Generic drugs and their role in bringing next generation products: An FDA perspective

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Disclaimer

- The opinions and conclusions expressed in this forum are the viewpoints of the speaker(s) and do not necessarily reflect the official position of the U.S. Food and Drug Administration.

Generic Drugs:

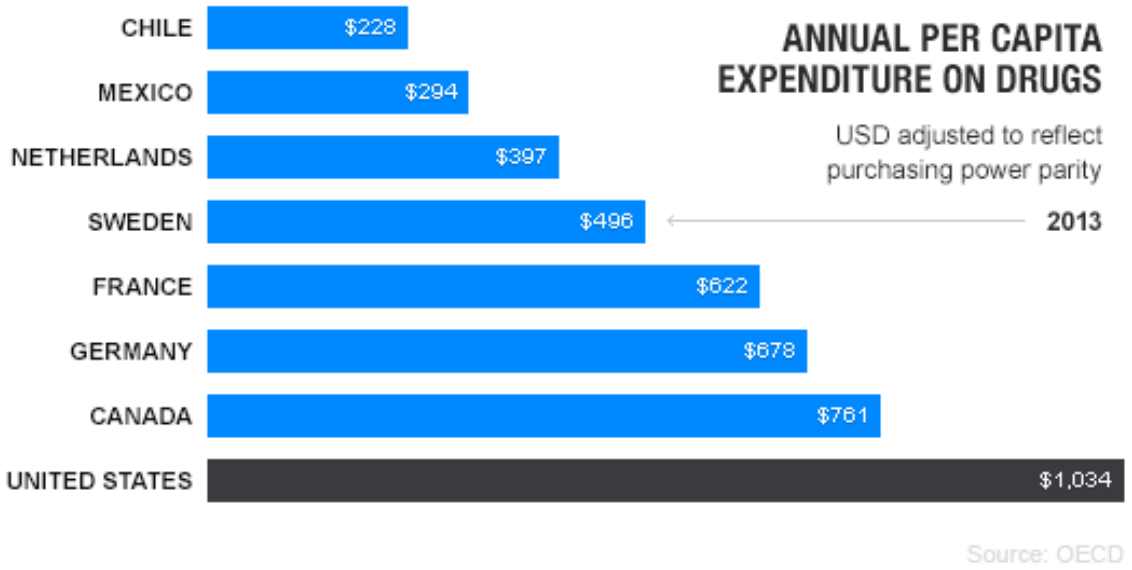
- Are duplicates of brand-name drugs
- Are the same as those brand-name drugs in active ingredients, dosage form, strength, route of administration, quality, performance characteristics, safety, efficacy, and intended use

From FDA website – Understanding Generic Drugs

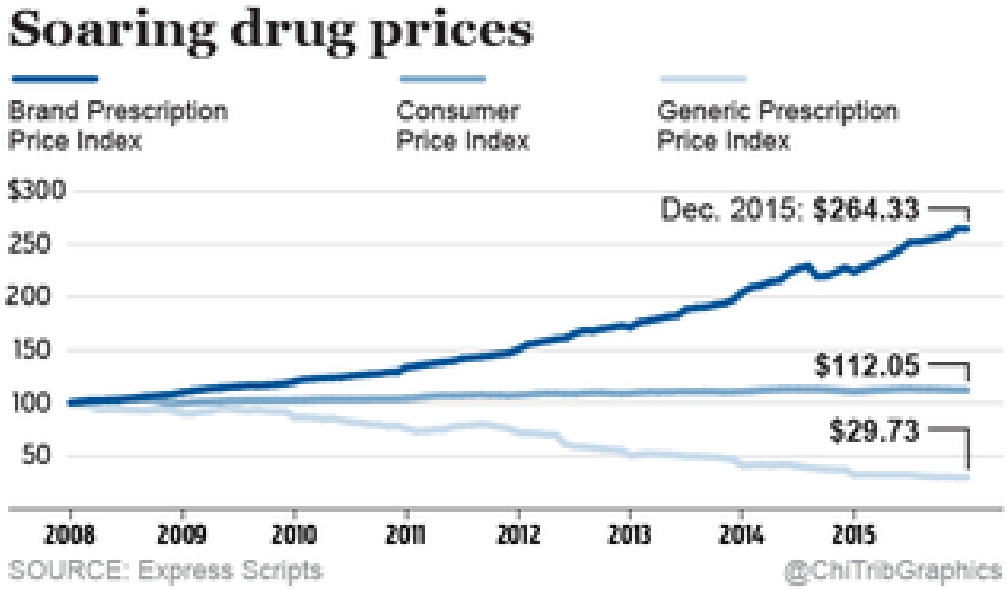
https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/default.htm

Generic Drugs

- Each ANDA (Abbreviated New Drug Application) relies on a reference listed drug (RLD)
- Generic drugs mostly cost less to develop because applicants do not repeat the safety and efficacy studies used to approve the RLD.

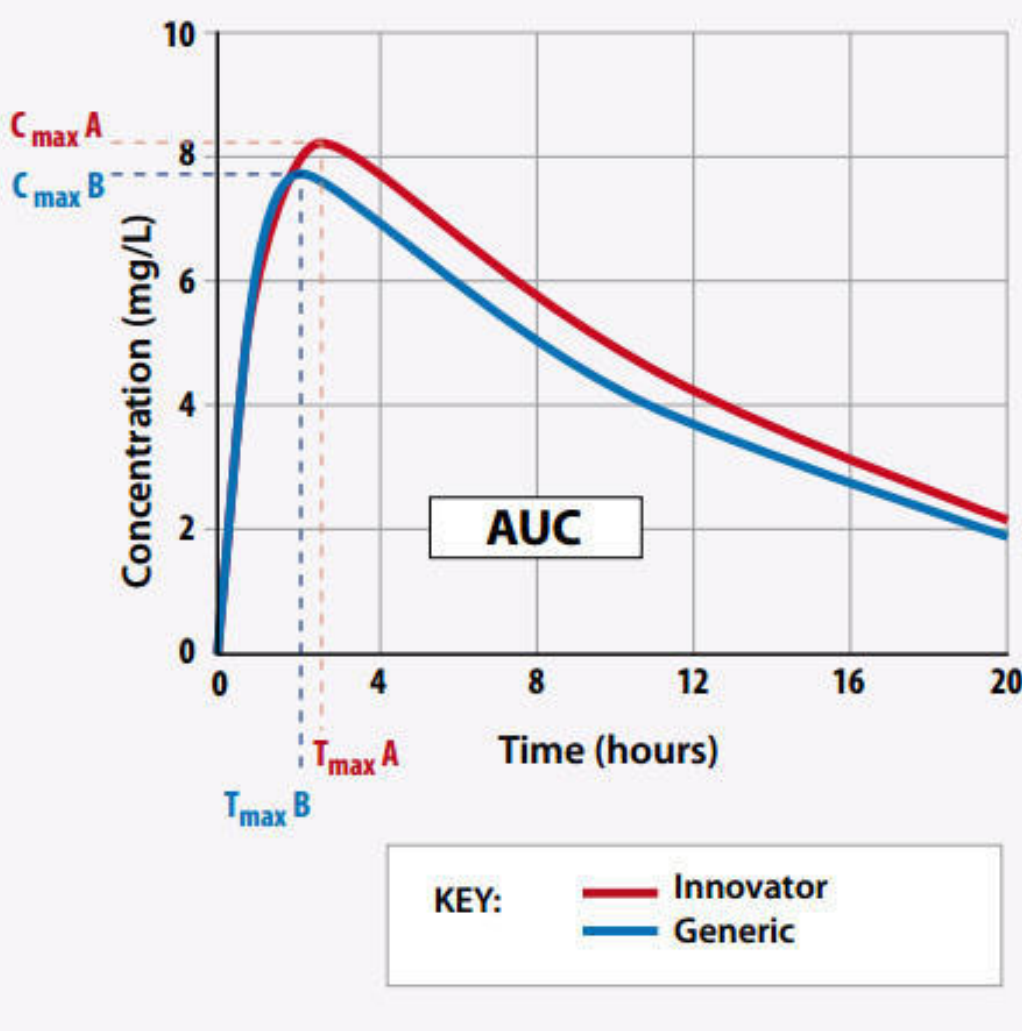


Fortune, 2015



Chicago Tribune, 2016

Bioequivalence Determinations



- For products with systemic site of action, BE via systemic PK endpoints (e.g. C_{max} and AUC) helps infer comparable safety and efficacy
- For products that are locally acting, it is more difficult to assess local exposure
- The site of action may not be directly correlated with systemic PK

Generic Competition for Ophthalmologics

Dosage Form (2016 sales)	Number of marketed Reference products	% products that have a generic	% products that have more than 3 generics
Solutions ($3.9B)	~79	60%	40%
Suspension ($1.2B)	~20	10%❖	0%
Emulsion ($2.0B)	2	0	0
Ointment ($400M)	21	24%	10%

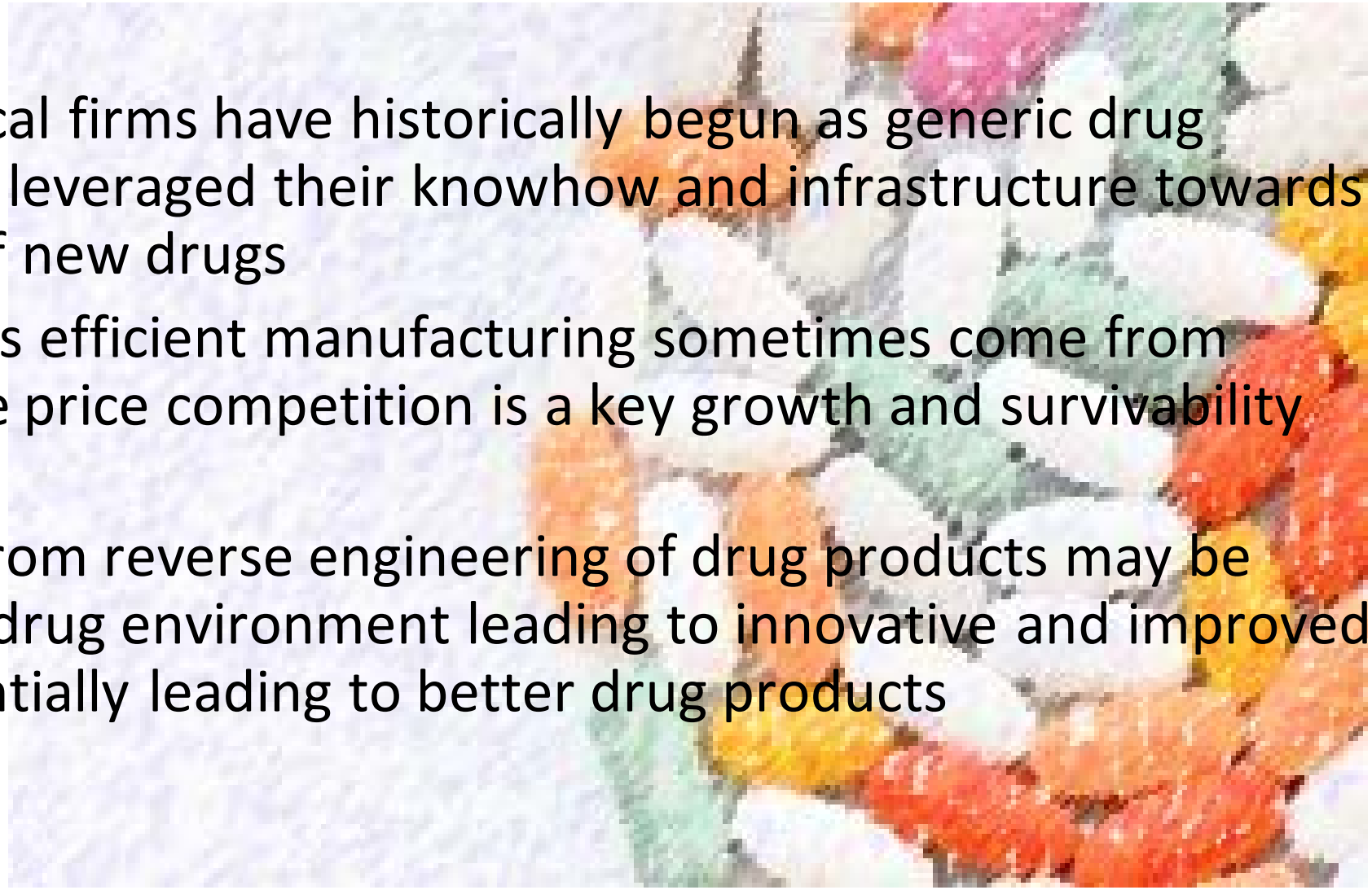
❖All were approved pre-2000, most in the 1980's

Complex Generic Products in GDUFA II

- Complex active ingredients
  - Complex mixtures of APIs, polymeric compounds, peptides
- Complex formulations
  - Liposomes, suspensions, emulsions, gels
- Complex routes of delivery
  - Locally acting such as dermatological and inhalational drugs
- Complex dosage forms
  - Long acting injectables, implantable drugs
- Complex drug-device combination products
  - Transdermals, metered dose inhalers (MDIs)
- Other products where complexity or uncertainty concerning the approval pathway or other alternative approach would benefit from early scientific engagement

https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf

Generic Drug Industry as a Teaching Lab

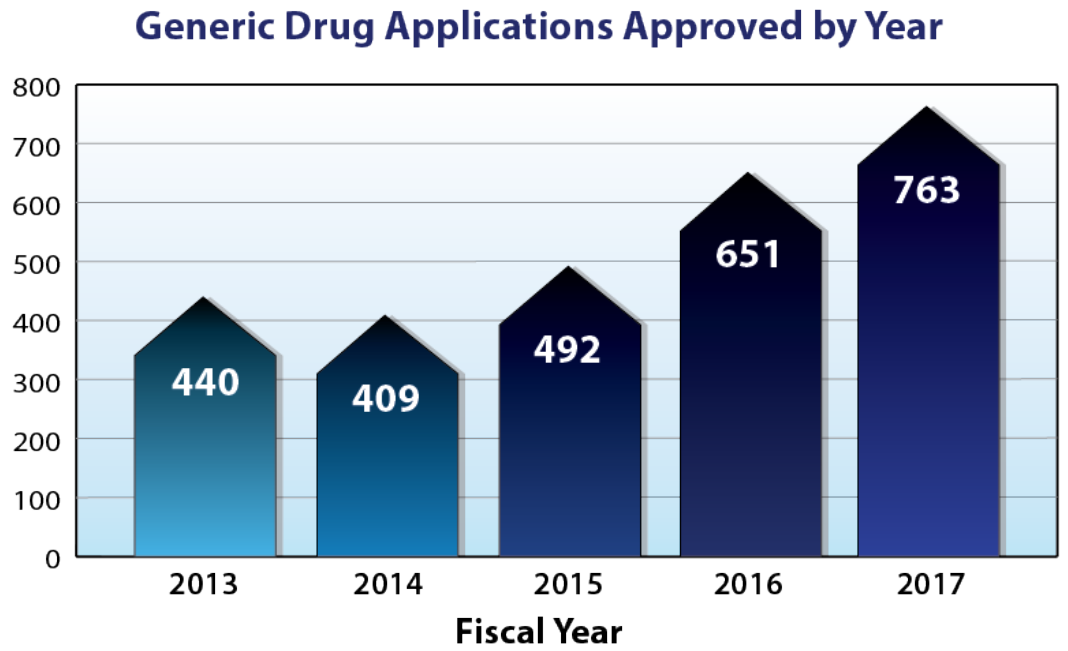


- Some pharmaceutical firms have historically begun as generic drug manufacturers, but leveraged their knowhow and infrastructure towards the development of new drugs
- Innovations towards efficient manufacturing sometimes come from generic firms where price competition is a key growth and survivability driver
- Lessons and tools from reverse engineering of drug products may be applied in the new drug environment leading to innovative and improved formulations, potentially leading to better drug products

GDUFA Regulatory Science

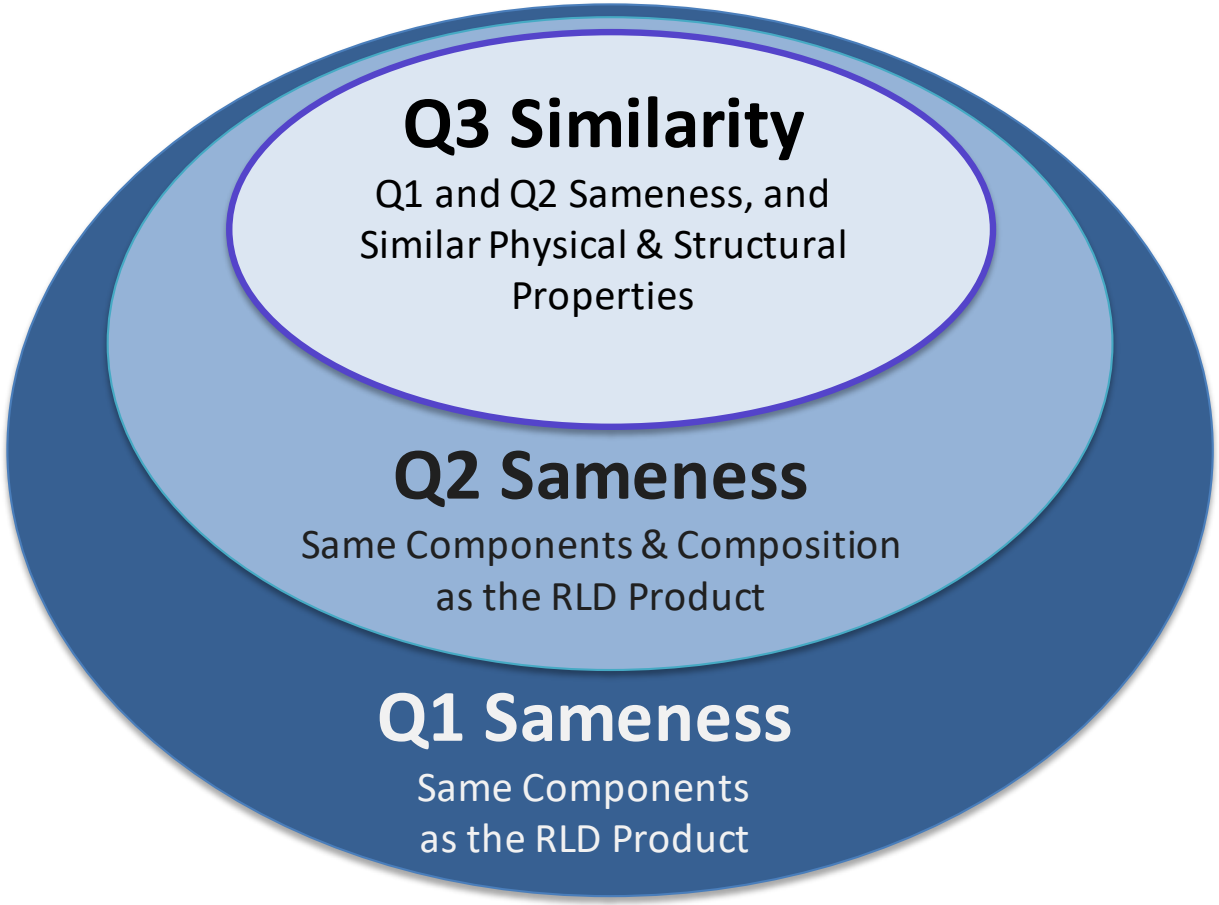
- FDA has been playing a more active role in performing and funding research to advance drug science
- This provides new tools for FDA and industry to evaluate generic drug equivalence, to enable more efficient development of generic drugs and thus improve access
- ~$30 million per year for stakeholder-driven generic drug regulatory science
  - Goal: Access to generics in all product categories
  - 90+ on-going projects
  - Recent focus on complex drug products

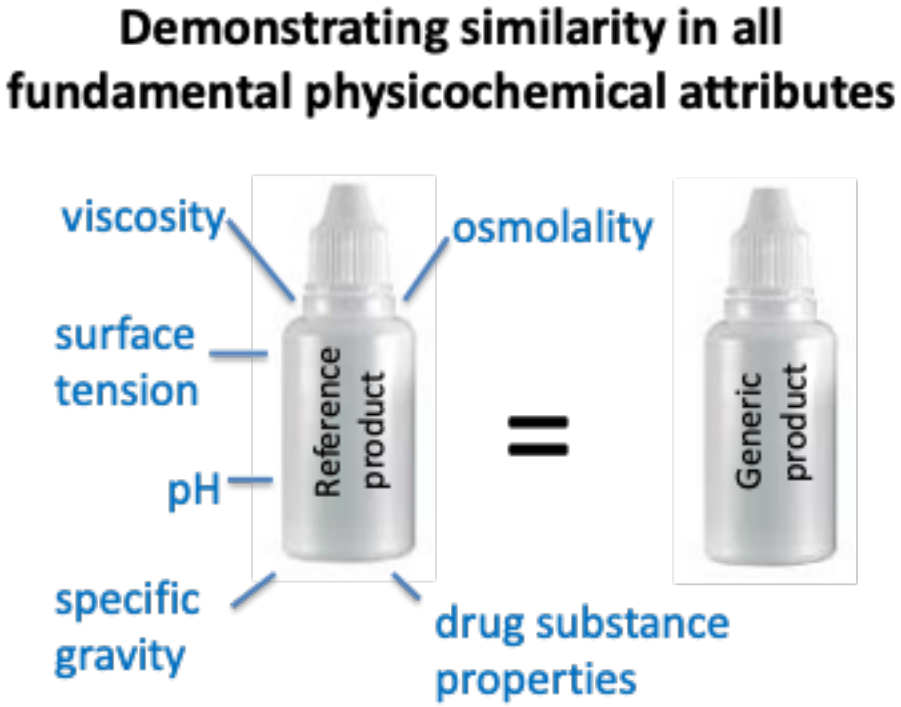
Generic Drug Science & Research Website:
https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm



Topical Formulation Quality Concepts

- What are Q1, Q2, and Q3?





Product Specific Guidances Intended to Assist Generic Drug Development

Drug	Dosage form	Indication Category	PSG posting
Alrex®	loteprednol etabonate suspension 0.2%	**Allergy:** relief of symptoms of seasonal allergic conjunctivitis	Q4 (Nov) 2017
Lotemax®	loteprednol etabonate suspension 0.3%	**Steroid:** treatment of inflammatory conditions of conjunctiva, cornea and anterior segment	Q1 (Feb) 2018
Lotemax®	loteprednol etabonate ointment 0.5%	**Steroid**: treatment of inflammatory conditions of conjunctiva, cornea and anterior segment	Q1 (Feb) 2018
Besivance®	besifloxacin suspension EQ 0.6% Base	**Anti-infective:** Antibiotic- anterior segment bacterial infections	Q2 (May) 2018
Natacyn®	Natamycin suspension 5%	**Anti-infective:** Antifungal -Fungal keratitis	Q2 (May) 2018
FML®	Fluorometholone ointment 0.1%	**Steroid:** treatment of inflammatory conditions of conjunctiva, cornea and anterior segment	Q3 (Aug) 2018
FML®	Fluorometholone suspension 0.1%	**Steroid:** treatment of inflammatory conditions of conjunctiva, cornea and anterior segment	Q3 (Aug) 2018

Future Directions

- Non-invasive methods to determine drug concentrations
- Studies to better understand and measure the characteristics of complex formulation.
- Impact of formulation physicochemical attributes on
  - drug pharmacokinetics at the site of action
  - product use and other patient-centric issues
- Develop Physiologically Based Pharmaco-Kinetic ~~(PBPK)~~ models to facilitate in vitro approaches for establishing BE.
- Economics of niche drug products in the context of competition, pricing, and accessibility

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Questions?


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