

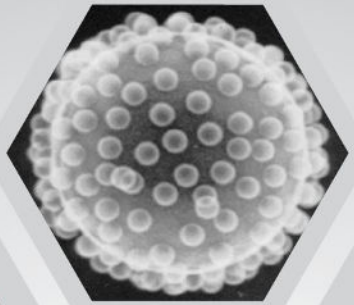



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Microparticles as Controlled Release Drug Delivery Systems

Kimberly Zubris, Ph.D.
Director, Drug Delivery Technologies

Lubrizol

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Introductions

- Located in Bethlehem, PA, ~50,000 sq ft integrated facility, 90+ employees
- Full service CDMO including commercial production and traditional CMC services
- Wide range of dosage forms, specialize in complexity
- 7,000+ sq. ft. of GMP production suites: sterile, non-sterile, and high potency
- FDA registered, DEA licensed

Kimberly Zubris Ph.D.

Director, Drug Delivery Technologies

PhD - Biomedical Engineering from Boston University

Focus Areas: Development, scale-up and manufacturing of a broad spectrum of drug products

Extensive experience in microparticulate formulations

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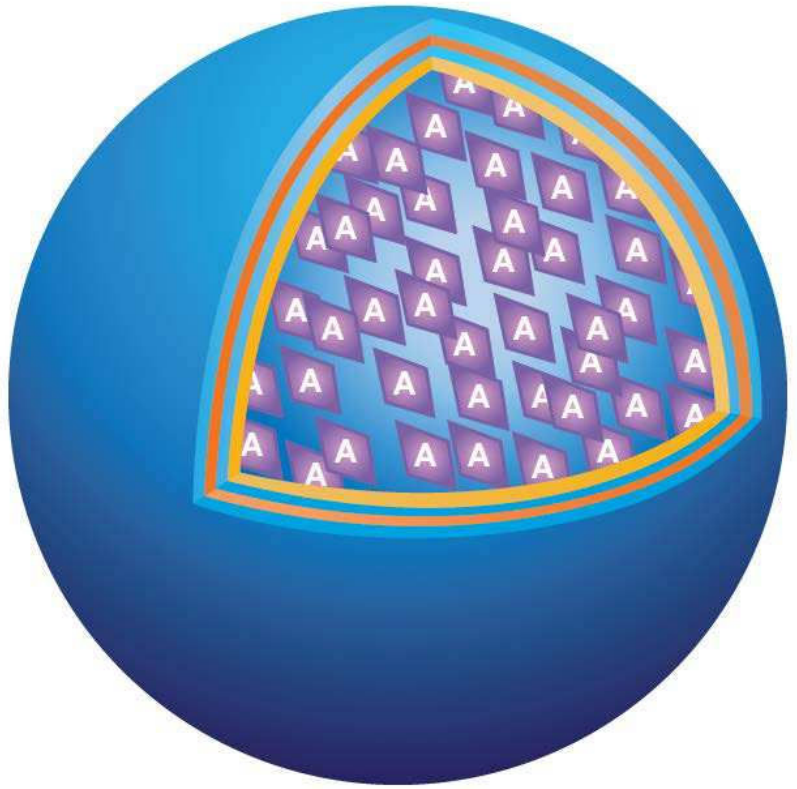
Agenda: Microparticles as Controlled Release Drug Delivery Systems

- What are microparticles?
- Why choose microparticles?
- Commercial microparticulate products
- Methods of preparation
- Preparation considerations
- Particle Sciences' microparticle capabilities



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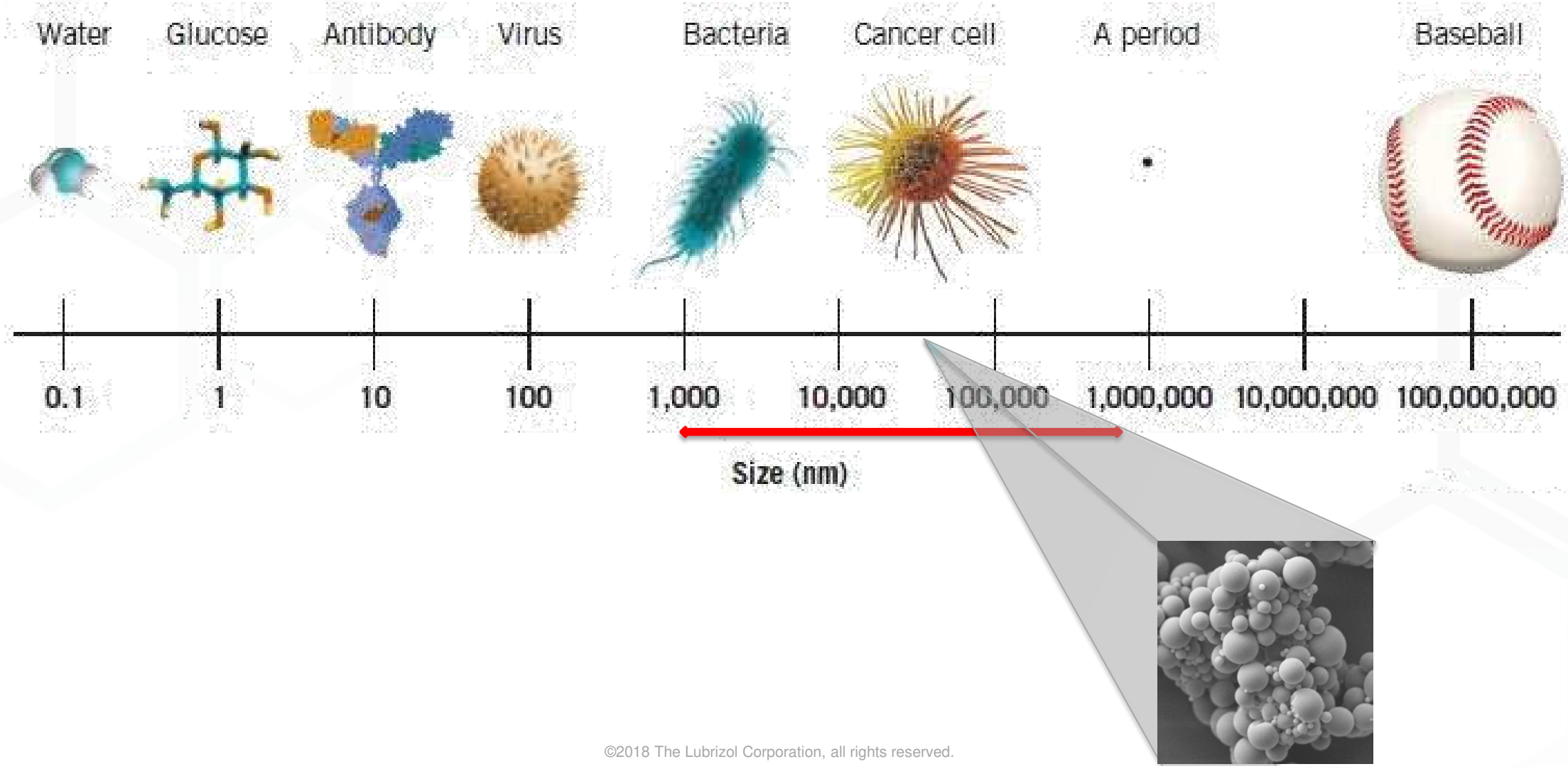
What Are Microparticles?



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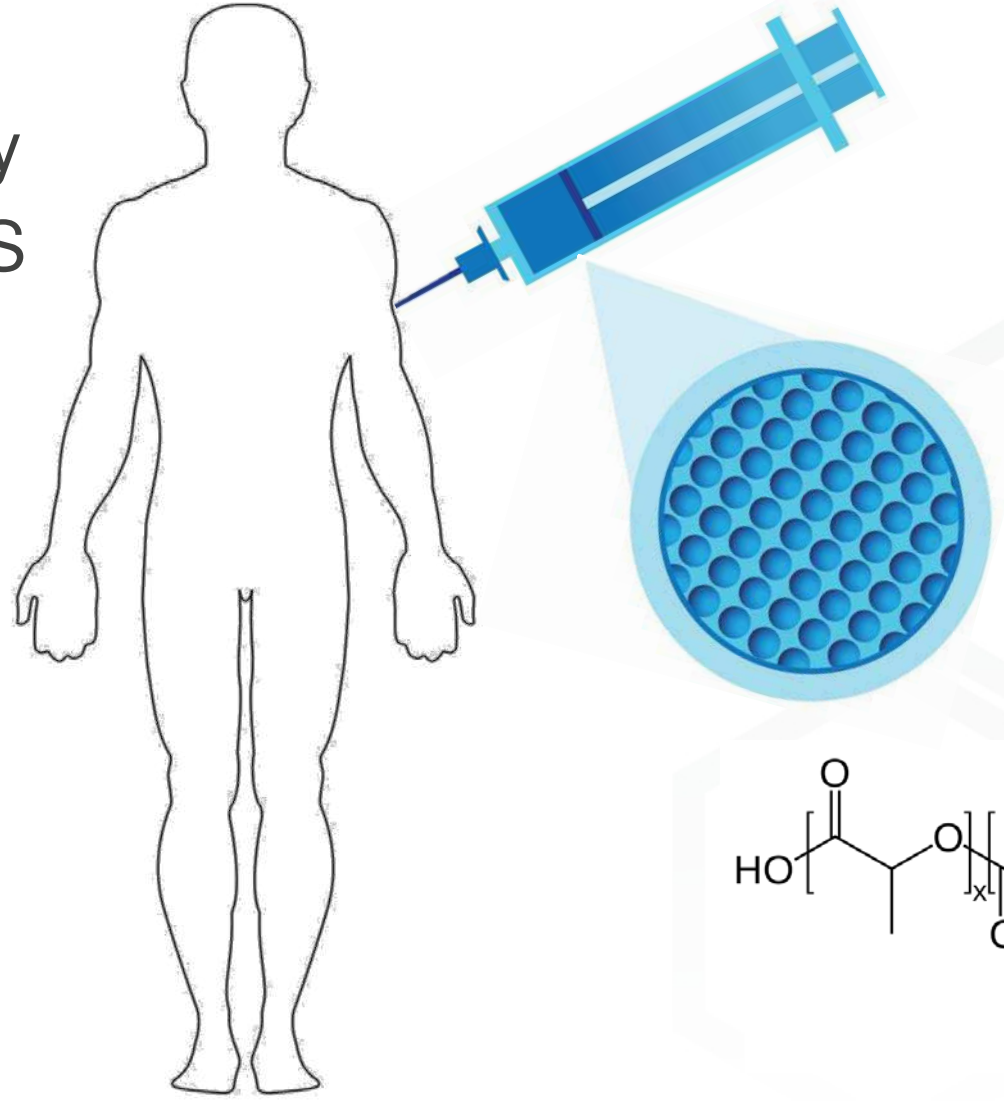
Microparticle Drug Delivery Systems Can Align with Important Goals

- Controlled release from single injection-tunable duration of efficacy
- Biodegradable/biocompatible GRAS carrier materials
- Small molecules and biologics
- Range of loading capability
- Delivery of water soluble or insoluble products



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Why Choose Microparticles?

- Protect unstable drugs
  - Before and after administration
- Provide accurate delivery of small quantities of potent drugs
- Provide ability to manipulate:
  - pK profile
  - Cellular and tissue interactions
  - *In vivo* action of drugs
- Enable controlled release

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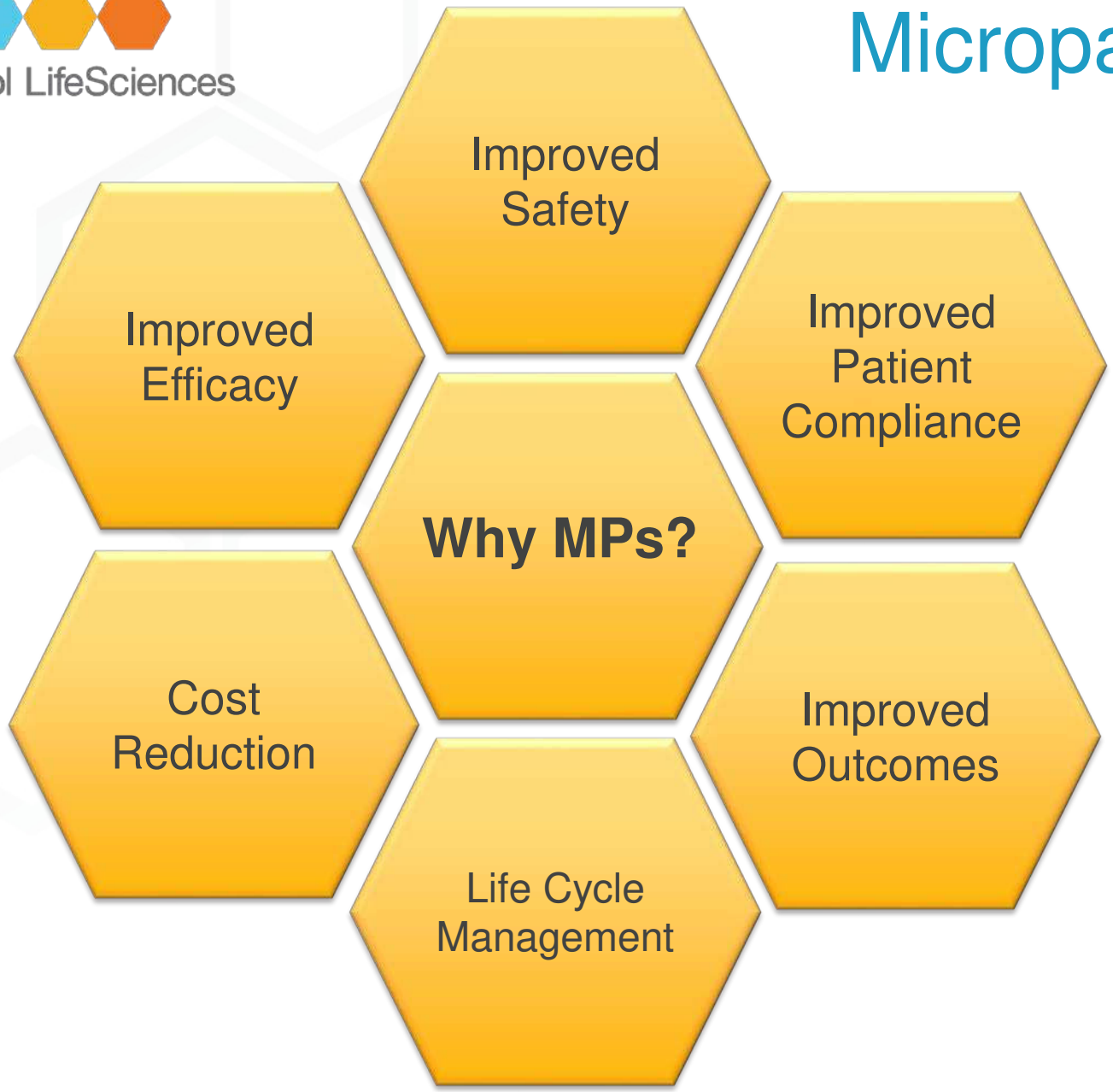
Microparticle Advantages



Sustained and **Controlled** delivery of an active over long periods of time

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Microparticle Advantages

- Effective delivery of insoluble actives
- Bolus delivery instead slower IV administration
- Targeted drug delivery to specific sites
- Reduction of dose frequency and toxicity
- Ability to maintain drug in amorphous form
- Reduction of local side effects
- Maintenance of therapeutic plasma concentrations

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Examples of FDA-Approved Microparticulate Products

		Dosing Frequency
Vivitrol (naltrexone for extended-release injectable suspension)	**Vivitrol® by Alkermes** – Active Ingredient: Naltrexone – Route of Administration: Intramuscular – Approval Date: 1984 – Indicated for the treatment of alcohol/opioid dependence	**Every 4 weeks**
Sandostatin® LAR Depot (octreotide acetate for injectable suspension) 10mg • 20mg • 30mg	**Sandostatin® LAR Depot by Novartis** – Active Ingredient: Octreotide – Route of Administration: Subcutaneous – Approval Date: 1998 – Indicated for treatment of acromegaly, severe diarrhea/flushing episodes associated with metastatic carcinoid tumors and VIP-secreting tumors	**Every 4 weeks**
Arestin® minocycline HCl 1mg MICROSPHERES	**Arestin® by OraPharma** – Active Ingredient: Minocycline HCl – Route of Administration: Periodontal – Approval Date: 2001 – Indicated as an adjunct to scaling and root planing (SRP) procedures for reduction of pocket depth in patients with adult periodontitis	**Variable**
RisperdalCONSTA risperidone Long-Acting Injection 12.5mg, 25mg, 37.5mg, 50mg	**Risperdal Consta® by Janssen** – Active Ingredient: Risperidone – Route of Administration: Intramuscular – Approval Date: 2003 – Indicated for the treatment of schizophrenia and bipolar I disorder	**Every 2 weeks**
LuproDepot® (leuprolide acetate for depot suspension)	**Lupron Depotstin® by AbbVie** – Active Ingredient: Leuprolide acetate – Route of Administration: Intramuscular – Approval Date: 1989 – Multiple indications including prostate cancer, central precocious puberty, fibroids and endometriosis	**Every 1, 3 or 6 months**

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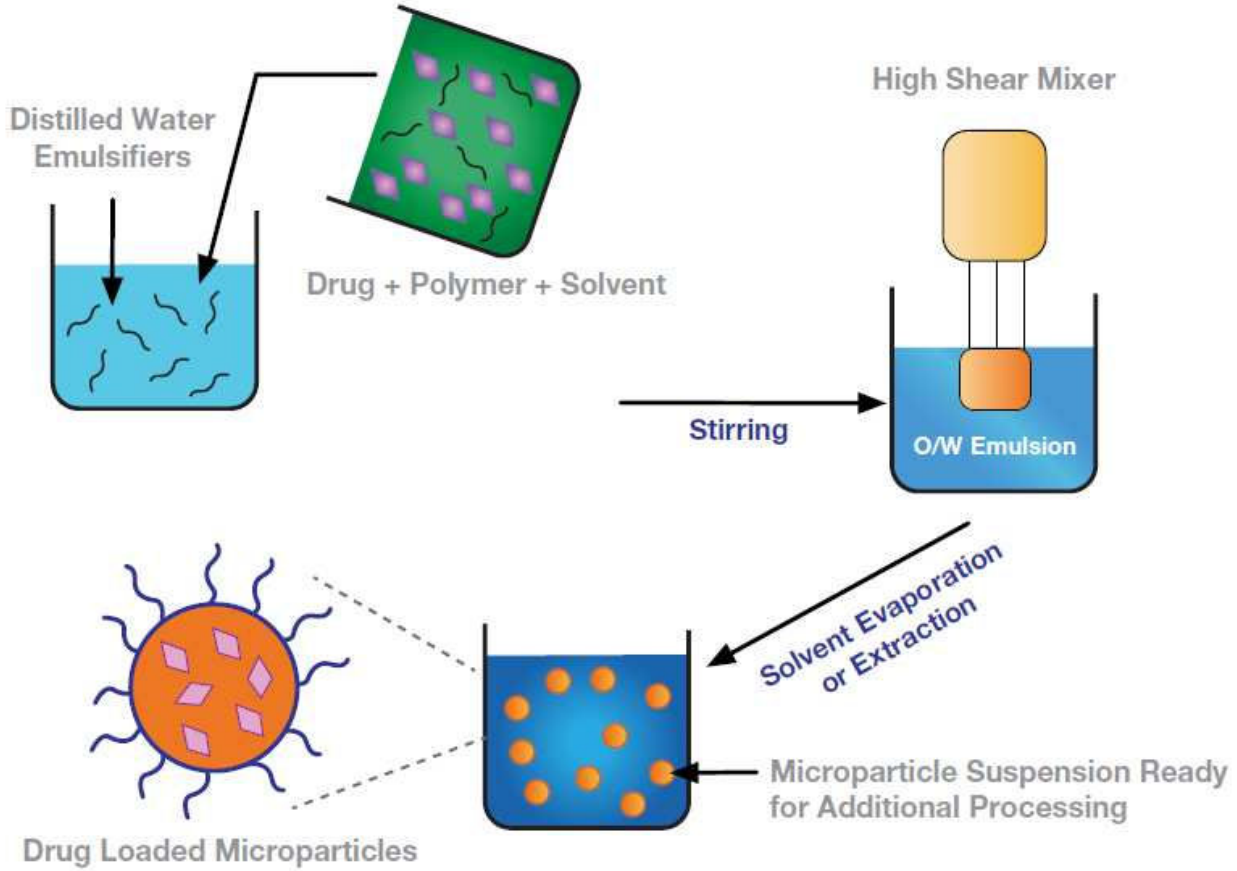
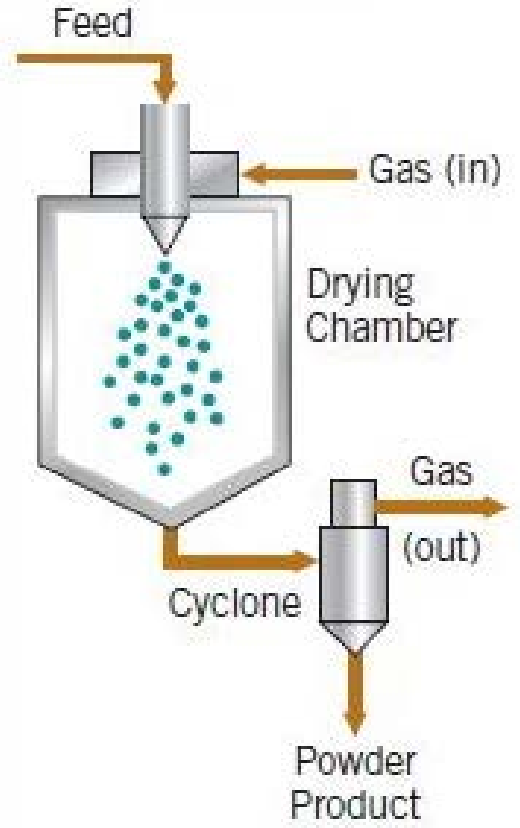
Methods of Preparation

Preparation of Microparticles via Emulsion



Spray Drying



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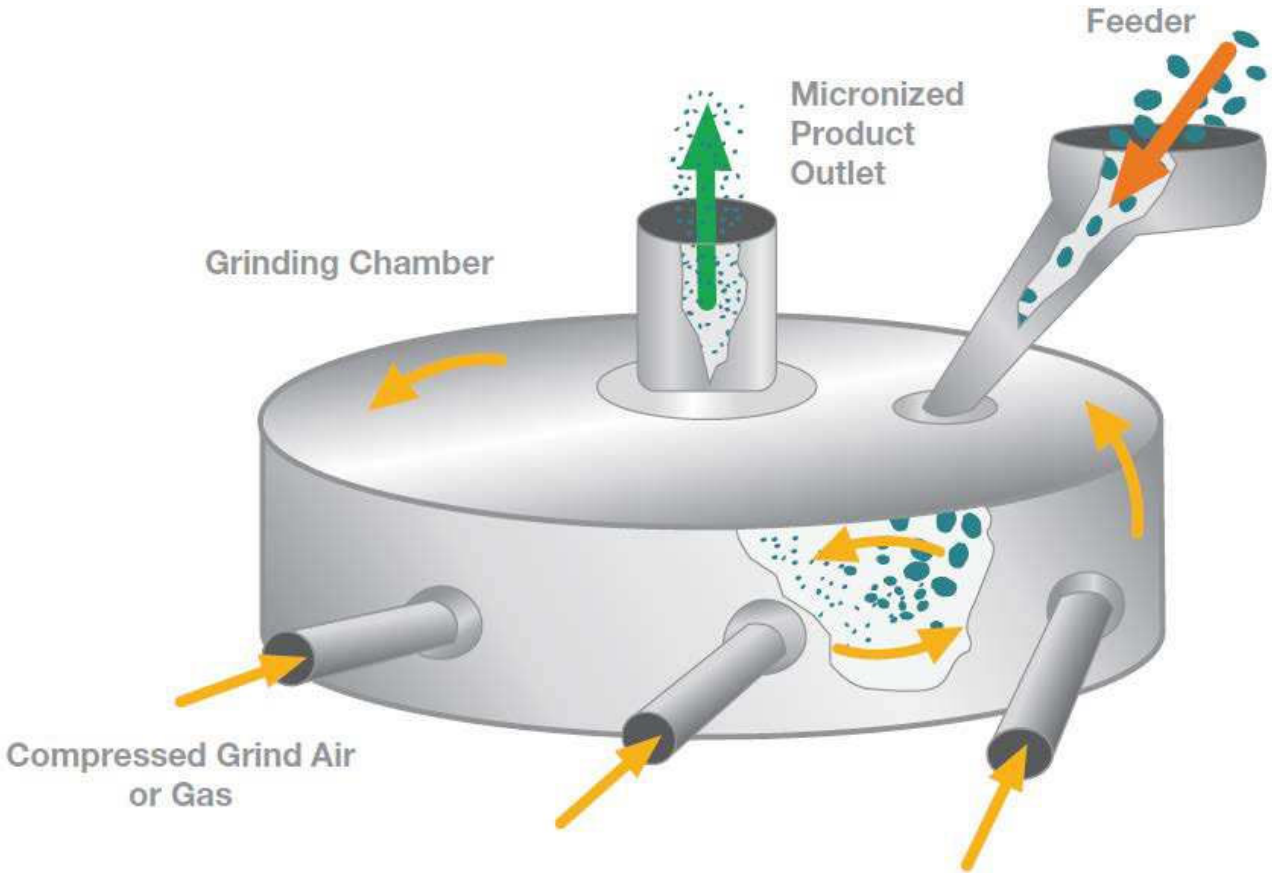
Methods of Preparation

Jet Milling



Augmented Drip Casting

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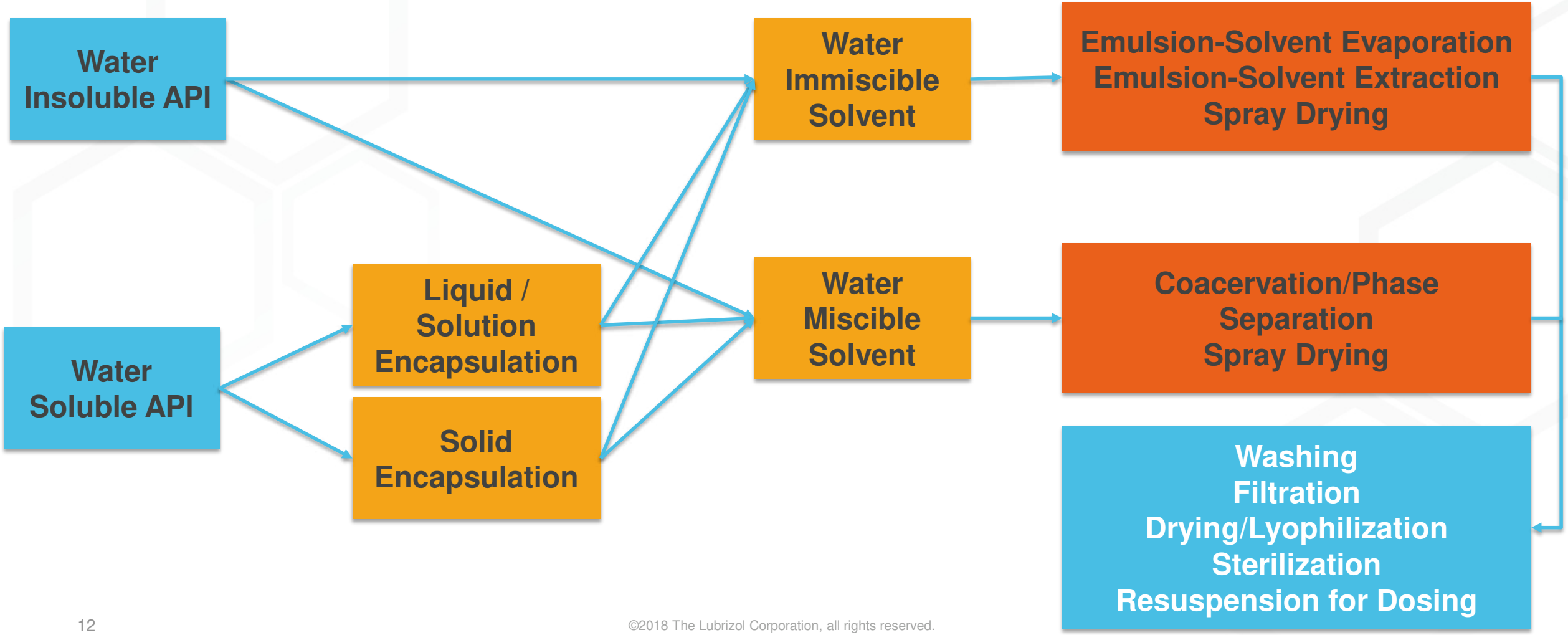
Preparation Considerations



PSI Processing Capabilities

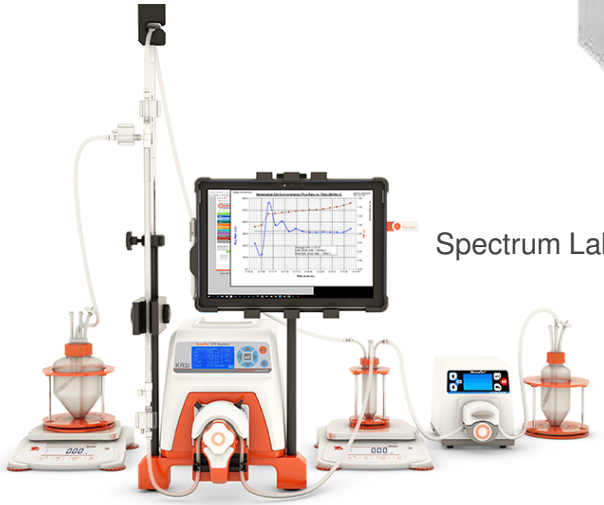
Chemglass

Eagle Stainless

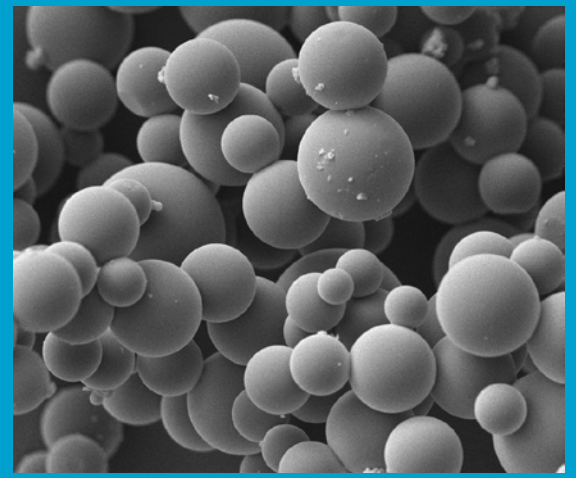
PSL

SP Scientific

Silverson



Spectrum Labs



Over 20 *microparticle formulations in development at PSI over past 18 months from R&D through clinical production*

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PSI Processing Capabilities

Buchi

Retsch

Microfluidics

Buchi

Sturtevant

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End-to-End Product Services

When it comes to microparticulate formulations, Particle Sciences has the:

Equipment

Fully equipped for development services and moving into commercial-scale equipment

Facilities

7,000+ sq. ft. of GMP production suites to accommodate 1 - 2 kg commercial batches

Personnel

Decades of cumulative experience formulating and manufacturing microparticulate formulations

Lubrizol LifeSciences

Concept to Commercialization

We Deliver®