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

MAY 22, 2019

Day 2 Breakout Session C
1:30 – 3:30 PM

Session C1 (Group G3), Pharmacy Hall N211, Time 1:30-2:30 PM
Session C2 (Group G1), Pharmacy Hall N306, Time 2.30-3.30 PM

Day2 Breakout Session C (Group G1 and G3)

- How to Design a Robust Statistical Approach In the Assessment of Dissolution Profile Comparisons -- Part 1
  - Moderators: Yanbing Zheng (AbbVie), Meiyu Shen (FDA)
  - Scribes: Om Anand (FDA), Ivelisse Colon-Rivera (Vertex)

Session Background

- **Discussion on**
  - Definition of similarity
  - For each method (*f*2, MSD, bootstrap, Bayesian vs frequentist, profile model vs model independent), what is the appropriate situation that it can be applied? How should statistical methods be prioritized in the construction of decision tree?
  - What is scientific and regulatory rationale for switching from *f*2 to other statistical methods such as multivariate statistical distance (MSD) based on intra-lot variability?
  - Many similarities and differences for comparability criteria across the regions have been identified. Based on participants experience which criteria can be standardized and which must remain, and why or why not they can be standardized.

Question 1 (G3)

- Should the definition of similarity include limits on differences in variance as well as mean?

Question 2 (G3)

- For each method (*f*2, MSD, bootstrap, Bayesian vs frequentist, profile model vs model independent), what is the appropriate situation that it can be applied? Not all tests are conducted for the same statistical or practical purpose.

Question 3 (G3)

- What is scientific and regulatory rationale for switching from *f*2 to other statistical methods such as multivariate statistical distance (MSD) based on intra-lot variability? Doing so alters the definition of similarity.

Question 4 (G3)

- What quality should a good statistical method have in similarity assessment?

Question 5 (G3)

- Many similarities and differences for comparability criteria across the regions have been identified. Based on participants experience which criteria can be standardized and which must remain, and why or why not they can be standardized.

Question 1 (G1)

- Should the definition of similarity depend on product (e.g., IR vs CR, narrow vs wide therapeutic range)?

Question 2 (G1)

- What challenges do users and regulators have in implementing each method (*f*2, MSD, bootstrap, Bayesian vs frequentist, profile model vs model independent)? How should statistical methods be prioritized in the construction of decision tree?

Question 3 (G1)

- If there are slight violations of f2 variability assumptions and f2 is large, e.g. above 60, can we still use f2 or should we go to other methods for similarity assessment?

Question 4 (G1)

- Do we need to take multiplicity adjustments when conducting multiple comparisons?

Question 5 (G1)

- Many similarities and differences for comparability criteria across the regions have been identified. Based on participants experience which criteria can be standardized and which must remain, and why or why not they can be standardized.

Action Day 2 BO Session C Q1

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G3				

Action Day 2 BO Session C Q2

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G3				

Action Day 2 BO Session C Q3

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G3				

Action Day 2 BO Session C Q4

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G3				

Action Day 2 BO Session C Q5

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G3				

Action Day 2 BO Session C Q1

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G1				

Action Day 2 BO Session C Q2

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G1				

Action Day 2 BO Session C Q3

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G1				

Action Day 2 BO Session C Q4

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G1				

Action Day 2 BO Session C Q5

Group	Key points discussed (related to the Question)	Consensus or Agreement reached	Possible scenarios or options (if no consensus is reached)	Action items and responsible person(s)
G1				