Beyond the API:
Role of Formulation in Topical Product Development

Society of Investigational Dermatology

From Laboratory Tools to Product Approval

Priyanka Ghosh, PhD

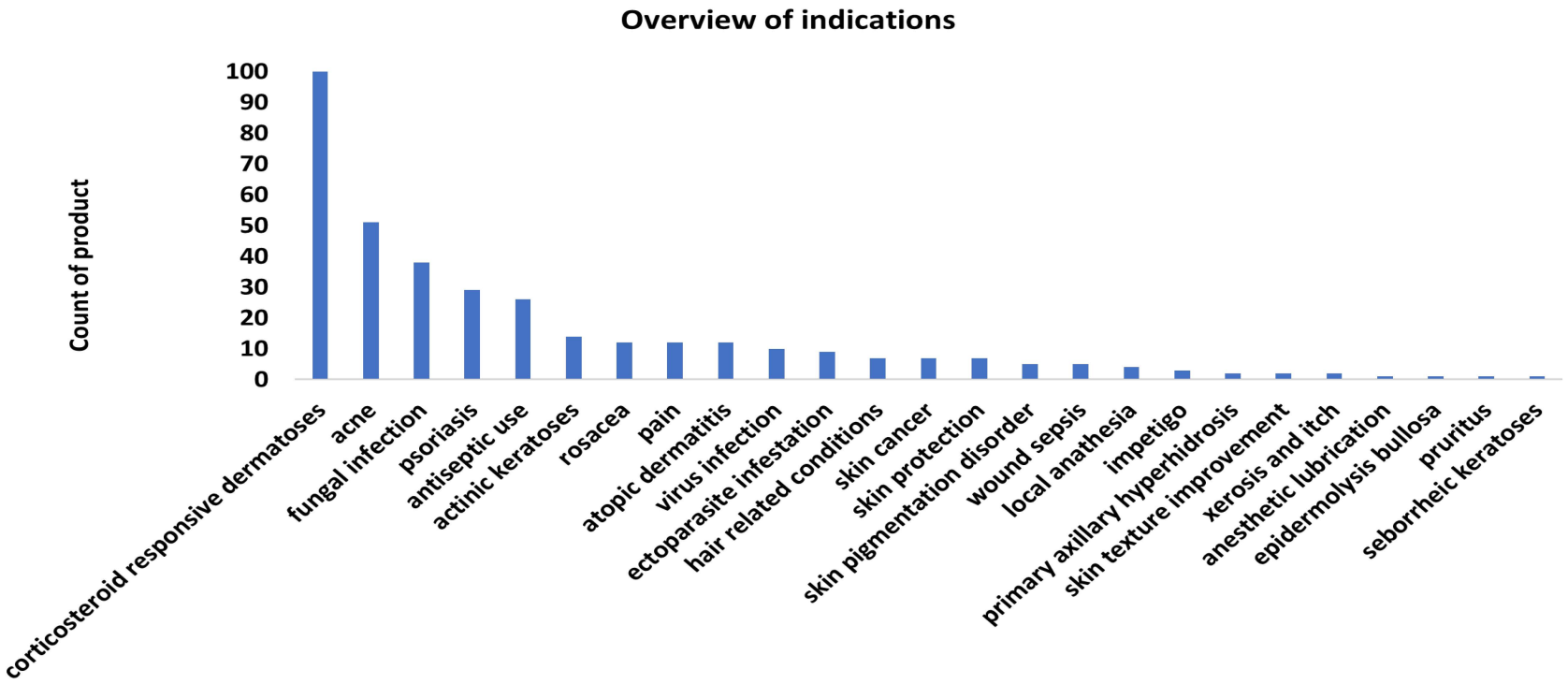
Lead Pharmacologist

Office of Research and Standards

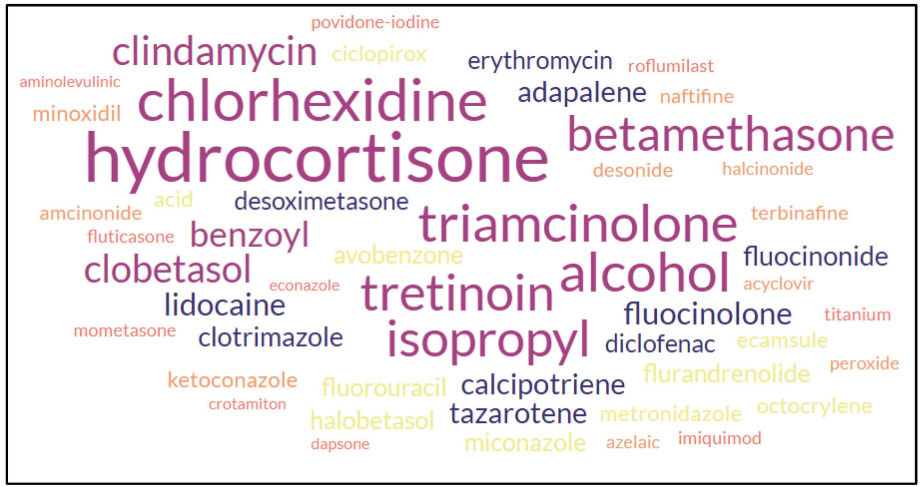
Office of Generic Drugs| CDER | U.S. FDA

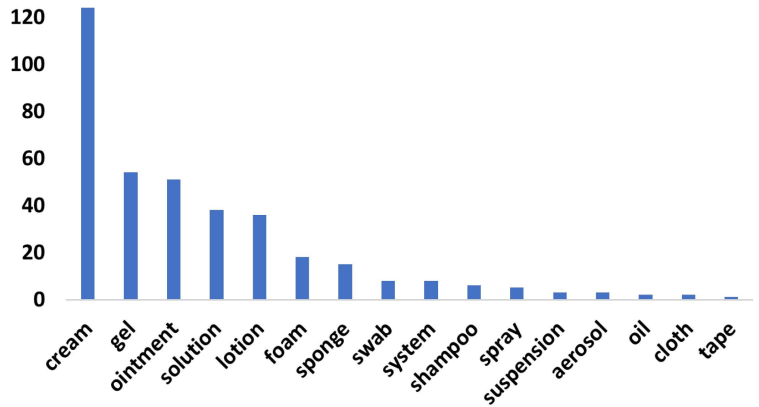
May 10, 2025

Approved Products Indications



Approved APIs and Dosage Forms

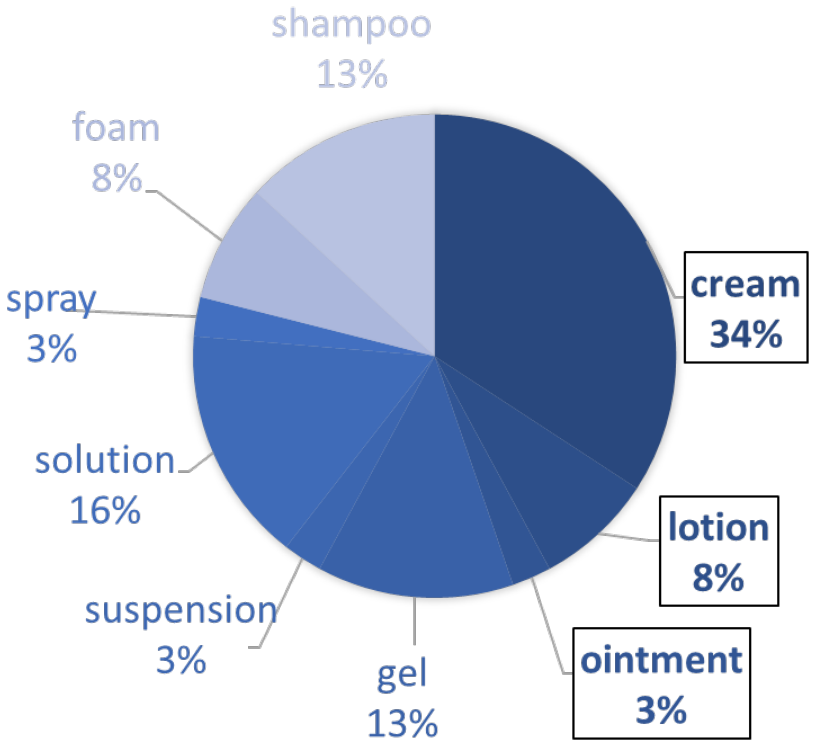




Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"), API- Active Pharmaceutical Ingredient

Role of Formulation

FUNGAL INFECTION



Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"), API- Active Pharmaceutical Ingredient

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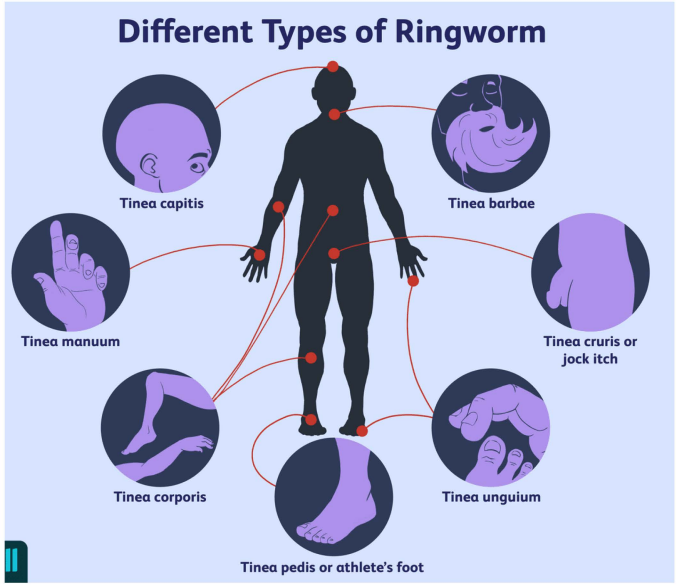

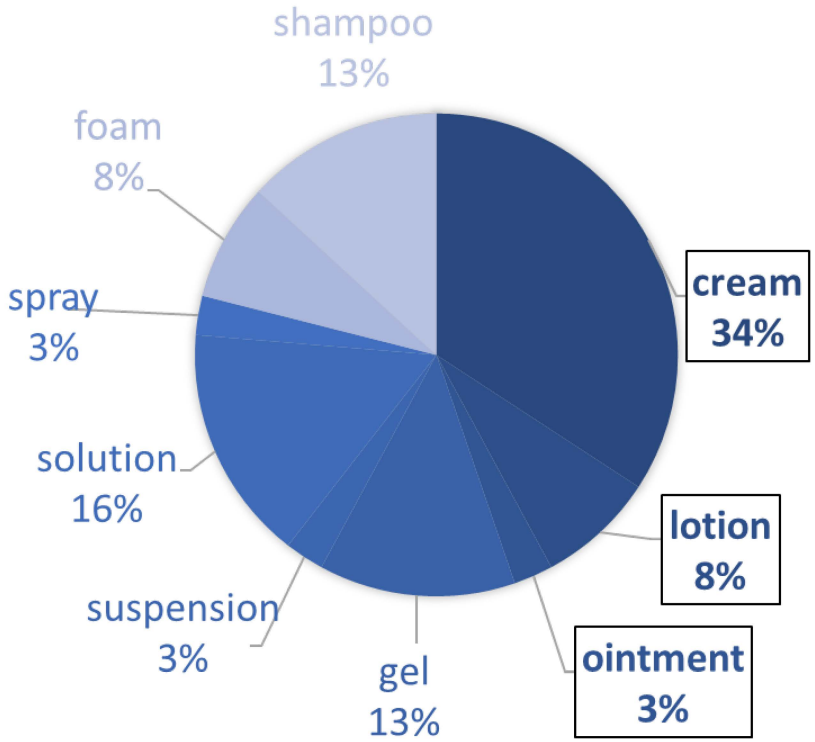

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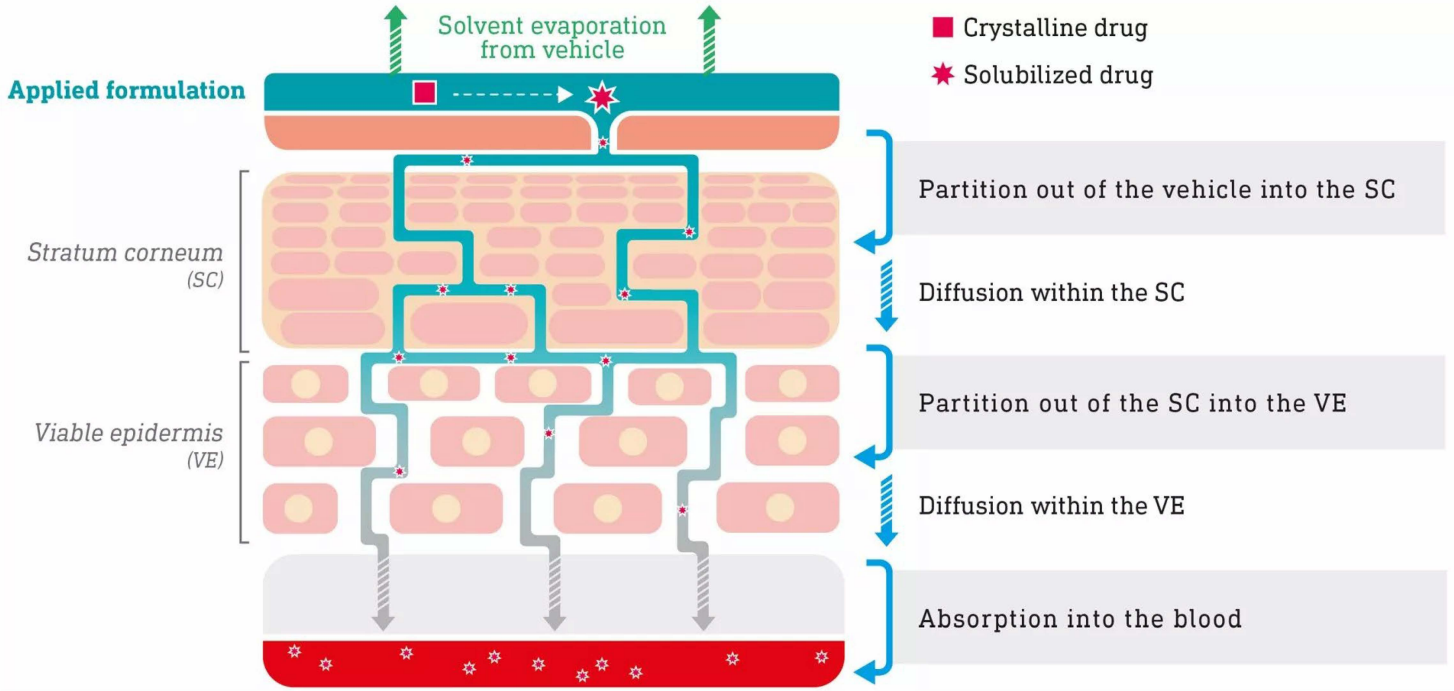
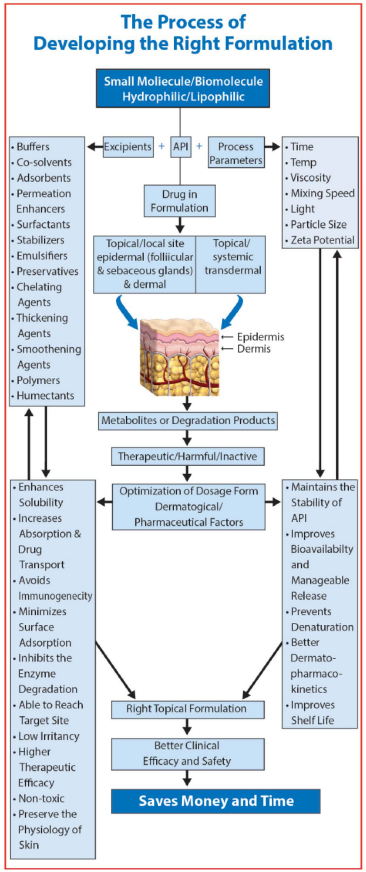
Formulation & Bioavailability



https://www.gattefosse.com/formulation-technologies/solubilizing-drugs-skin-delivery-decisive-step

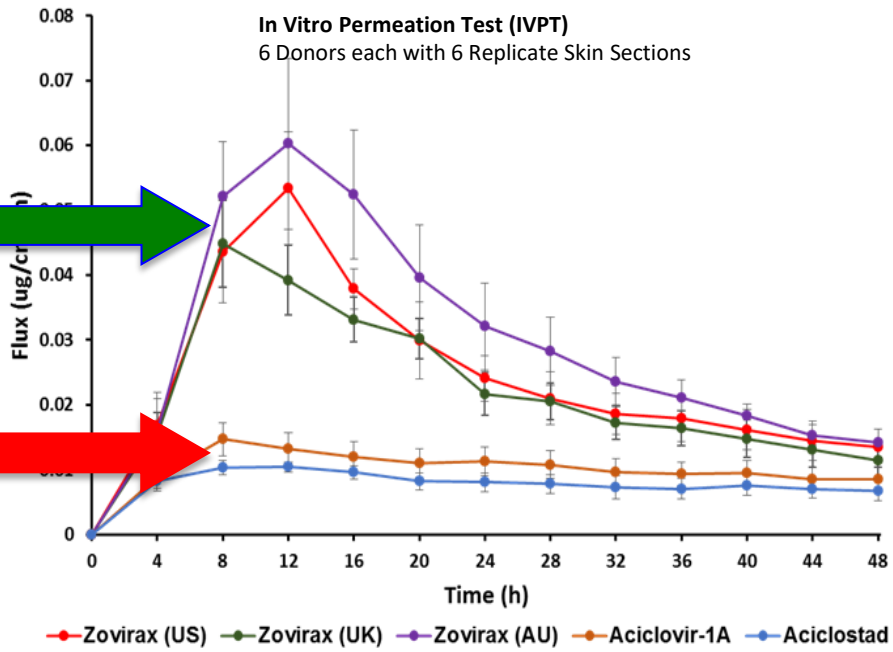
Formulation & Bioavailability



https://drug-dev.com/topical-delivery-the-importance-of-the-right-formulation-in-topical-drug-development/

Formulation & Bioavailability

	Zovirax (USA)	Zovirax (UK)	Zovirax (Austria)	Aciclostad (Austria)	Aciclovir-1A (Austria)
	Water	Water	Purified water	Water	Water
	Propylene glycol	Propylene glycol	Propylene glycol	Propylene glycol	Propylene glycol
	Mineral oil	Liquid Paraffin	Liquid Paraffin	Liquid Paraffin	Viscous Paraffin
	White petrolatum	White soft paraffin	White Vaseline	White Vaseline	White Vaseline
	Cetostearyl alcohol	Cetostearyl alcohol	Cetostearyl alcoh	Cetyl alcohol	Cetyl alcohol
	SLS	SLS	SLS		
	Poloxamer 407	Poloxamer 407	Poloxamer 407		
		Dimethicone 20	Dimethicone 20	Dimethicone	Dimethicone
		Arlacel 165	Glyceryl Mono Stearate	Glyceryl Mono Stearate	Glyceryl Mono Stearate
		Arlacel 165	Polyoxyethylene stearate	Macrogol Stearate	Polyoxyethylene stearate
Density (g/cc)	1.02	1.02	1.02	1.02	1.01
Content Uniformity (%)	97.9 ± 0.7	99.6 ± 1.4	100 ± 2.2	99.7 ± 1.7	98.3 ± 2.6
Polymorphic Form	2,3 hydrate	2,3 hydrate	2,3 hydrate	2,3 hydrate	2,3 hydrate
Crystilline Habit	Rectangular	Rectangular	Rectangular	Ovoid	Ovoid
Particle size (d50) (µm)	3.8	2.5	3.4	6.8	6
pH	7.74	7.96	7.54	4.58	6.05
Work of Adhesion	59	81	60	17	18
Drug in Aq (mg/g)	0.49	0.64	0.49	0.37	0.26
Drying Rate (T-30%)	>12h	~8h	~7h	<1h	<1h
Water Activity	0.75	0.73	0.74	0.95	0.95



Data provided courtesy of Dr. Narasimha Murthy associated with FDA funding for award U01FD005233

Correlation Between Q3 & Bioavailability

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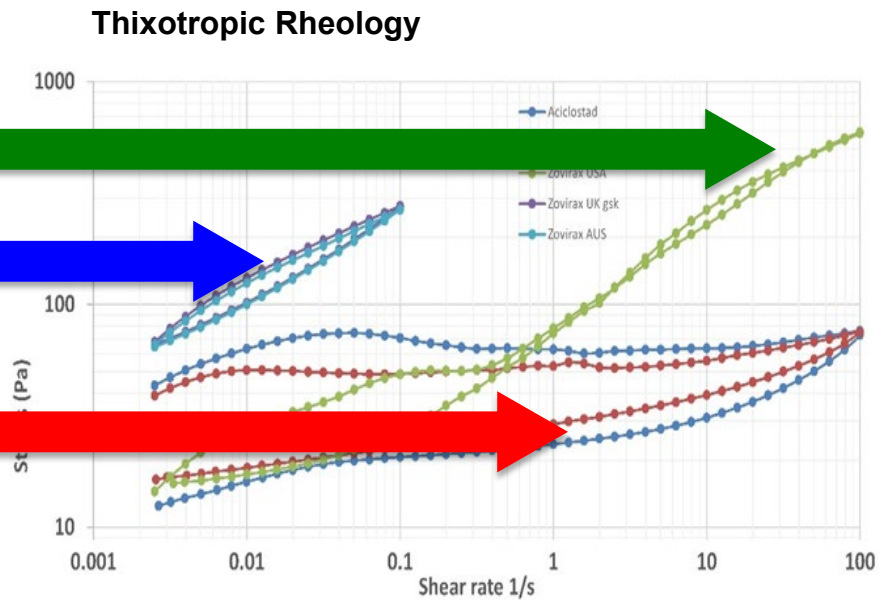

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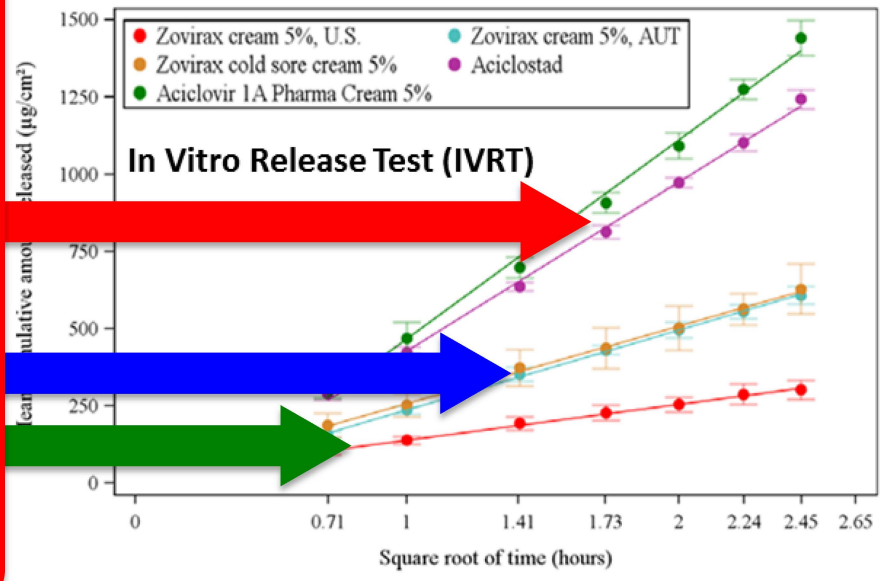

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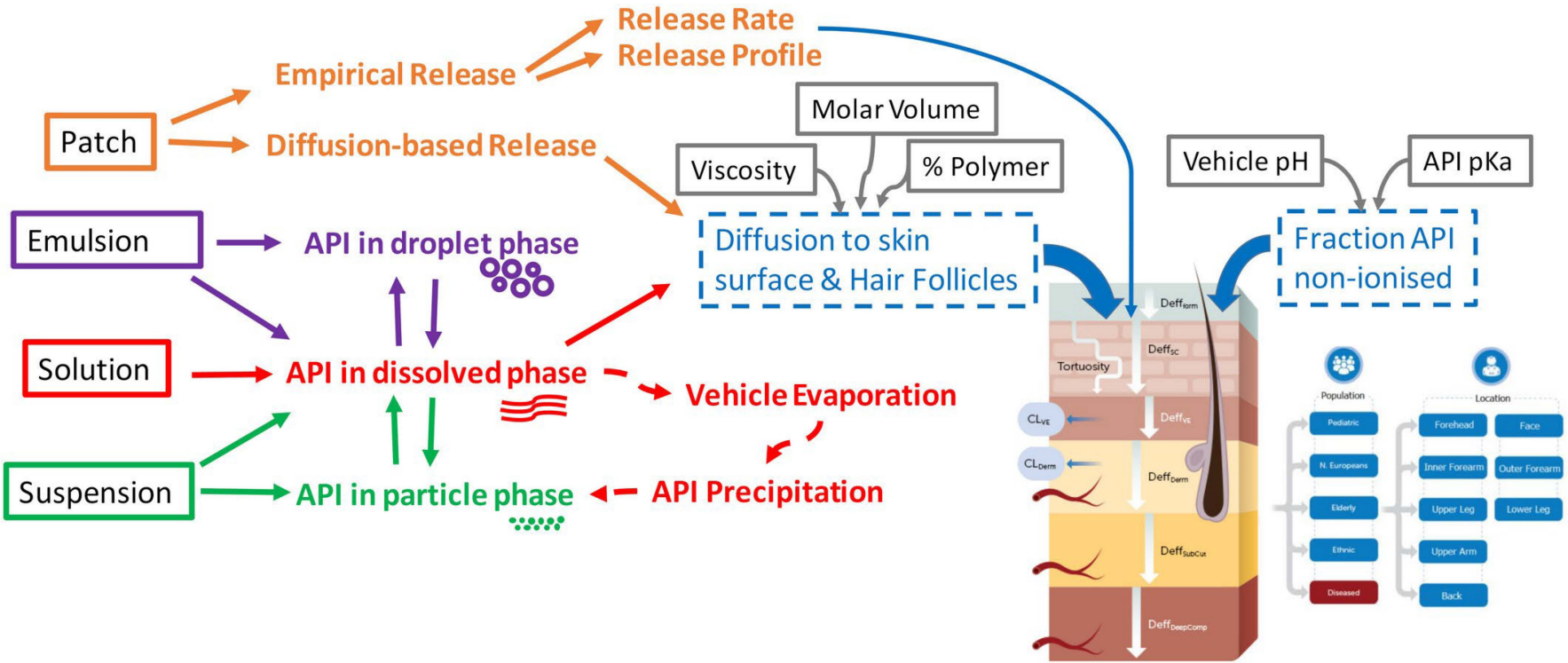
Modeling and Simulation Tools



Arora et al. Mol Pharm. 2022;19(9):3139-3152. doi:10.1021/acs.molpharmaceut.2c00229
Tsakalozou et al. CPT Pharmacometrics Syst Pharmacol. 2021;10(5):399-411. doi:10.1002/psp4.12600

Generic Drugs

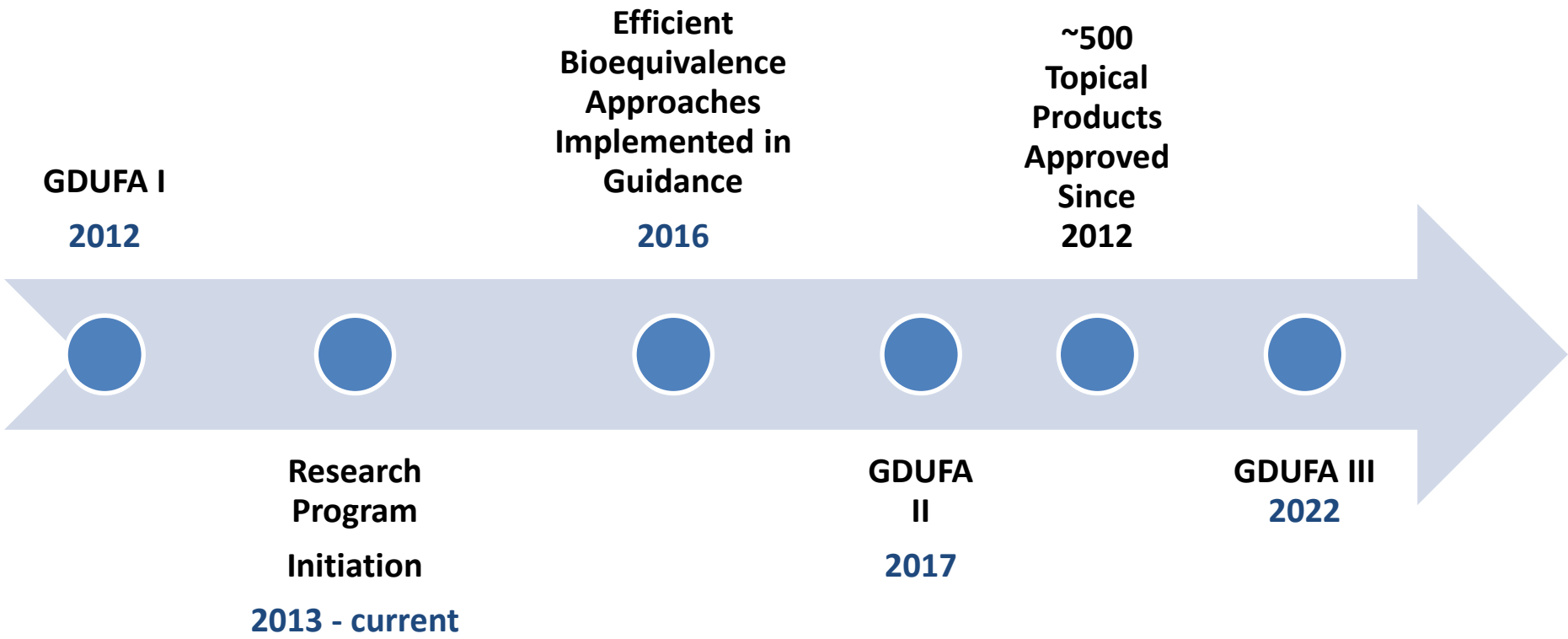
- Generic drug products use the same active ingredient(s) and can be expected to have the same clinical effect and safety profile when administered under conditions specified in the labeling, as the brand-name (reference) listed drug products
- Generic drug products can be substituted for the reference listed drug product
- ….And they can cost less money

https://www.fda.gov/drugs/generic-drugs/generic-drug-facts

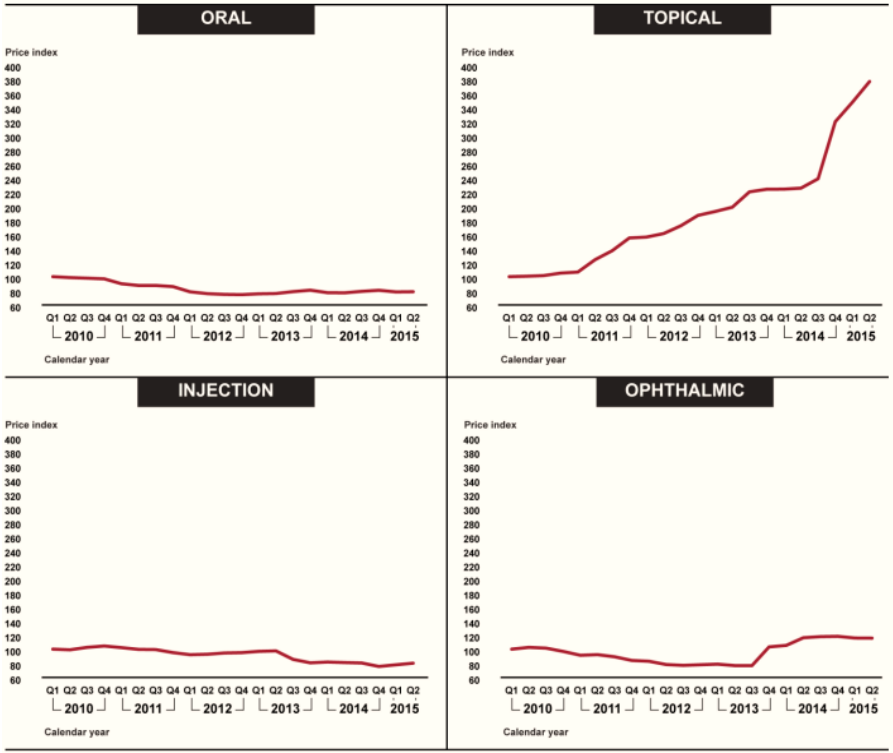
Formulation and Generic Drugs

- Most generic drugs may have differences in formulation compared to the reference listed drug
  - Pharmaceutical Equivalence
    - Same Active Ingredient
    - Same Dosage Form
    - Same Route of Administration
    - Same Dose
  - Bioequivalence
    - Rate and extent of bioavailability is the same

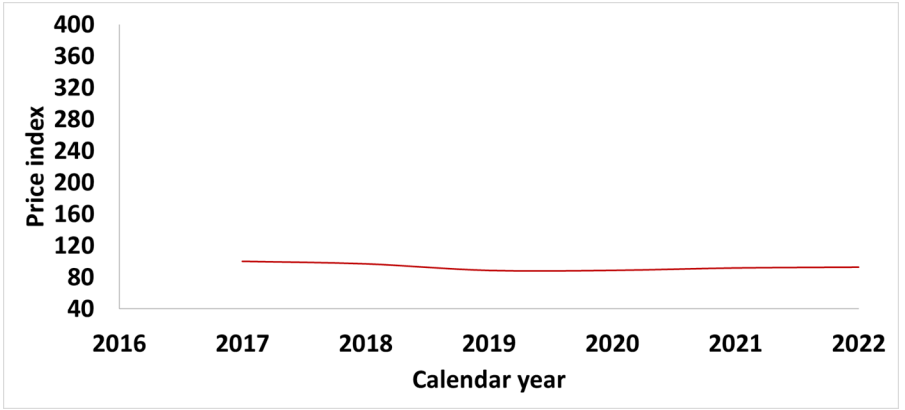
Timeline for the Program



Impact of Generic Product Availability



Data was collected from Medicare Part D database for 1441 generic drug products, including 117 topical drugs.



Data was collected from IQVIA. A chained Fisher Price index was constructed for the set of 17 topical generic product families between 2017 and 2022.

"Price Trends for Established Generic Drugs under Medicare Part D by Route of Administration, First Quarter 2010 through the Second Quarter of 2015" from 2016 GAO report.

Russo et al. Correlation between generic product approvals and price for drug products applied to the skin, AAD Annual Meeting, 2024

Summary

- Topical drug products are generally complex dosage forms
- Formulation plays a key role in topical product bioavailability
- A mechanistic understanding of the impact of formulation on drug product microstructure and bioavailability can facilitate topical product development
- The goal of the GDUFA regulatory science and research program is to facilitate research to enhance our understanding of how formulation influences microstructure and bioavailability
- Availability of tools within the scope of the program have contributed to the availability of more generic products on the market, and a corresponding decrease in price

Acknowledgements

U.S. Food & Drug Administration

- Sam Raney, PhD
- Tannaz Ramezanli, PharmD, PhD
- Ying Jiang, PhD
- Jackson Russo, PhD
- Megan Kelchen, PhD
- Eleftheria Tsakalozou, PhD
- Markham Luke, MD PhD
- Robert Lionberger, PhD

Research Collaborators

Collaborations within FDA

All of our collaborators within the GDUFA Regulatory Science and Research Program

U.S. FOOD & DRUG ADMINISTRATION

Thank You

Priyanka Ghosh, Ph.D.
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Office of Research and Standards (ORS), Office of Generic Drugs (OGD)
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