

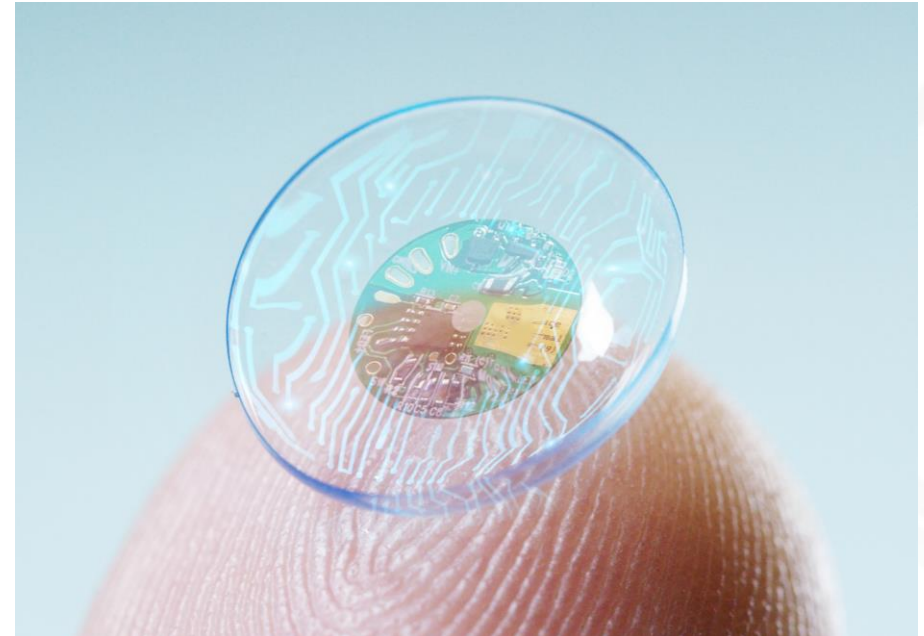
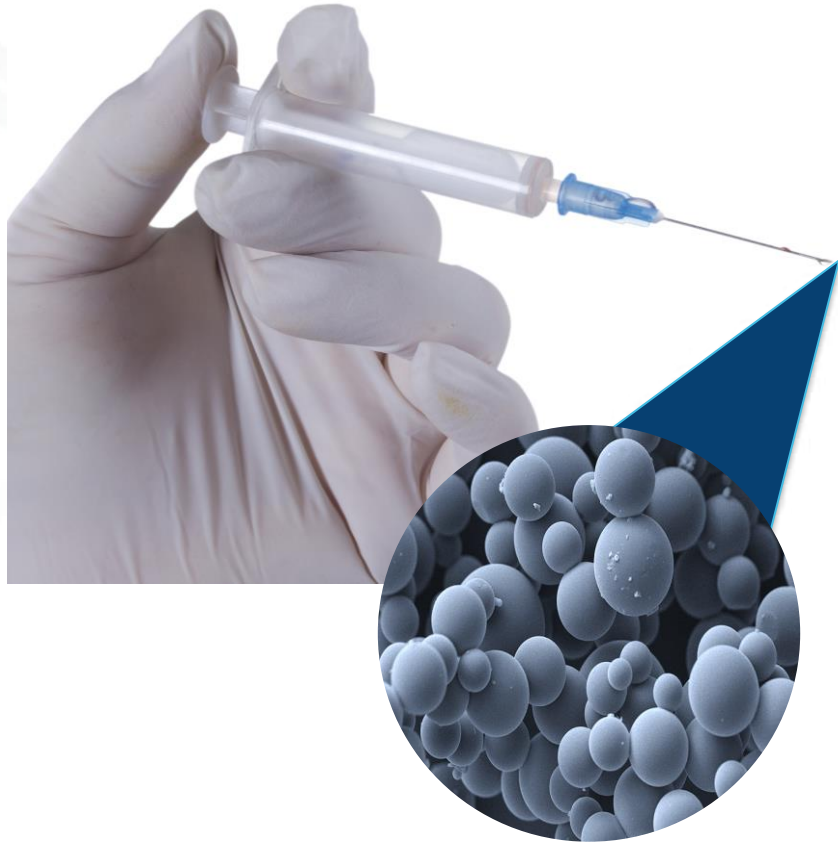


Lubrizon LifeSciences

Webinar: Overcoming Challenges in Ophthalmic Drug Delivery including Bioavailability and Sterility
6/19/2019



Ophthalmics – The Future has become Reality



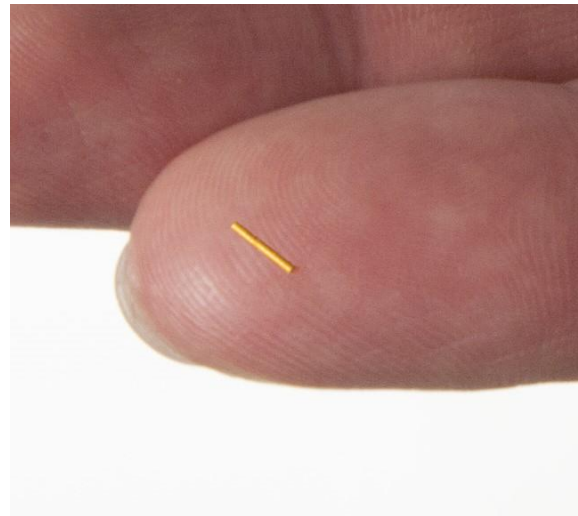
Agenda

- Introduction
- Industry trends
- Anterior and Posterior Drug Delivery
- Challenges
 - API
 - Patient Compliance & Sustained Release
 - Sterility, Containment, & Packaging



Introduction

What is ophthalmic drug delivery?





Lubrizol LifeSciences

Marketed Products

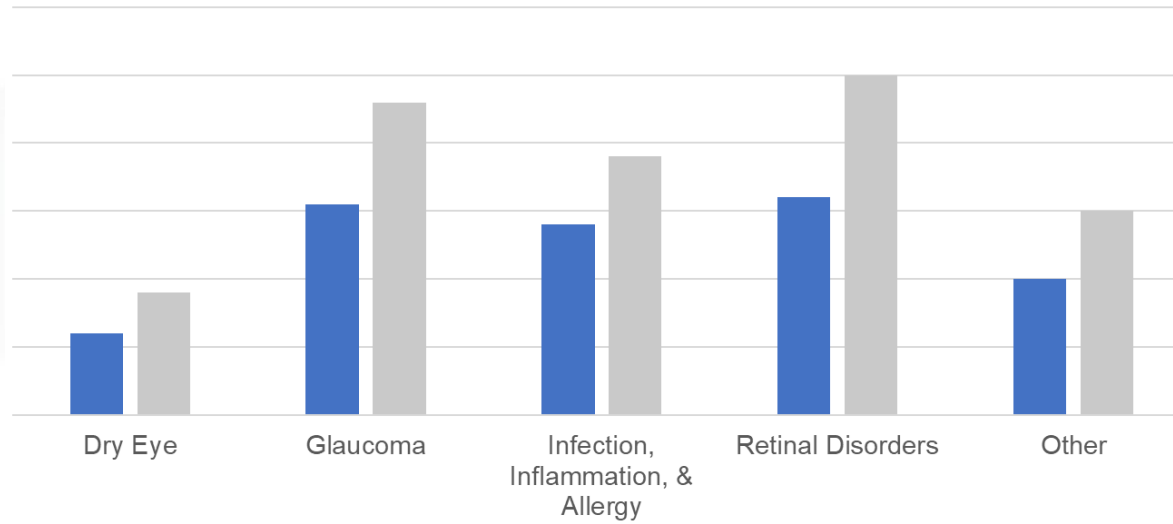


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2. Eylea® is a registered trademark of Regeneron Pharmaceuticals, Inc.

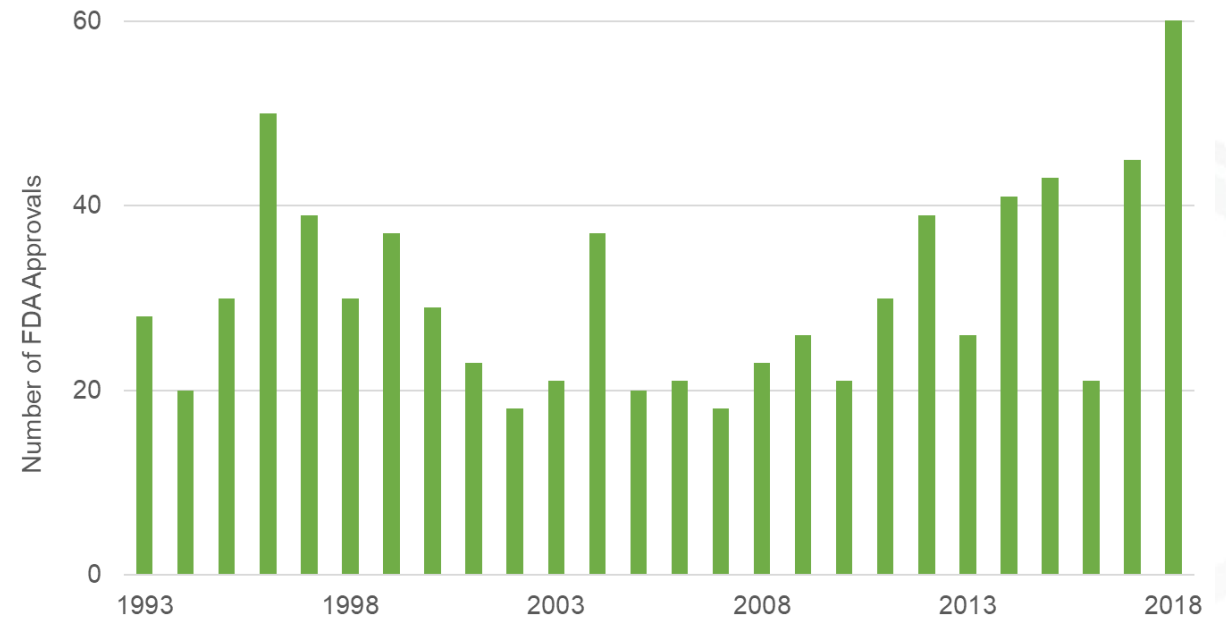
Industry Trends

Ocular Drug Development by Disease State*
2016 vs 2023 Projection

■ 2016 ■ 2023

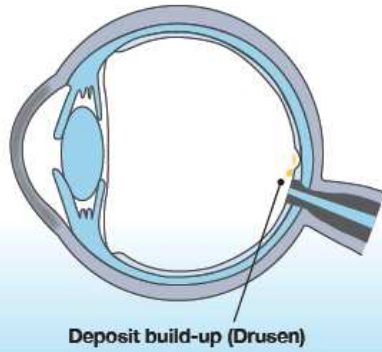


FDA Ophthalmic Drug Product Approvals by Year

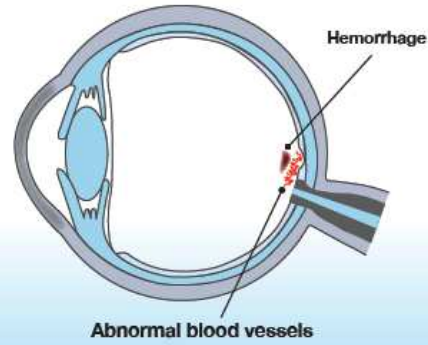


Common Disease States

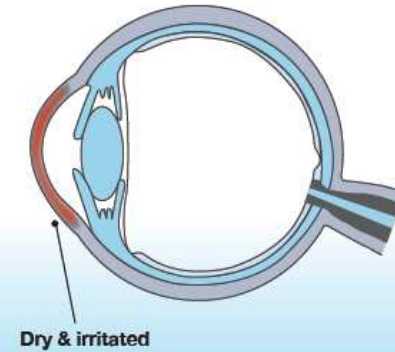
“Dry” Age-Related Macular Degeneration (Dry AMD)



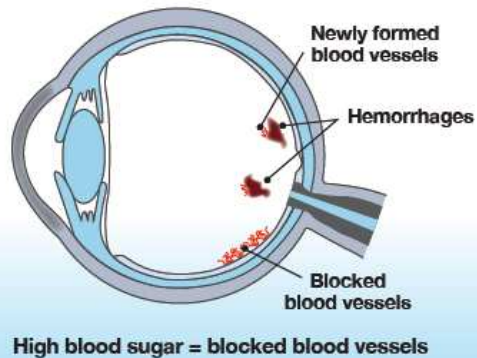
“Wet” Age-Related Macular Degeneration (Wet AMD)



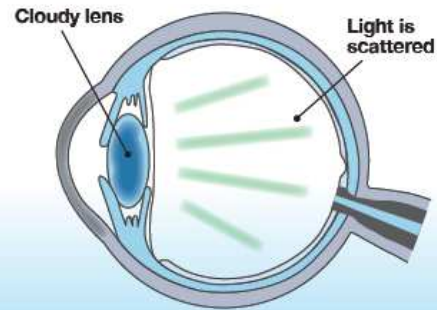
Dry Eye



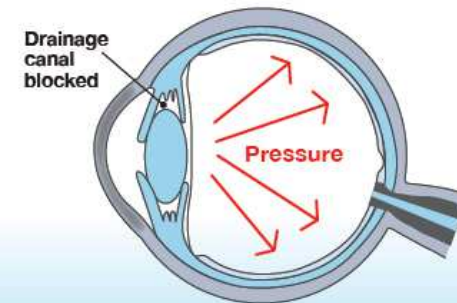
Diabetic Retinopathy



Cataracts



Glaucoma

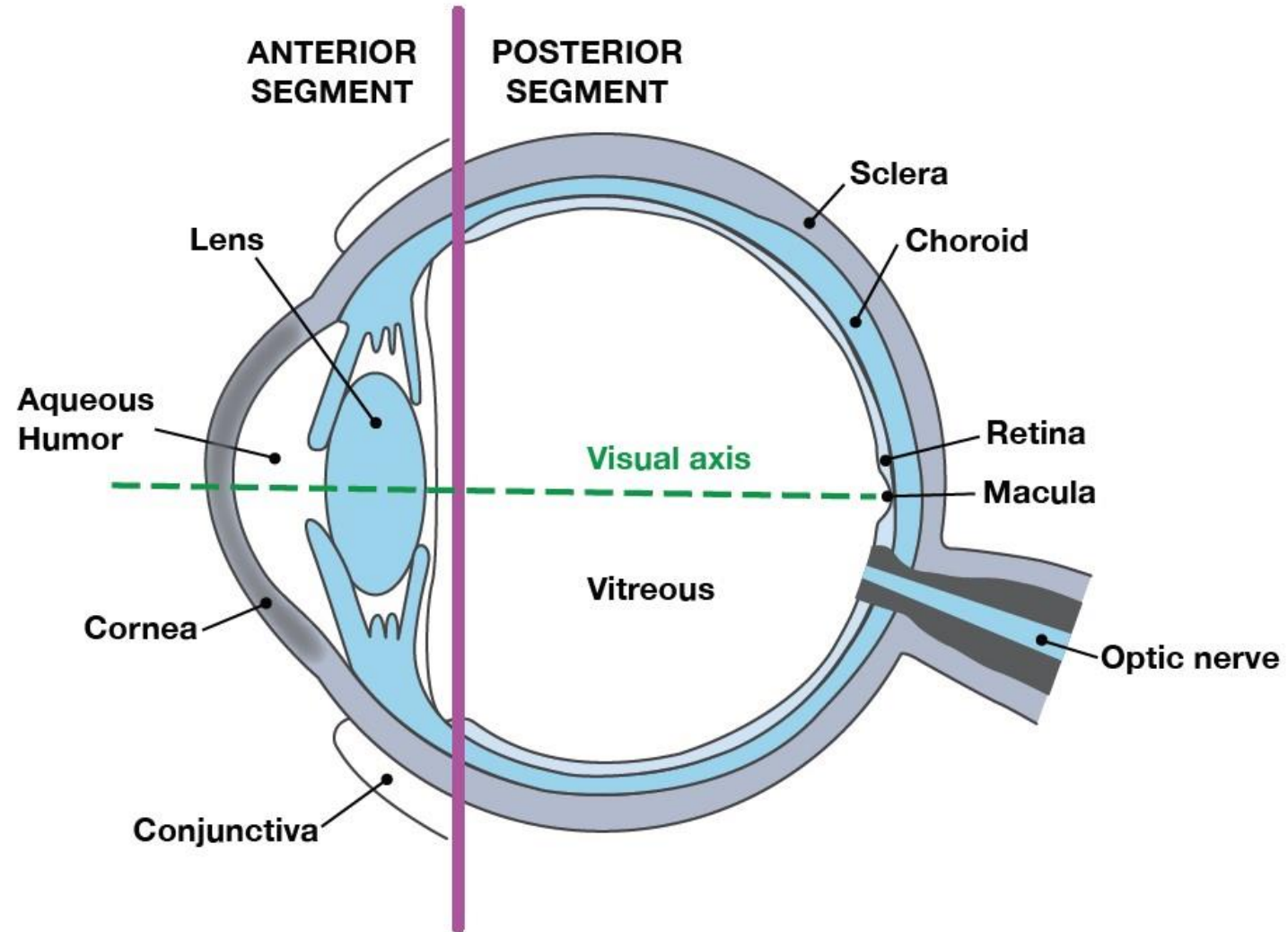




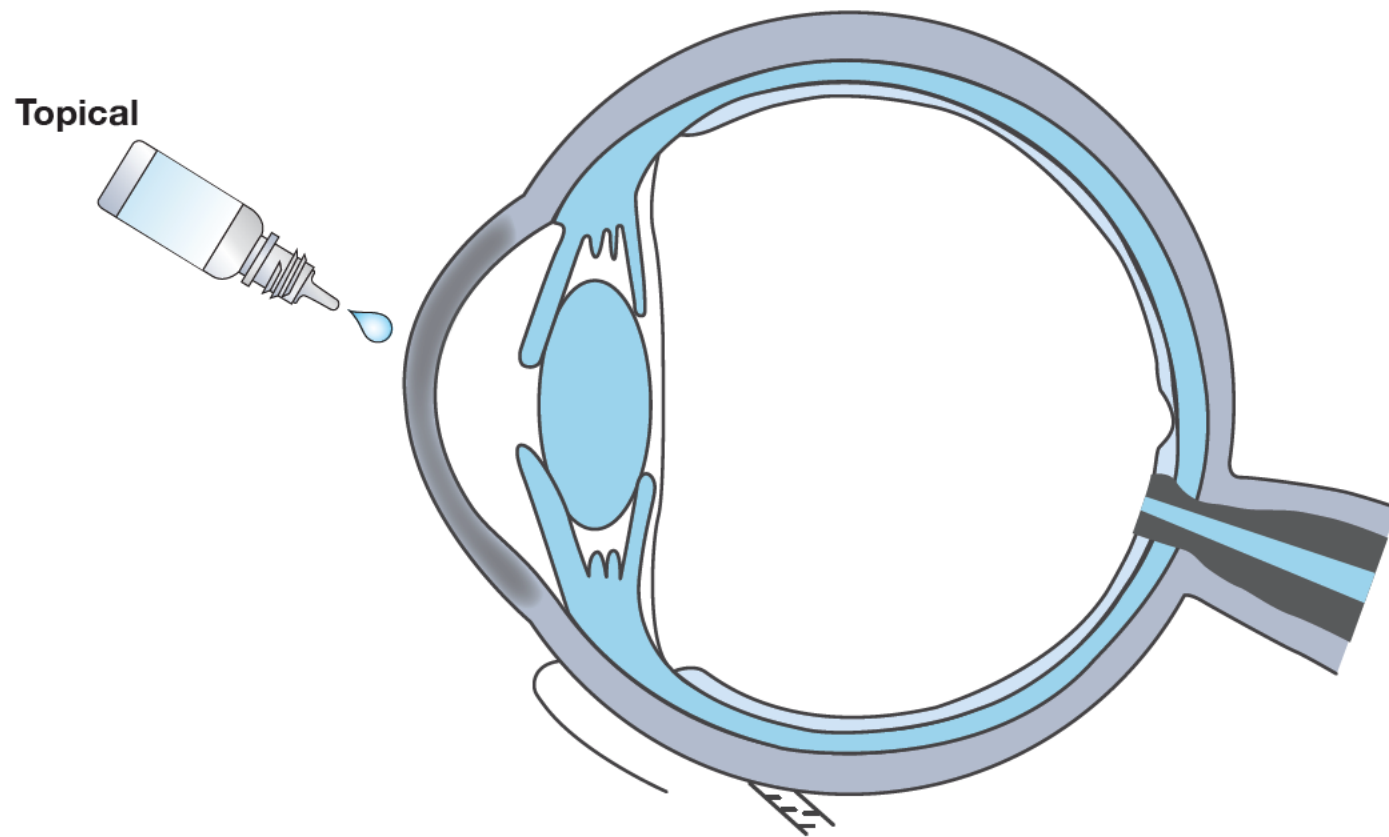
Anterior & Posterior Ocular Delivery

Ocular Anatomy

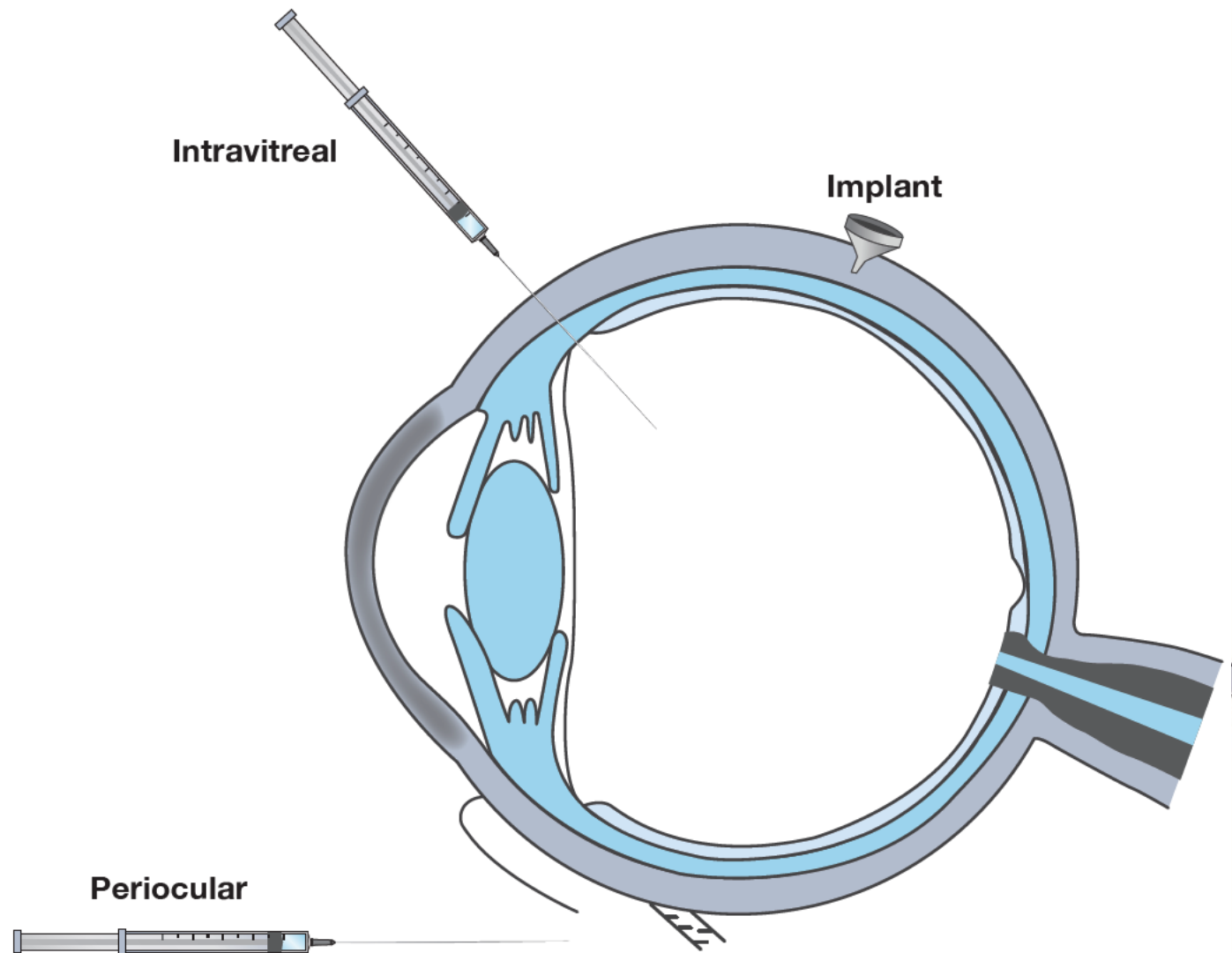
- Anterior
 - Cornea
- Posterior
 - Retina
 - Macula
 - Vitreous



Anterior Drug Delivery



Posterior Drug Delivery





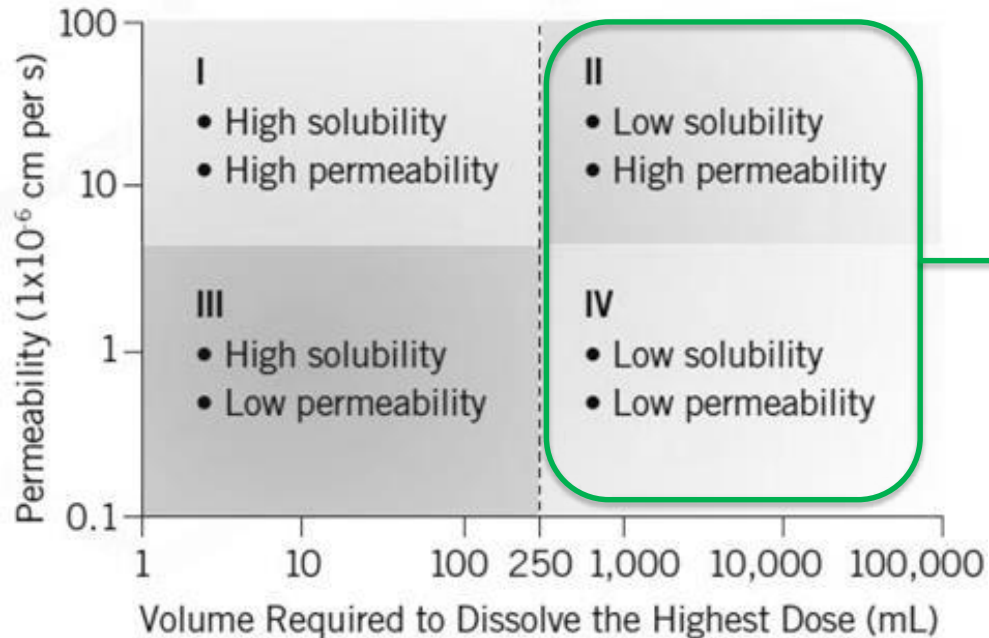
The Challenges



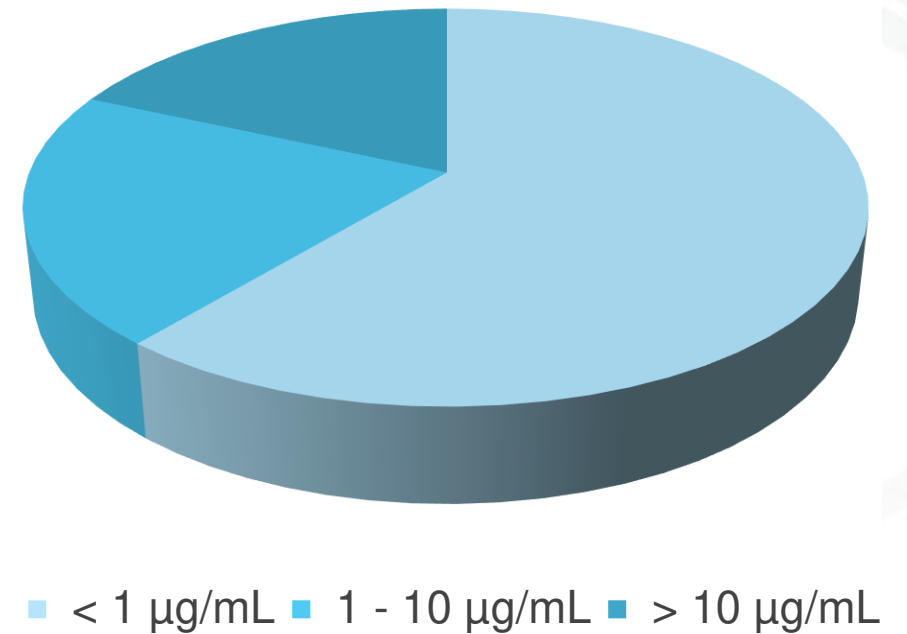
API Issues

Low Bioavailability Due to Poorly Soluble APIs

Biopharmaceutical Classification System (BCS)



PSI Projects - Aqueous Solubility

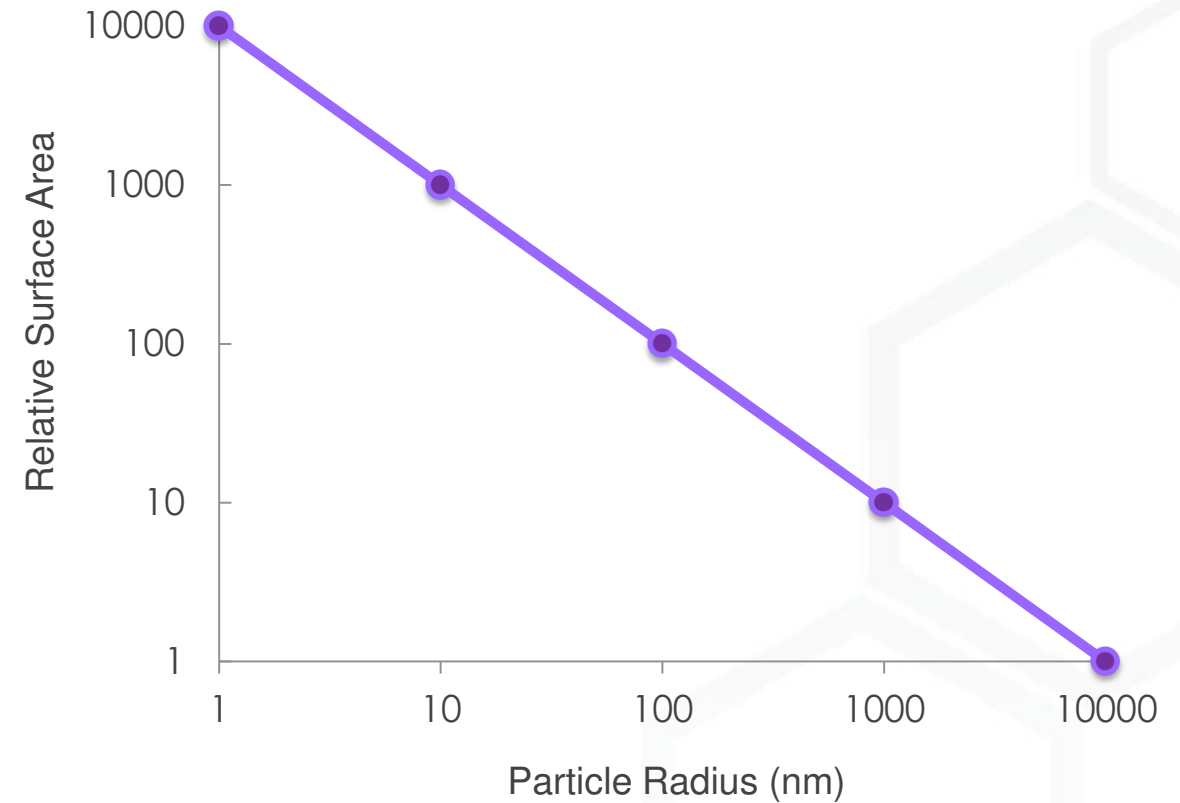
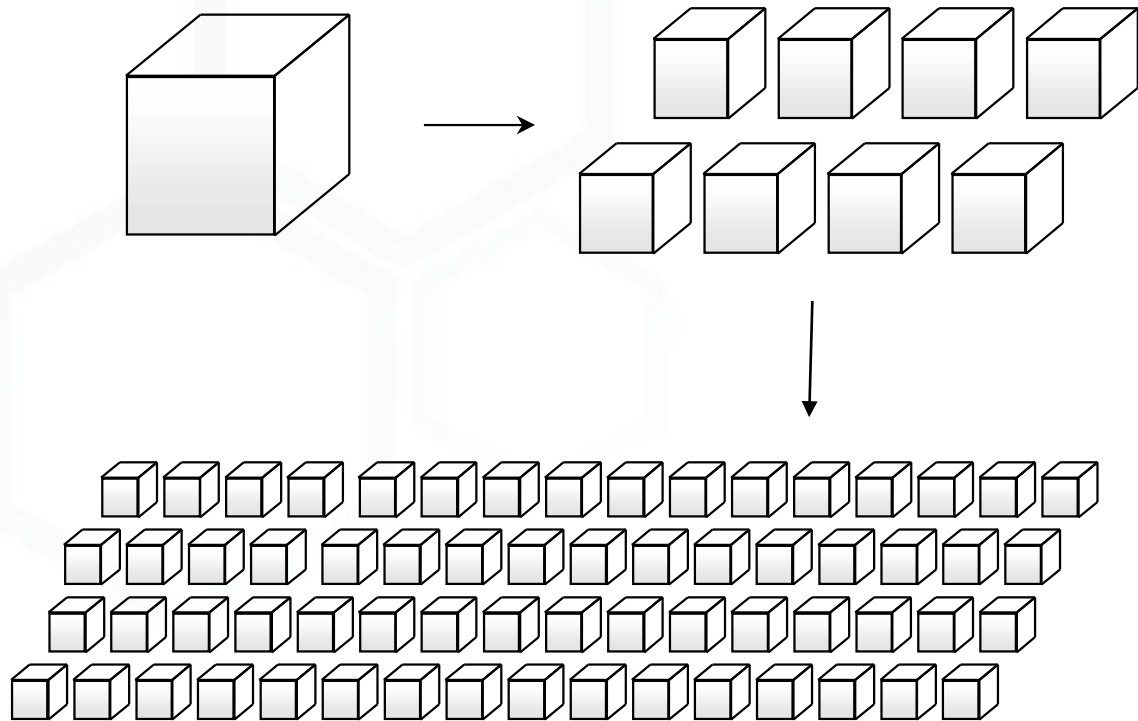


API Stability Issues

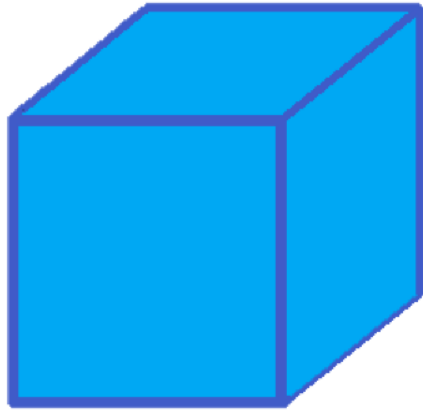
- Shelf-life and enzymatic stability
- Many drugs are highly sensitive to specific conditions (light, humidity, temperature, pH, etc.)
- Stability impacts integrity and therefore efficiency and safety of the final drug product



Particle Size Reduction

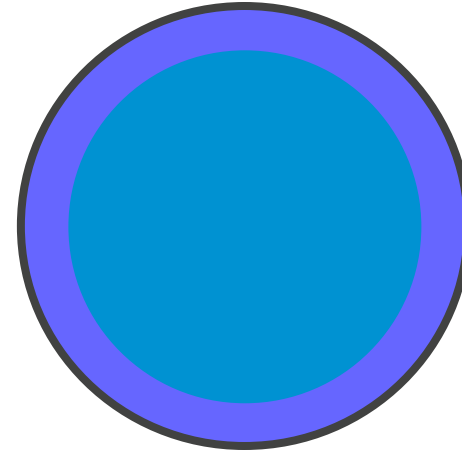


Nanoparticles



Nanoparticle

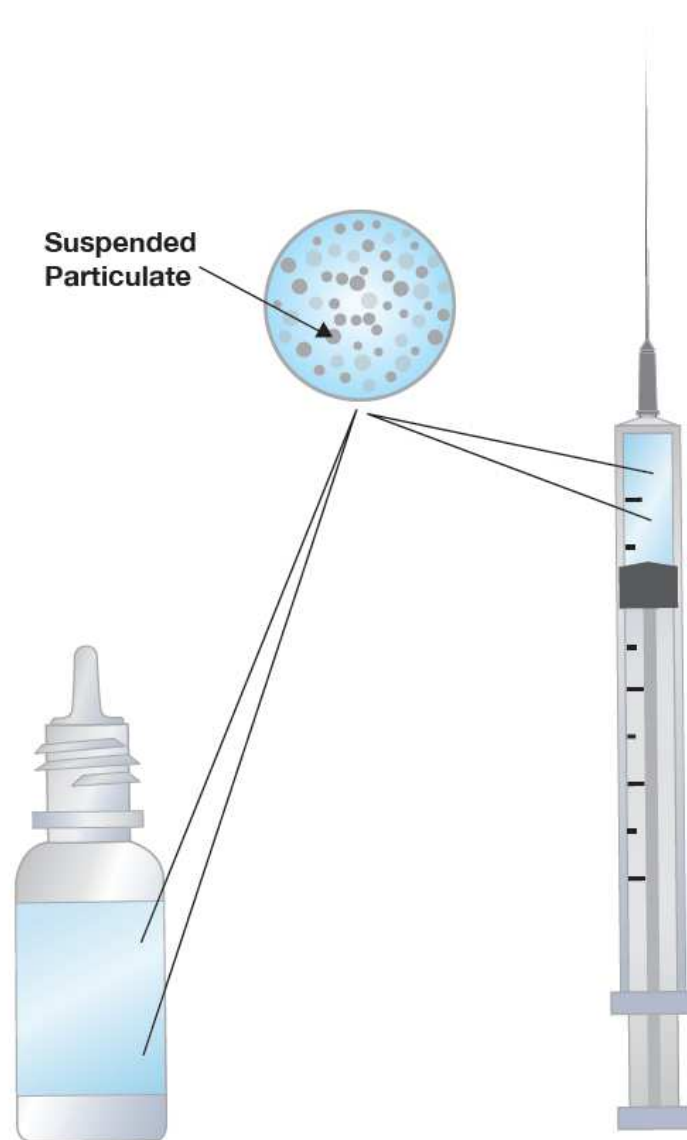
- Nanoparticulate suspensions
- Solid lipid nanoparticles
- Polymeric nanoparticles



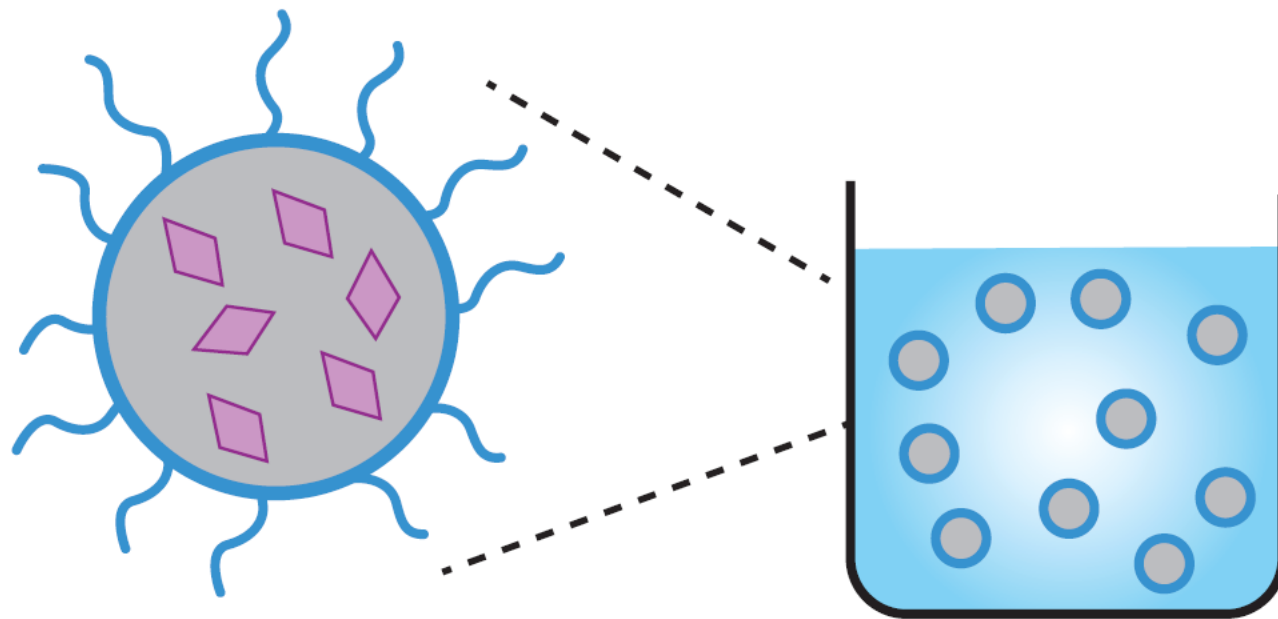
Nanocapsule

- Liposomes
- Emulsions

Suspensions & Emulsions



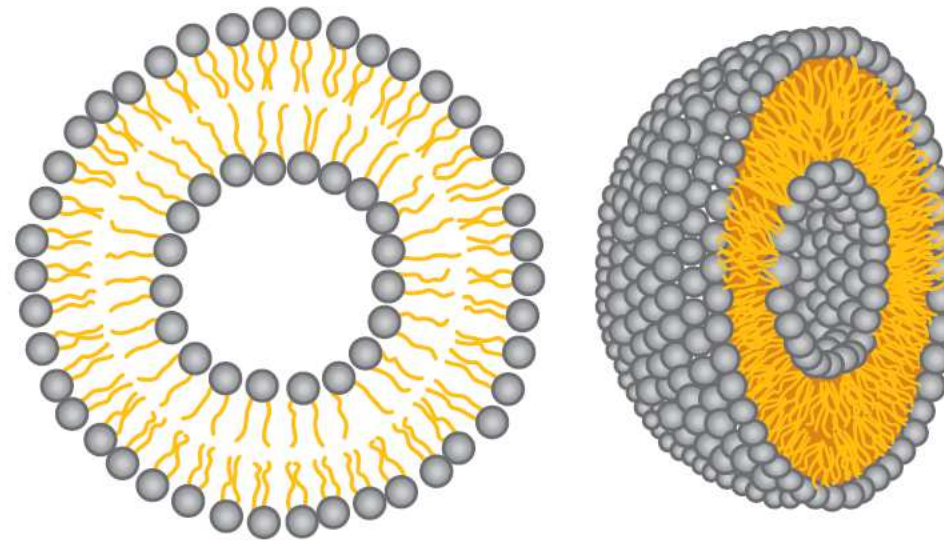
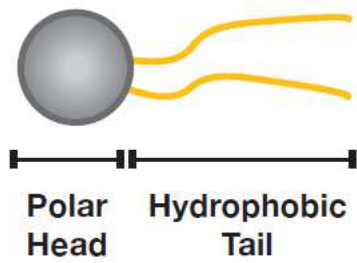
Solid Lipid Nanoparticles



Solid Lipid Nanoparticles

Liposomes

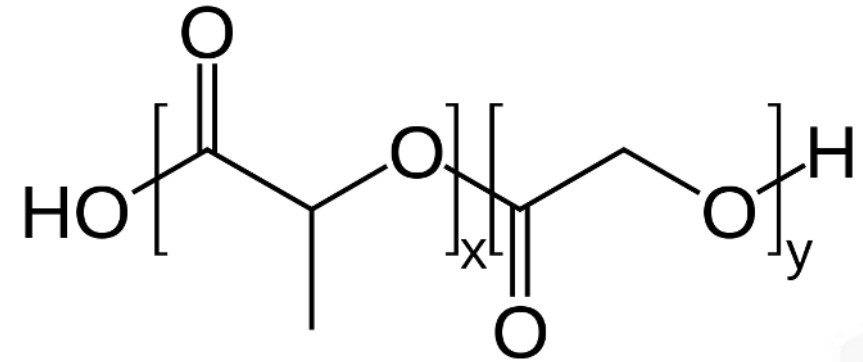
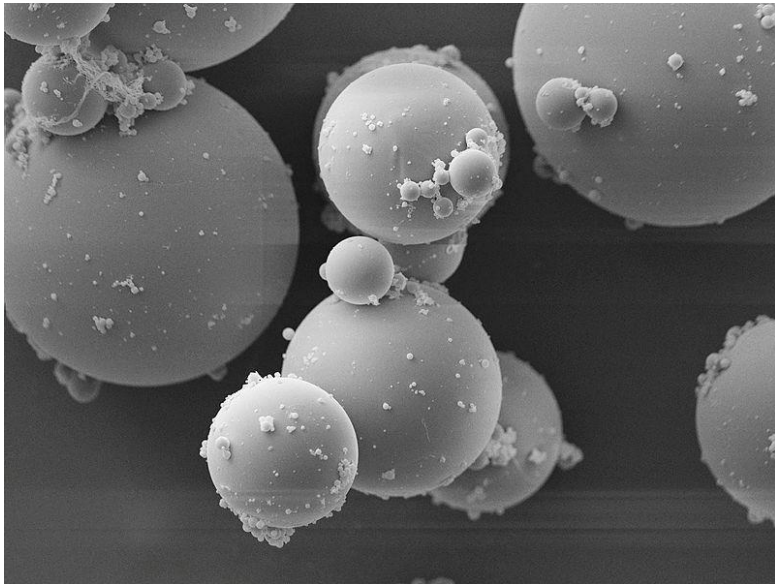
Phospholipid



Liposome
Sizes: 0.025 μm to 2.5 μm

Microparticles

- PLGA



Cold Storage

- Refrigeration: 2 - 8° C
- Important for biologics
- ICH Guidelines
- All intravitreal injections currently on the market are refrigerated + one frozen



Lyophilization





Patient Compliance & Sustained Release

Looking Out for Patients

- Valuable organ vital to everyday life
- Frequent dosing = decreased quality of life
 - Pain & discomfort
 - Inconvenience
 - Risk with injectables including infection
 - Side effects, such as blurred vision
- Sustained release = less interference =



Mucoadhesive Topicals

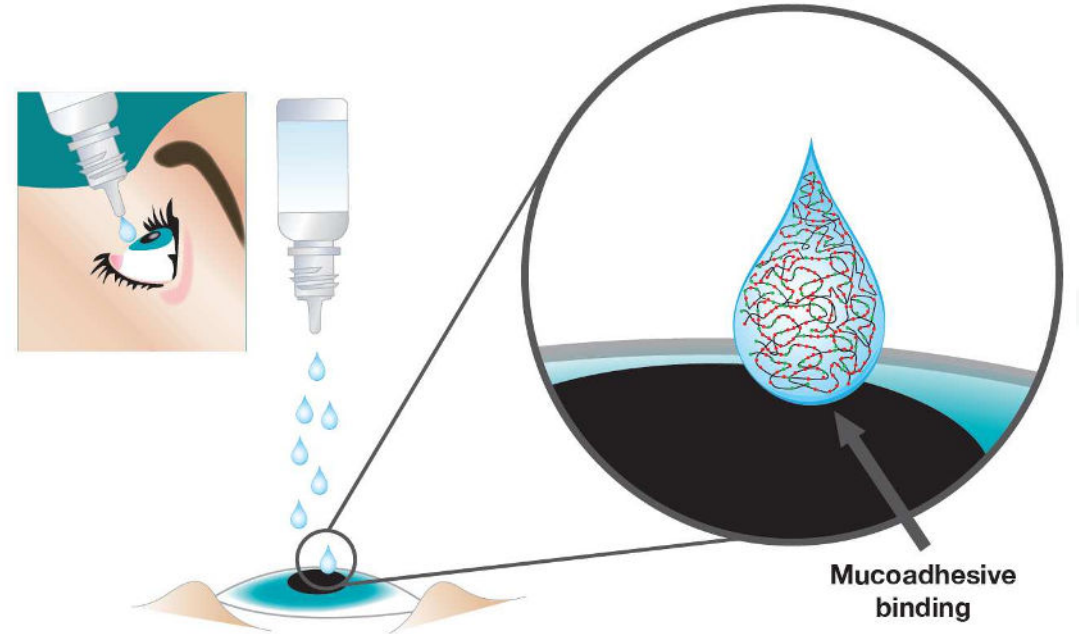
Mucoadhesive Polymers in Ophthalmic Drug Delivery

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Table 1 Some Representative Mucoadhesives with Their Relative Mucoadhesive Performance

Substance	Adhesive performance
Carboxymethylcellulose	Excellent
Carbopol	Excellent
Carbopol and hydroxypropylcellulose	Good
Carbopol base with white petrolatum/hydrophilic petrolatum	Fair
Carbopol 934 and EX 55	Good
Poly(methyl methacrylate)	Excellent
Polyacrylamide	Good
Poly(acrylic acid)	Excellent
Polycarbophil	Excellent
Homopolymers and copolymers of acrylic acid and butyl acrylate	Good
Gelatin	Fair
Sodium alginate	Excellent

This table was borrowed from Ophthalmic Drug Delivery Systems, Second Edition by Mitra

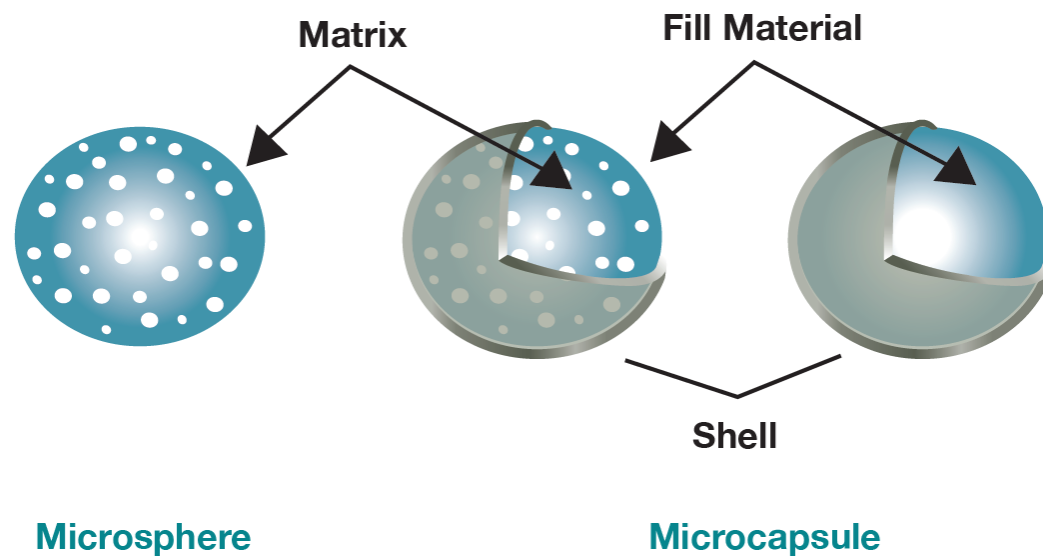


Implants

- Biodegradable and non-biodegradable
- Injectable, suprachoroidal, punctal



Long-acting Injectable Systems





Sterility, Containment, & Packaging

The Importance

- Human eye is sensitive
- Sterility is an absolute requirement because products come in direct contact with tissue that is critical to sight



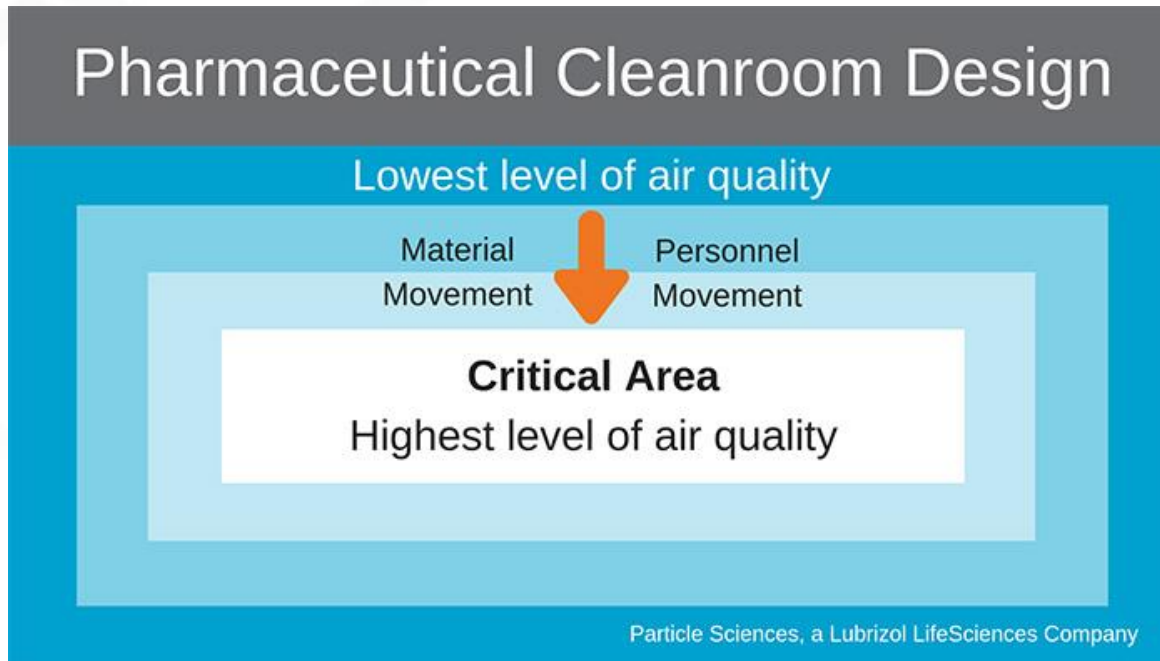
Sterilization Methods

- Terminal vs Aseptic + Sterile Fill-Finish
 - Method depends on dosage form
 - Can affect properties such as stability, viscosity, globule size
 - Heat sterilization
 - Radiation
 - Filtering
 - Ethylene oxide sterilization



Highly Potent Compound Handling

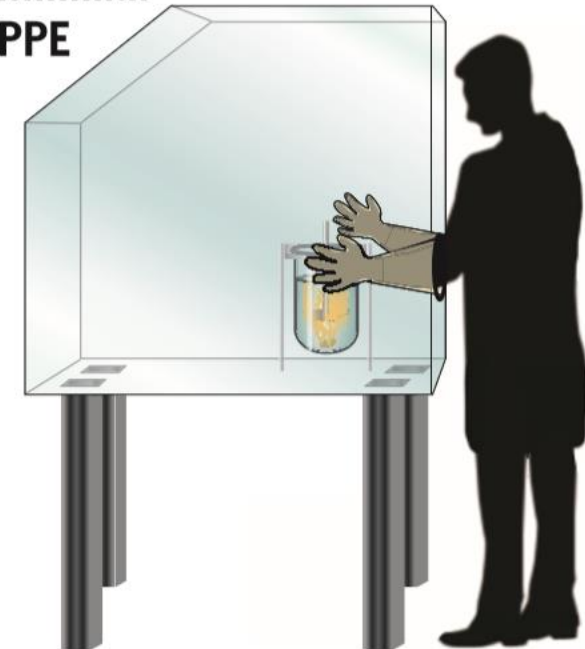
- Steroids and VEGF inhibitors



CONTAINMENT USING ISOLATOR

Isolated process using a negative pressure isolator

Minimal PPE



Fillers



Sterile Multidose Bottles



1. Restasis Multidose® is a registered trademarks of Allergan plc
2. Novelia® is a registered trademark of Nemera
3. Image courtesy of Aero Pump GmbH
4. Image courtesy of Aptar Pharma

Case Study

Eyenovia Optejet™,
novel microtherapeutic
technology designed for
optimal drug delivery¹

- Piezo-print micro dosing to increase precision and reduce waste
- Approximately 80% less drug, less exposure to preservatives
- Can eliminate drug overflow for a more comfortable patient experience
- Non-protruding nozzle for no-touch spray application which can potentially minimize the risk of cross contamination seen with traditional eye dropper bottles



Vials and Pre-Filled Syringes



Conclusion

- Most important consideration = the patient
- Industry increasingly moving towards the complex
- Ocular products have unique considerations
 - Anatomy of the eye & API (bioavailability, solubility, stability)
 - Sterility and patient compliance
- Don't be discouraged! Success is possible and rewarding with the right partner



Concept to Commercialization.

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Questions...