Ocular drug delivery: Fundamentals, challenges, and technologies

Organizers
Ash Jayagopal, PhD, Kodiak Sciences Inc. and Uday Kompella, PhD, University of Colorado, Anschutz Medical Campus

Description
How are therapeutics delivered for eye diseases? What are the fundamental principles that one must understand to successfully design ophthalmic drugs for ocular diseases? What ocular and other tissue anatomical barriers are relevant to drug targeting and delivery? What key drug delivery technologies are available for anterior and posterior segment now and in the future? What regulatory considerations must be made when evaluating drug delivery devices and formulations for approval? How can modeling and simulation strategies approximate drug distribution and clearance, to enable improved drug design, predict preclinical or clinical outcomes, and reduce reliance on animal models?

This course provides answers to these questions and will instruct attendees on how to apply key concepts in drug delivery toward their own research.

Learning objectives
After attending this course, participants will be able to:

- Identify significant ocular tissue barriers for drug delivery and clearance in the eye
- Develop competency in comparing ocular drug delivery systems and formulations to propose optimal strategies for delivery of small molecules and macromolecules including oligonucleotides, gene therapies, and protein drugs
- Describe the regulatory process for approval of drug delivery devices and formulations
- Identify and apply state-of-the-art platform technologies for ocular drug delivery in anterior and posterior segment diseases, including those based on polymer, lipid, implant, and nanoparticulate technologies

Agenda
Presenters and presentations may change.

8 – 8:20am  Introduction and history of ophthalmic product development
Sesha Neervannan, PhD, Pharmaceutical Development, Allergan, Irvine, CA

8:20 – 8:45am  Overview of fundamentals of ocular drug delivery
Uday B. Kompella, PhD, FARVO, Professor, University of Colorado, Anschutz Medical Campus, Aurora, CO
This presentation will provide an overview of the fundamentals determining the selection and development of various types of drug molecules, routes of administration, and delivery systems for treating eye diseases. Special emphasis will be placed on the rate limiting biological factors for ocular drug delivery and how they can be overcome, at least in part, by using conventional and novel delivery systems.

8:45 – 9:10am  Ocular Drug Delivery Technologies: A Clinical Perspective
Diana V. Do, MD, Professor of Ophthalmology, Stanford University School of Medicine, Palo Alto, CA
9:10 – 9:35am  
**Potentials and Pitfalls of Animal Models**

*John S. Penn, PhD, FARVO, Snyder Professor & Vice Chairman, Vanderbilt University School of Medicine, Nashville, TN*

The goal of this presentation is to describe common rodent models of eye disease, with an emphasis on diseases of the retinal and choroidal vasculatures. The focus of the presentation will be on the pitfalls associated with certain experimental eye disease models, how they work, their clinical relevance, and what they can and cannot tell us about the pathogenesis of human eye diseases. Specific models to be discussed include oxygen-induced retinopathy (OIR), laser-induced choroidal neovascularization (LCNV), diabetic retinopathy, retinal vein occlusion, ischemia reperfusion injury. Brief mention will made of models of glaucoma and inherited retinal dystrophies.

9:35 – 9:50am  
**Morning Break**

9:50 – 10:15am  
**Pharmacokinetics and modeling of drug delivery to the anterior segment**

*Micheal B. Bolger, PhD, Chief Scientist, Simulations Plus, Inc., Lancaster, CA*

10:15 – 10:40am  
**Pharmacokinetics and modeling of drug delivery to the back of the eye**

*Arto Urtti, PhD, Professor, Centre for Drug Research, University of Helsinki, Helsinki, Finland*

The lecture will describe the main factors in the posterior eye segment pharmacokinetics, test models, their clinical relevance and modeling approaches for generalized understanding of the processes.

10:40 – 11:05am  
**Eye drop formulations for drug delivery**

*Clive G. Wilson, PhD, J.P. Todd Professor of Pharmaceutics, University of Strathclyde, Glasgow, Scotland, UK*

11:05 – 11:30am  
**Ocular Suspension and Nanosuspension Products: Formulation Development, scale up and manufacturing Considerations**

*Onkar N. Singh, PhD, MBA, Director, Pharmaceutical Development, CONRAD, Eastern Virginia Medical School (EVMS), Norfolk, VA*

Drug delivery to the ocular diseases requires strategic approaches due to the existence of several anatomical/static and physiological/dynamic barriers. Several ophthalmic conventional topical formulations are designed as solutions, suspensions, nanosuspension, ointments or emulsions to achieve an effective drug dose to the ocular tissues. In addition, various novel nanoformulation-based delivery systems have been explored through various routes of administration and showed promising results. I will also present how the various routes of ocular administrations play a key role in designing and developing a suspension formulation and other drug delivery systems. The considerations in formulation development of suspension dosage forms will be presented to facilitate the development of
safe, stable, and efficacious drug products meeting ideal target product profile (TPP). Stability studies per ICH guidelines will be summarized. I will also touch upon process scale up and manufacturing of a sterile ocular suspension products.

11:30 – 12:30pm  Lunch

12:30 – 12:55pm  Emulsions for drug delivery to the eye
Frederic Lallemand, PhD, Novagali Pharma, Evry, France
This presentation will firstly present a brief state of the art on the use of emulsions in ophthalmology either as artificial tears for the relief of dry eye or as vehicle for active molecules. We will review the main physicochemical and thermodynamic parameters driving the stability and efficacy of the emulsions after topical application. Manufacturing processes will be examined and discussed with their pros and cons as well as sterilization processes. A good physicochemical characterization is key in understanding the emulsion and appropriate in vivo model should be chosen. The course will be concluded by listing the gaps to be filled to better understand the behavior of emulsions after ocular administration. During the talk, reference to regulatory standards will be done to ensure that emulsion developments are done according to ICH, FDA and EMA requirements.

12:55 – 1:20pm  Slow release drug products for ocular delivery
Susan S. Lee, PhD, Director, Clinical Development, Allergan, Inc., Irvine, CA

1:20 – 1:45pm  Nanoparticles and microparticles for ophthalmic drug delivery
Rocio Herrero-Vanrell, PhD, Professor, Complutense University, Madrid, Spain
Nanoparticles and microparticles are intended to provide controlled delivery of therapeutic agents. For ophthalmic purposes they can be administered by topical, intraocular or periocular routes. Depending on the biomaterial used for their preparation, particles can be biodegradable or non bioerodible. The right choice of the appropriate drug delivery system depends on the ophthalmic disease, route of administration and the site of action. There are several methods to fabricate nanoparticles and microparticles. Once prepared they are characterized in terms of size, morphology, encapsulation efficiency and release profile.

1:45 – 2:00pm  Afternoon break

2:00 – 2:25pm  Hydrogels and novel materials for ocular delivery
Hu Yang, PhD, Professor, Virginia Commonwealth University, Glen Allen, VA
Challenges to ocular drug delivery come from the physiological barriers of the eye. Hydrogels have been widely explored to address the medication challenges of the ocular environment. In this workshop, I will review the latest hydrogel formulations and their associated chemistries for use in ocular therapies, spanning from external anterior to internal posterior regions of the eye in order to evaluate the state of recent research. I will discuss the utility of hydrogels in soft contact lens, wound dressings, intraocular lens, vitreous substitutes, vitreous drug release hydrogels, and cell-based therapies for regeneration. Additional focus is placed on the pre-formulation, formulation considerations of the hydrogels as well as new materials based on individual components (polymer chains, linkers, and therapeutics).
2:25 – 2:50pm  Targeted Drug Delivery Systems  
Ashwath Jayagopal, PhD, Executive Director, Discovery Medicine, Kodiak Sciences Inc., Palo Alto, CA

2:50 – 3:15pm  Regulatory Considerations for Drugs and Devices (FDA/EMA)  
Speaker request pending

3:15 – 3:45pm  Q&A: Panel Discussion: Focus on anterior segment

3:45 – 4:15pm  Q&A: Panel Discussion: Focus on posterior segment

4:15 – 4:30pm  Wrap and key takeaways  
Ash Jayagopal, PhD, and Uday Kompella, PhD