Regulatory Education for Industry (REdI):
GENERIC DRUGS FORUM

Sheraton | Silver Spring, MD | April 22-23, 2015

Dissolution Method Development for Generic Drug Products

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This presentation reflects the views of the presenter and should not be construed to represent FDA's views of policies

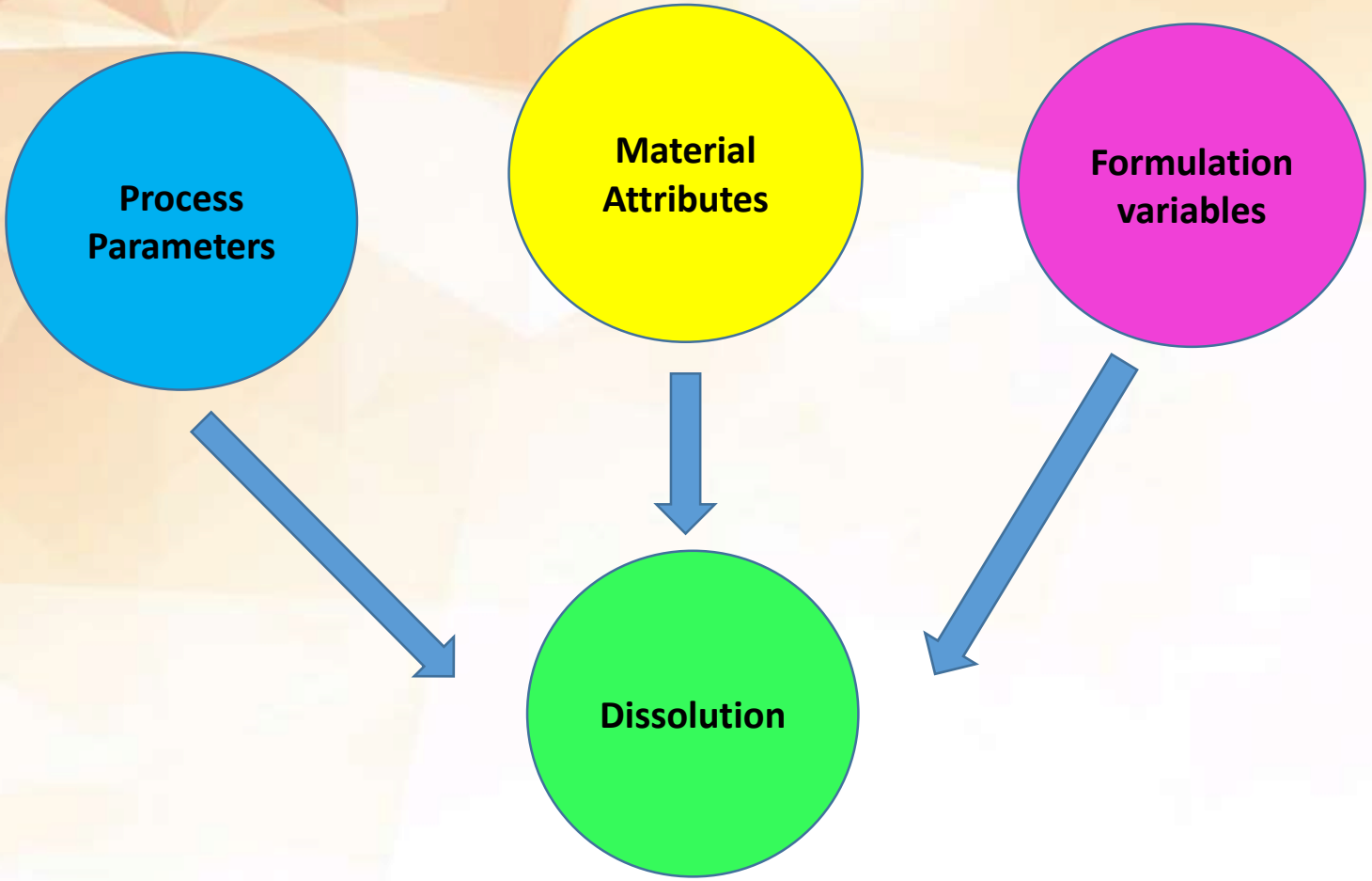
Outline

- Role of dissolution method development
- Current approaches for dissolution method development for generic drugs
- Product specific dissolution method
- Common deficiencies identified in the applications
- Summary

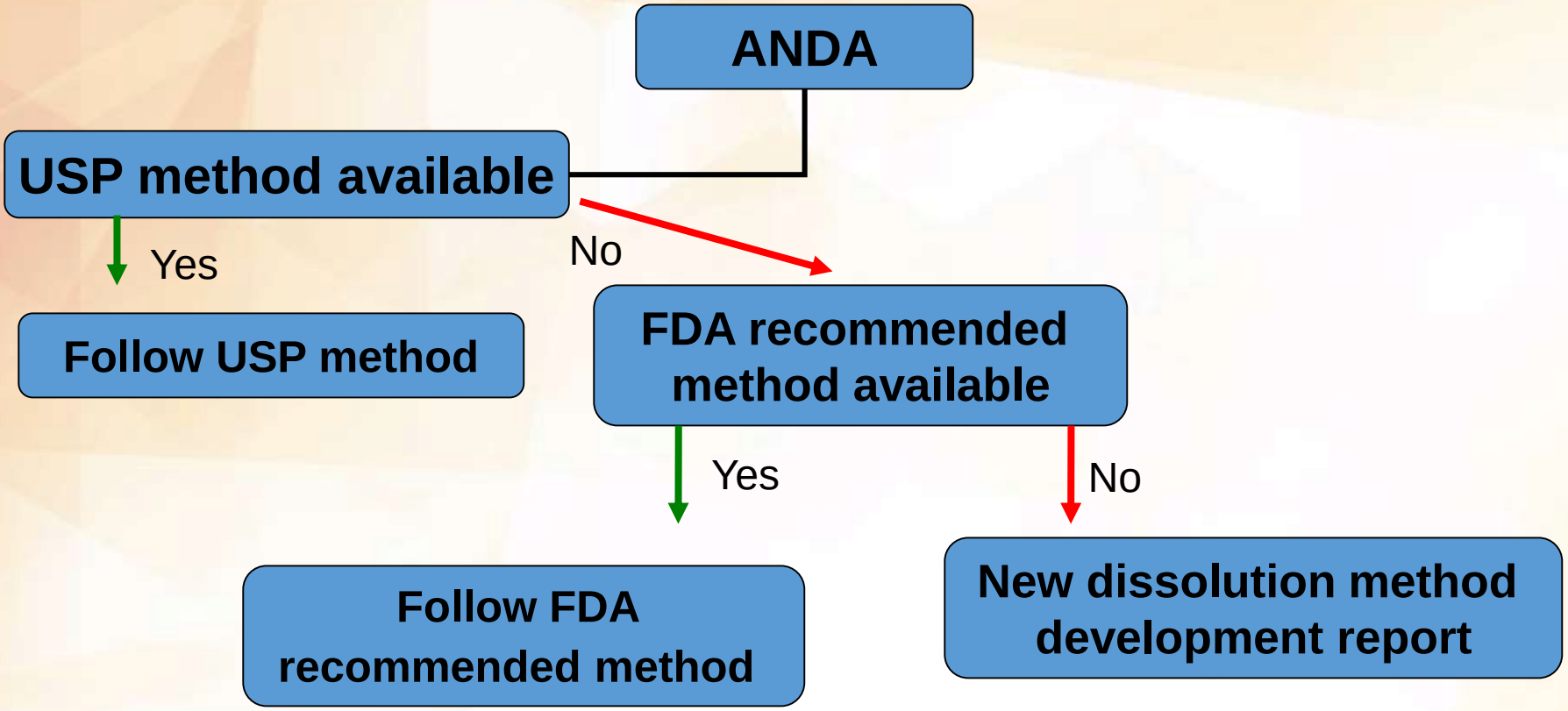
Dissolution testing as a tool…

- A quality control
  - Batch-to-batch consistency
  - Provide quality assurance
- Important for formulation development
- Biowaiver purposes
- In vitro BE studies
- Alcohol-induced dose dumping
- Post-approval manufacturing changes

Role of Dissolution Method Development



Current Approaches for Dissolution Method Development



FDA Dissolution Method

http://www.accessdata.fda.gov/scripts/cder/dissolution/dsp_SearchResults_Dissolutions.cfm?PrintAll=1

Product Specific Method Development

Three Components:

1. **Evaluation of the method**
2. **Discriminating ability**
3. **The acceptance criterion**

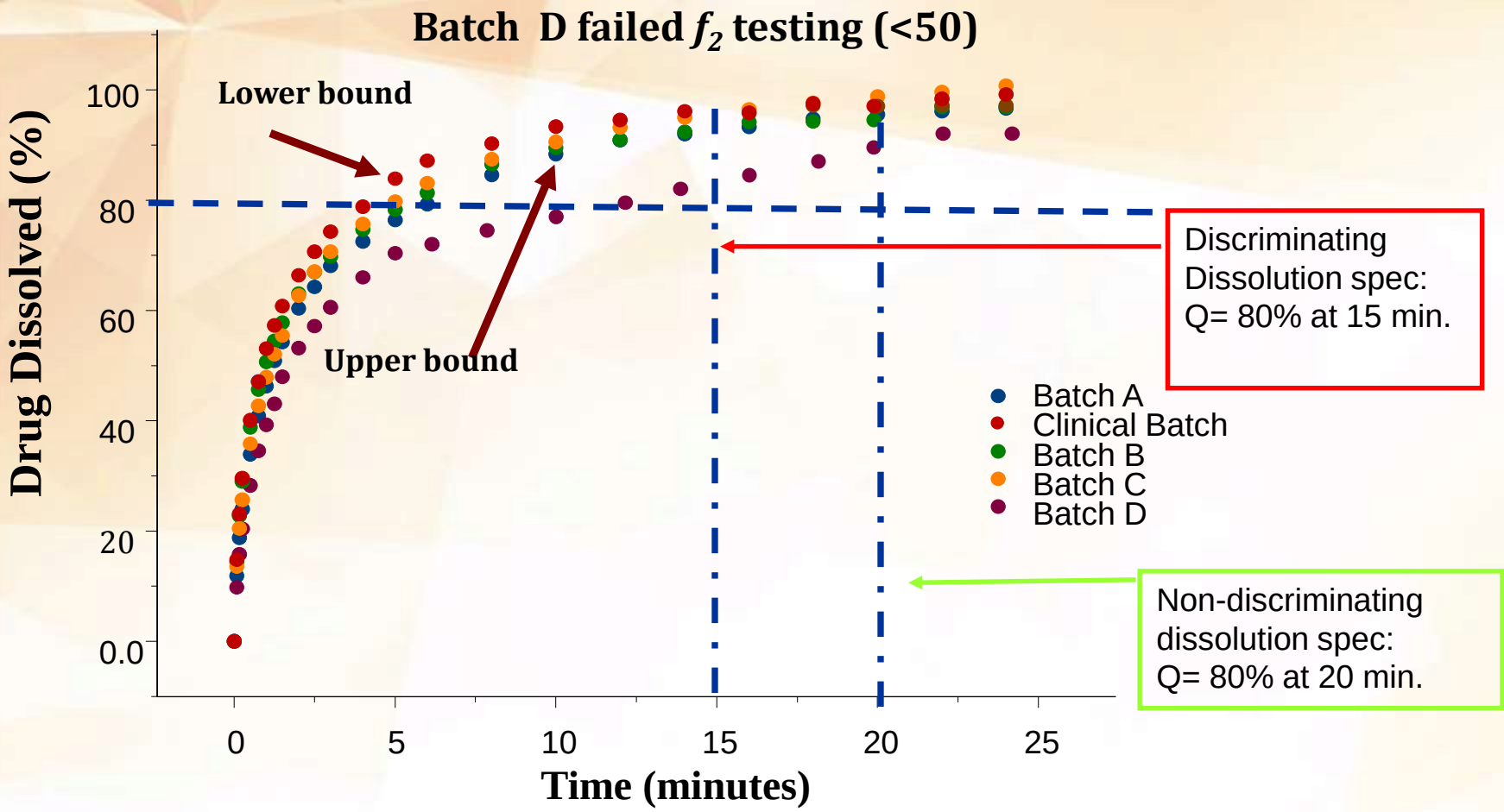
1. Evaluation of the method

- Solubility profile
- Selection of the apparatus
- In vitro dissolution/release media
- Rotation/Agitation speed
- Sink conditions
- Data to support selection of surfactant

2. Discriminating Dissolution Method

- **Differentiates drug products manufactured under target conditions vs. formulations with meaningful variations for the most relevant manufacturing variables**

Different Particle Size Ranges



Ref: 2012 AAPS presentation by Dr. Sandra Suarez Sharp

Based on bioequivalence batches

Manufacture product variants with different release characteristics

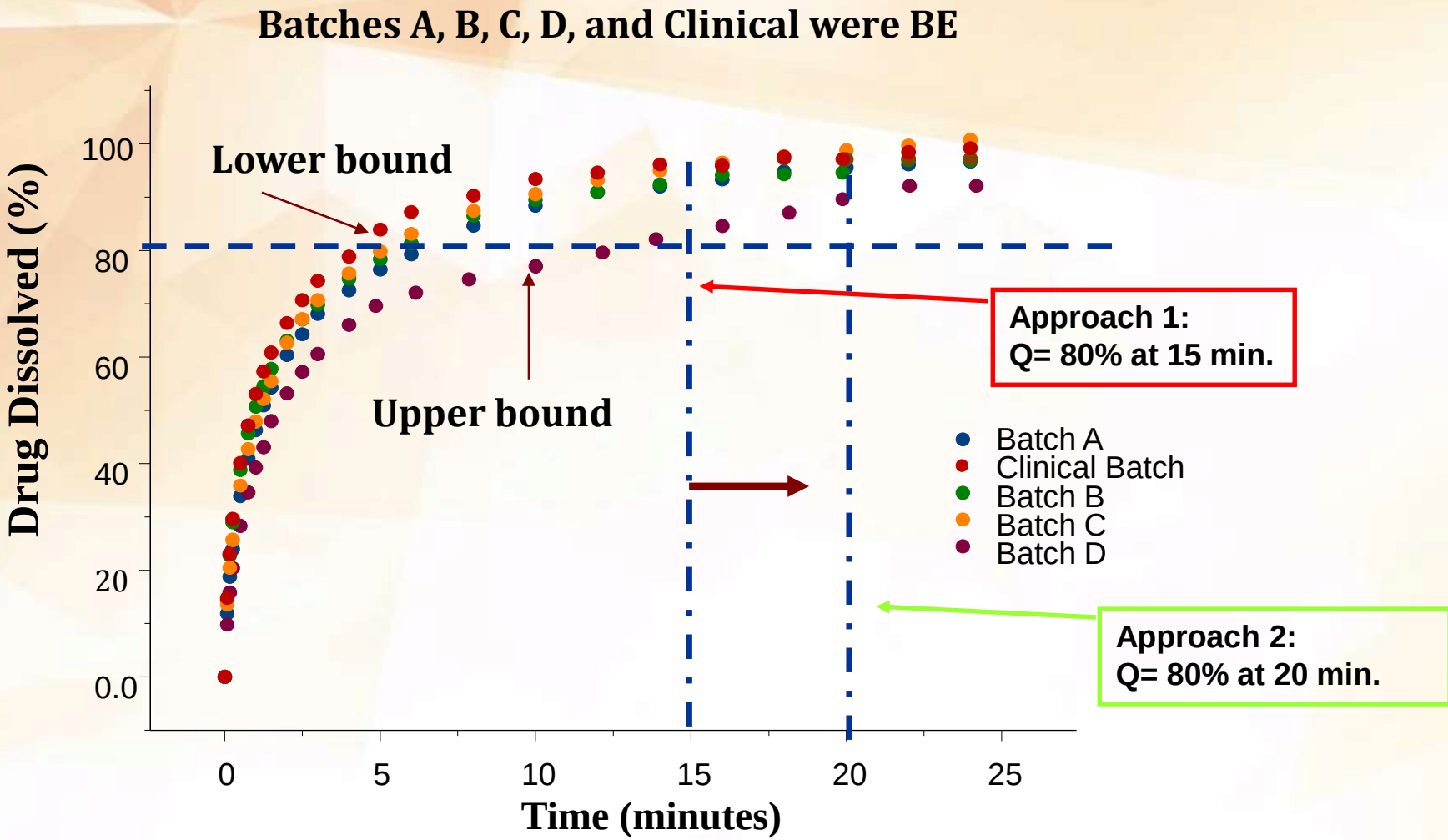
Select optimal dissolution method with adequate discriminating power

Determine bioavailability for product variants

Determine dissolution rates resulting in similar in vivo performance

Dissolution specifications chosen to ensure similar (BE) product performance

Illustration of the dissolution profiles based on BE batches



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3. Acceptance Criterion

- **Bioequivalence batches**
- **At least 85% of the drug is dissolved**

or

- **Where plateau of drug dissolved is reached**
- **The selection of time point should be where Q=80% of drug dissolved.**

Applications: Common deficiencies

- Dissolution method development is not included in the application
- Fails to demonstrate that dissolution method is discriminating
  - No information on critical material attributes and process parameters
- Data do not support the proposed acceptance criterion
- There is no dissolution data for lower strength waivers, alcohol dose dumping studies, multi-media testing for MR products.

Applications: Common deficiencies

- There is no method transfer report when method validation is conducted at a different site
- Dissolution data collected on aged lots
- Individual dissolution data is not submitted.

Ref: Common Deficiencies with BE submissions in ANDAs Assessed by FDA. AAPS Journal, Volume 14. No. 1, March 2012

Summary

- Dissolution method is product specific
- Three Components
  1. Evaluation of the method
  2. Discriminating ability
  3. The acceptance criterion

Acknowledgments

- Om Anand, Ph.D.
- Elsbeth Chikhale, Ph.D.
- Angelica Dorantes, Ph.D.
- Kelly Kitchens, Ph.D.
- Jing Li, Ph.D.
- Haritha Mandula, Ph.D.
- Mei Ou, Ph.D.
- Paul Seo, Ph.D.
- Sandra Suarez Sharp, Ph.D.

Questions?

Evaluation: surveymonkey.com/s/GDF-D2S8