

If multiple batches of test and reference are employed, should a single “pooled” comparison be made, or multiple comparisons of all combinations of batches?

## Question 7

What is the relationship between the hypothesis testing and inference space?  
Can descriptive statistics (e.g.,  $f^2$ ) generate inference space?

# Action BO C1, Day 1, Q1

| Key points discussed<br>(related to the Question ) | Consensus or Agreement reached | Possible scenarios or options (if no consensus is reached) | Action items and responsible person(s) |
|----------------------------------------------------|--------------------------------|------------------------------------------------------------|----------------------------------------|
| Q1                                                 |                                |                                                            |                                        |

# Action BO C1, Day 1, Q2

| Key points discussed<br>(related to the Question ) | Consensus or Agreement reached | Possible scenarios or options (if no consensus is reached) | Action items and responsible person(s) |
|----------------------------------------------------|--------------------------------|------------------------------------------------------------|----------------------------------------|
| Q2                                                 |                                |                                                            |                                        |