

*FDA 2020 Generic Drug Regulatory Science Initiatives Public Workshop
Breakout Session 3: In Vitro Bioequivalence Methods*

Image-based Microstructure Bioequivalence Evaluation

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Solution for Bioequivalence

Qualitative

*Correlative 3D Imaging with
FIB-SEM and X-Ray Microscopy*

Quantitative

*Microstructure Characterization
with Artificial Intelligence*

Predictive

*Image-Based Simulation
Transport Properties*

10 μ m



Conventional

Bulk Measurement

- Geometry
- Density
- Appearance

Wet lab test

- In-vitro
- In-vivo

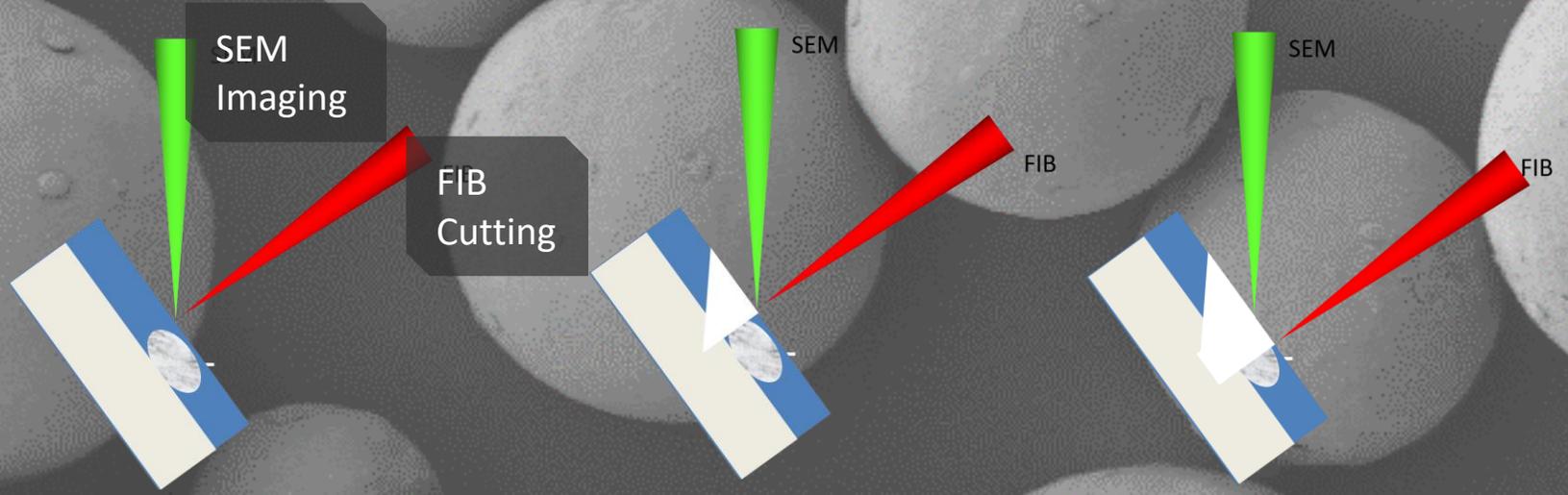
Destructive test

- Crushing
- Razor blade cutting

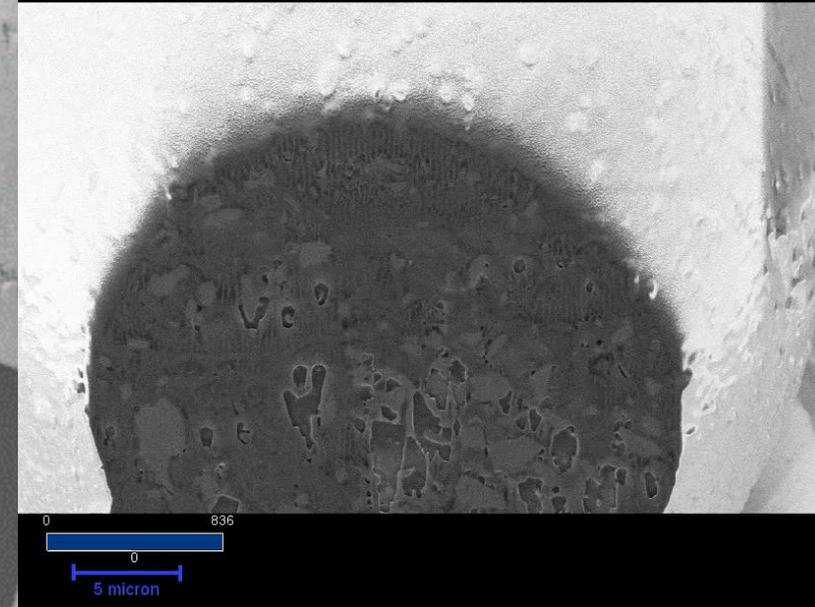
*PLGA Extended Release Microsphere
Sample Courtesy: Dr. Dan Wu, Bausch Health*



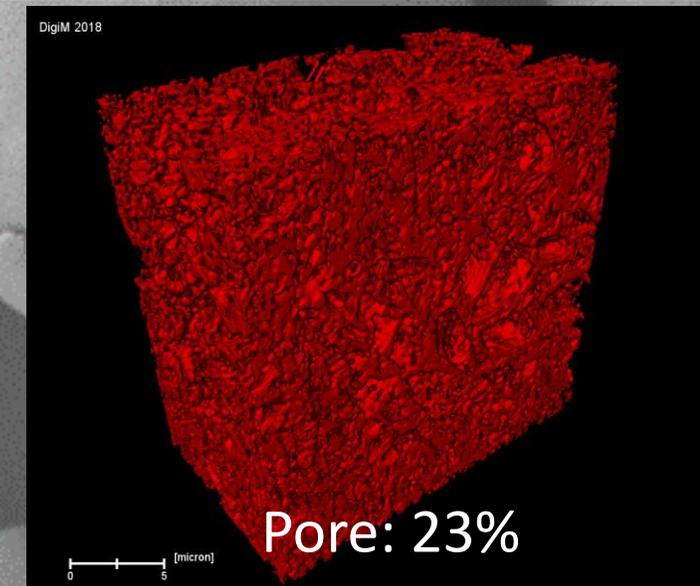
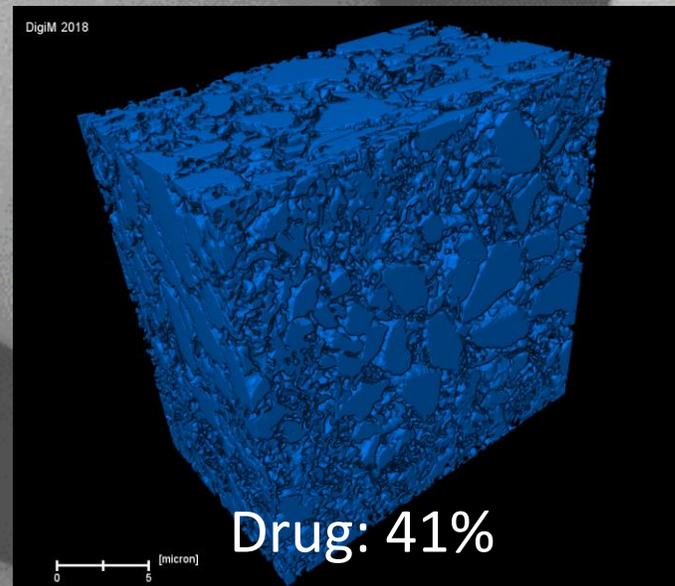
PLGA Extended Release Microsphere

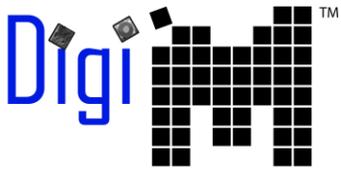


836 FIB-SEM slices at 20nm thickness

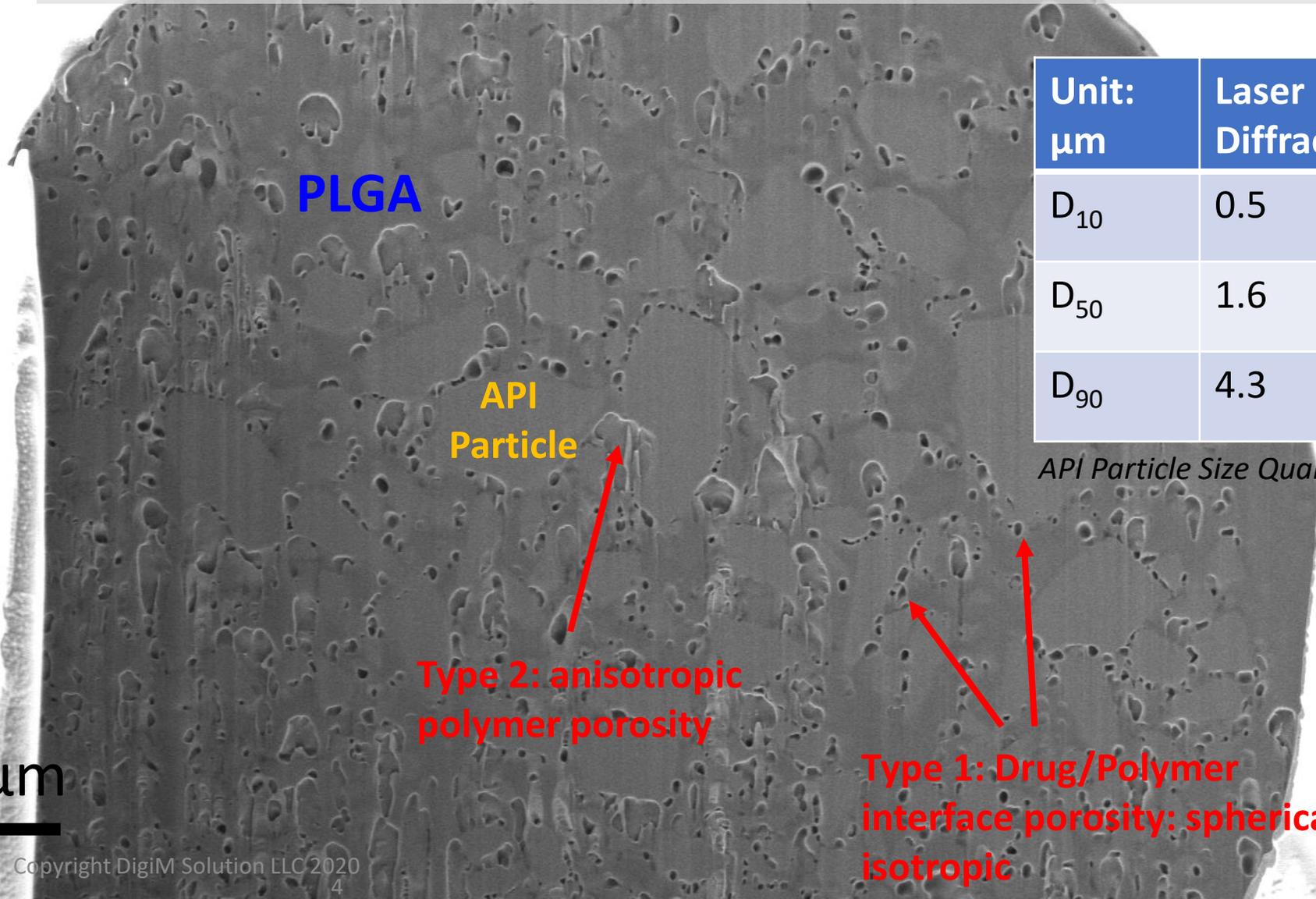


10 μ m





Example FIB-SEM Cross Section PLGA Controlled Release Microsphere



Unit: μm	Laser Diffraction	AI Image Analysis
D ₁₀	0.5	0.7
D ₅₀	1.6	1.7
D ₉₀	4.3	3.3

API Particle Size Quantification



Equivalent or not: Root cause analysis

Process 1

Process 2

Exterior SEM Surface Images

100 μm

Interior FIB-SEM Cross Section Images

Drug-Free Zone

4 μm

Illustrative Data Only.

Qualitative

High Resolution 3D Imaging with
FIB-SEM and X-Ray Microscopy

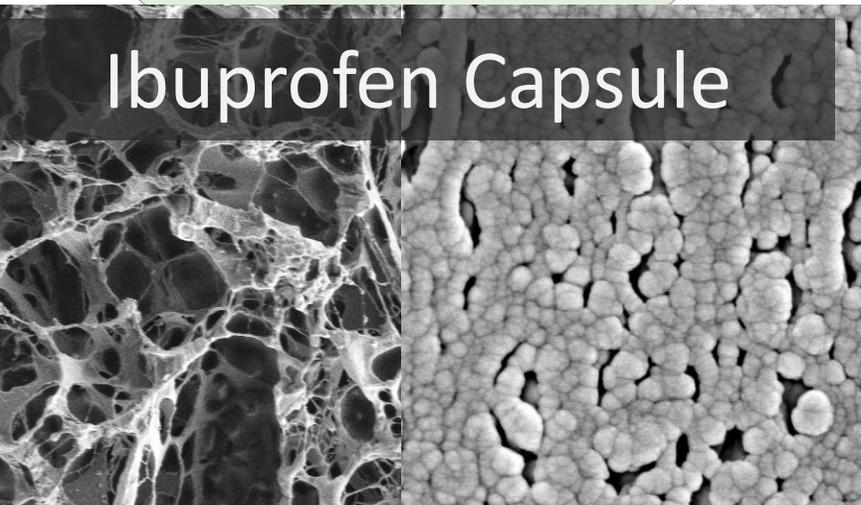
Quantitative

Microstructure Characterization
with Artificial Intelligence

Predictive

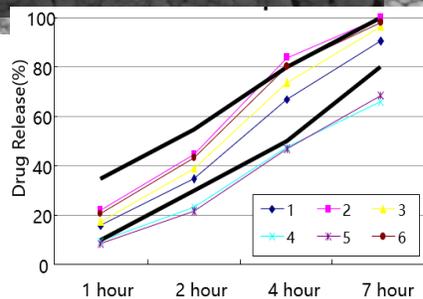
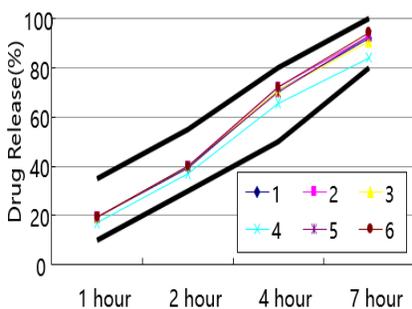
Image-Based Simulation
Transport Properties

Ibuprofen Capsule

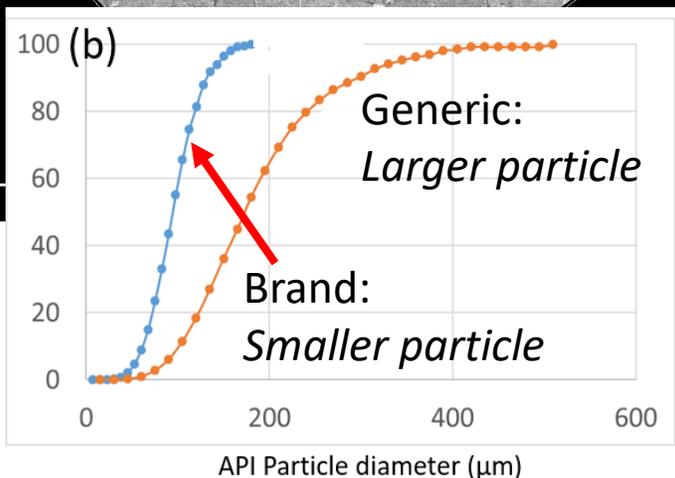


Brand:
API in porous
polymer matrix

Generic:
Lack of porosity



Indomethacin Tablet



Peptide Implant

