FDA Update: FDA and Dermatology DEIA

100th Annual AtlanticDerm Conference, Baltimore, MD

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CDER | U.S. FDA

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Disclaimer

This presentation reflects the views of the presenter and should not be construed to represent FDA's official views or policies.

FDA Centers

Most Relevant to Dermatology:

- **Center for Drug Evaluation and Research (CDER)**
  - Office of New Drugs (OND)
    - Division of Dermatology and Dental Drug Products
  - Office of Generic Drugs (OGD)
- **Center for Devices and Radiological Health (CDRH)**
- **Center for Biologics Evaluation and Research (CBER)**
- **Center for Food Science and Nutrition (CFSAN)**
  - Office of Cosmetics and Colors

Selected Dermatology Relevant 2022 New Drugs

Drug Name	Active Ingredient	Approval Date	FDA-Approved Use
NexoBrid	anacaulase	12/28/2022	To remove eschar in adults with deep partial thickness or full thickness thermal burns
Sotyktu	deucravacitinib	9/9/2022	To treat moderate-to-severe plaque psoriasis
Daxxify	daxibotulinumtoxinA	9/7/2022	To treat moderate-to-severe glabellar lines associated with corrugator and/or procerus muscle activity
Spevigo	spesolimab	9/1/2022	To treat generalized pustular psoriasis flares
Vtama	tapinarof	5/23/2022	To treat plaque psoriasis
Opdualag	nivolumab and relatlimab	3/18/2022	To treat unresectable or metastatic melanoma
Cibingo	abrocitinib	1/14/2022	To treat refractory moderate-to-severe atopic dermatitis

Diversity, Equity, Inclusion, Access

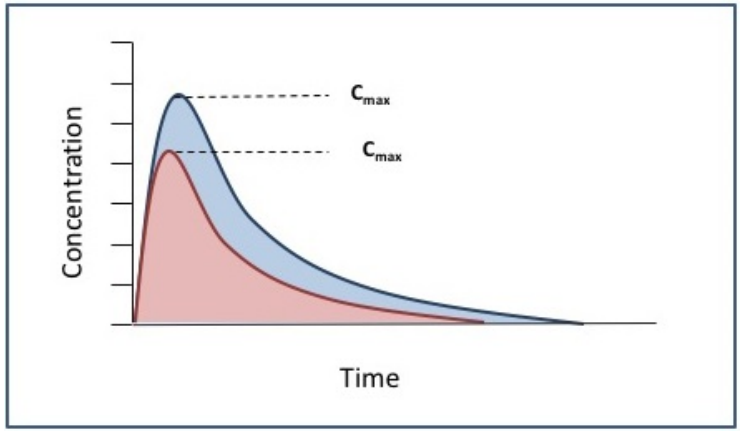
- Generic drugs epitomize a proposition for drug access, potentially providing better equity
- Examples of FDA's effort at understanding diversity and having an impact on product regulation
- Patient perspective and broadening enrolled study population are important to inclusion

The Promise of 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

How are Generic Drugs Approved?



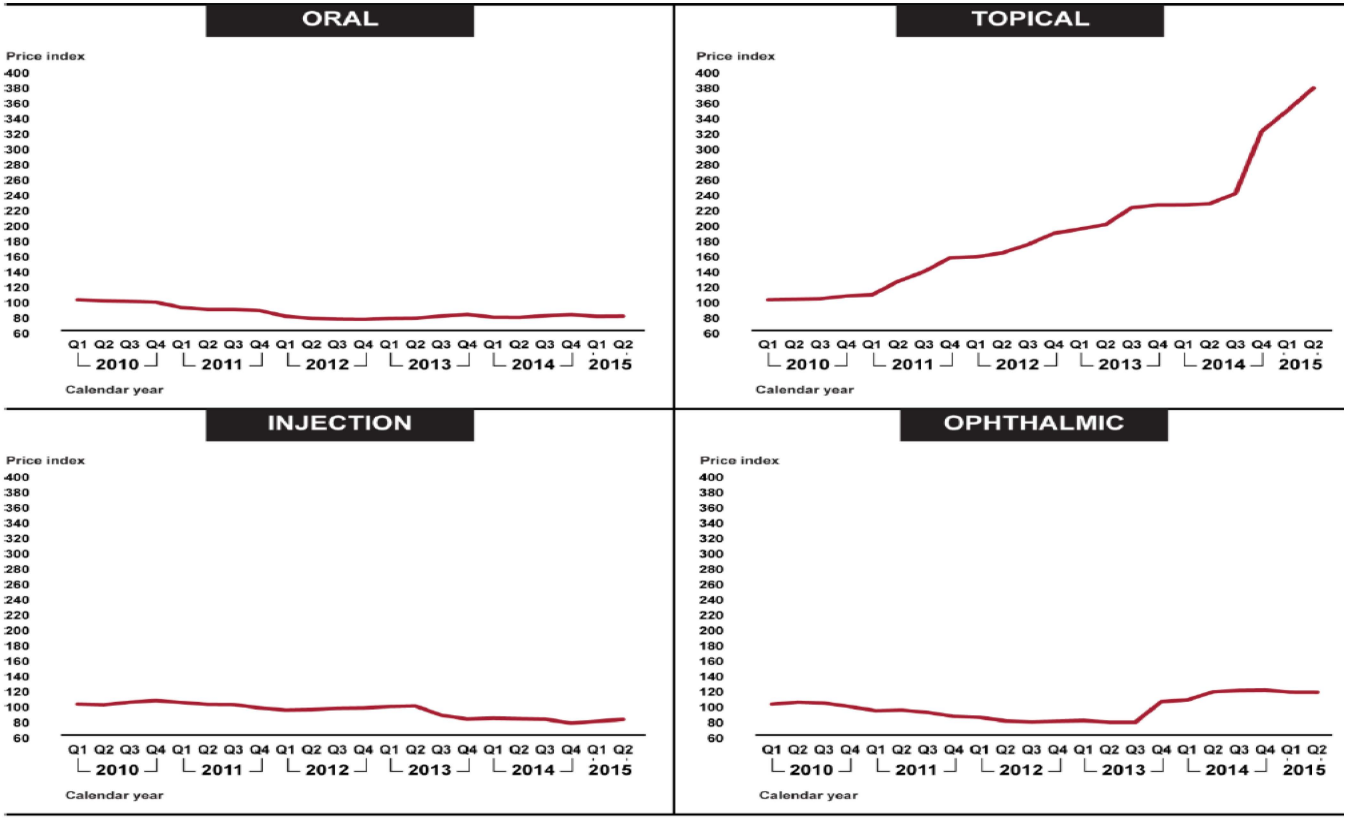
Bioavailability (BA) is assessed, and bioequivalence (BE) is typically established by showing that a generic drug product and the reference standard are similar in terms of their concentrations over time at the site of action (e.g., in the blood)

https://www.fda.gov/drugs/regulatory-science-action/impact-story-developing-new-ways-evaluate-bioequivalence-topical-drugs

The 2016 GAO Report

- The U.S. Government Accountability Office (GAO) Report (GAO-16-706; August 2016) had analyzed a period spanning Quarter 1 of 2010 through Quarter 2 of 2015
- **57%** of the topical drug products experienced an extraordinary price increase in that period
- The average price of topical generic drugs was **276% higher** by the end of the period analyzed
- Manufacturers and other stakeholders reported that market **competition**, influenced by various factors, drives generic drug prices

The GAO Report (GAO-16-706)



Source: GAO analysis of Medicare Part D prescription drug event data. | GAO-16-706

Retail Prices for Topical Products

Drug	Type	Price, US $ 2009	2011	2014	2015	Absolute Change, 2009-2015	% Change, 2009-2015
Altabax, 15 g	I	92.50	106.18	168.75	196.86	104.36	112.82
Benzaclin, 50 g	A	166.79	205.80	451.29	503.85	337.06	202.08
Carac cream, 30 g	N	159.40	227.16	2939.68	2864.70	2705.30	1697.18
Clobex spray, 4 oz	S	389.57	500.29	827.11	958.01	568.44	145.91
Cloderm cream, 30 g	S	96.47	132.92	220.75	360.02	263.55	273.19
Cutivate lotion 120 mL	S	305.00	493.92	918.63	1067.25	762.25	249.91
Derma-Smoothe FS oil, 4 oz	S	45.70	47.23	247.84	322.67	276.97	606.06
Finacea, 50 g	A	124.42	185.42	288.92	284.30	159.88	128.51
Olux-E foam, 100 g	S	307.58	382.79	750.79	841.76	534.18	173.67
Oracea, 40 mg (30 tablets)	A	439.01	416.09	632.80	702.46	263.45	60.01
Oxistat cream, 30 g	I	76.50	119.25	399.00	544.66	468.16	611.97
Oxsoralen-Ultra, 10 mg (50 capsules)	P	1227.32	2150.49	4568.54	5204.31	3976.99	324.04
Retin-A Micro, 0.1%, 50 g	A	178.05	335.73	791.47	914.52	736.47	413.64
Solaraze gel, 100 g	N	442.89	618.56	1738.91	1883.98	1441.09	325.38
Soriatane, 25 mg (30 capsules)	P	757.75	958.50	1452.50	1595.27	837.52	110.53
Taclonex, 60 g	P	465.99	522.58	848.21	962.90	496.91	106.64
Targretin gel, one 60-g tube	N	1686.78	1787.97	15 708.40	30 320.12	28 633.34	1697.51
Tazorac cream, 0.1%, 60 g	A	266.18	464.96	656.20	722.27	456.09	171.34
Xolegel, 30 g	I	212.50	278.00	389.25	641.96	429.46	202.10

Abbreviations: A, acne and rosacea; I, antiinfective; N, antineoplastic; P, psoriasis; S, corticosteroid.

Source: Miranda E. Rosenberg, BA and Steven P. Rosenberg, MD (2016) *Changes in Retail Prices of Prescription Dermatologic Drugs From 2009 to 2015*. JAMA Dermatology. 152(2):158-163. doi:10.1001/jamadermatol.2015.3897

Patient Access to Topical Products

- Most topical dermatological drug products had fewer than three generic competitors; for many products, no generics were available at all
- This may have been attributable to the historical challenges impacting the development of topical dermatological generic drug products, possibly including
  - Absence of efficient PK-based approaches by which to demonstrate BE
  - Inefficiency of high risk, costly, comparative clinical endpoint BE studies
  - The complex nature of topical formulations
- FDA had begun research to develop more efficient ways to demonstrate BE for complex generics, including topicals

GDUFA

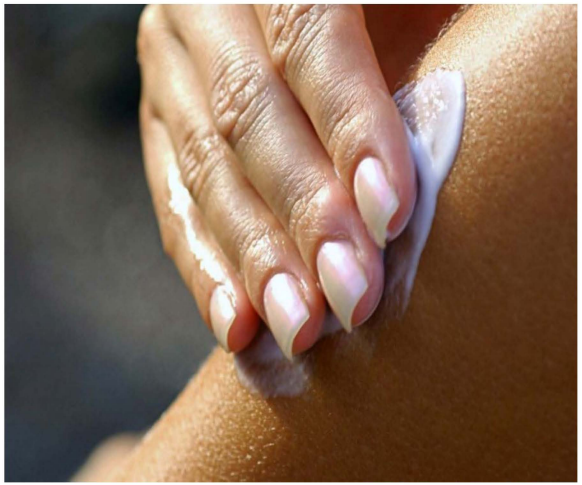
- The Generic Drug User Fee Amendments (GDUFA) was signed into law in July 2012, as part of the Food and Drug Administration Safety and Innovation Act (FDASIA)
- One out of numerous User Fee Programs that help the FDA to fulfill its mission of protecting the public health and accelerating innovation in the industry
- GDUFA is designed to speed the delivery of safe and effective generic drugs to the public and improve upon the predictability of the review process
- One unique feature of GDUFA is the Regulatory Science and Research Program ~ $20 million annually
- GDUFA must be reauthorized every 5 years (currently in GDUFA III)

https://www.fda.gov/industry/fda-user-fee-programs
https://www.fda.gov/industry/fda-user-fee-programs/generic-drug-user-fee-amendments

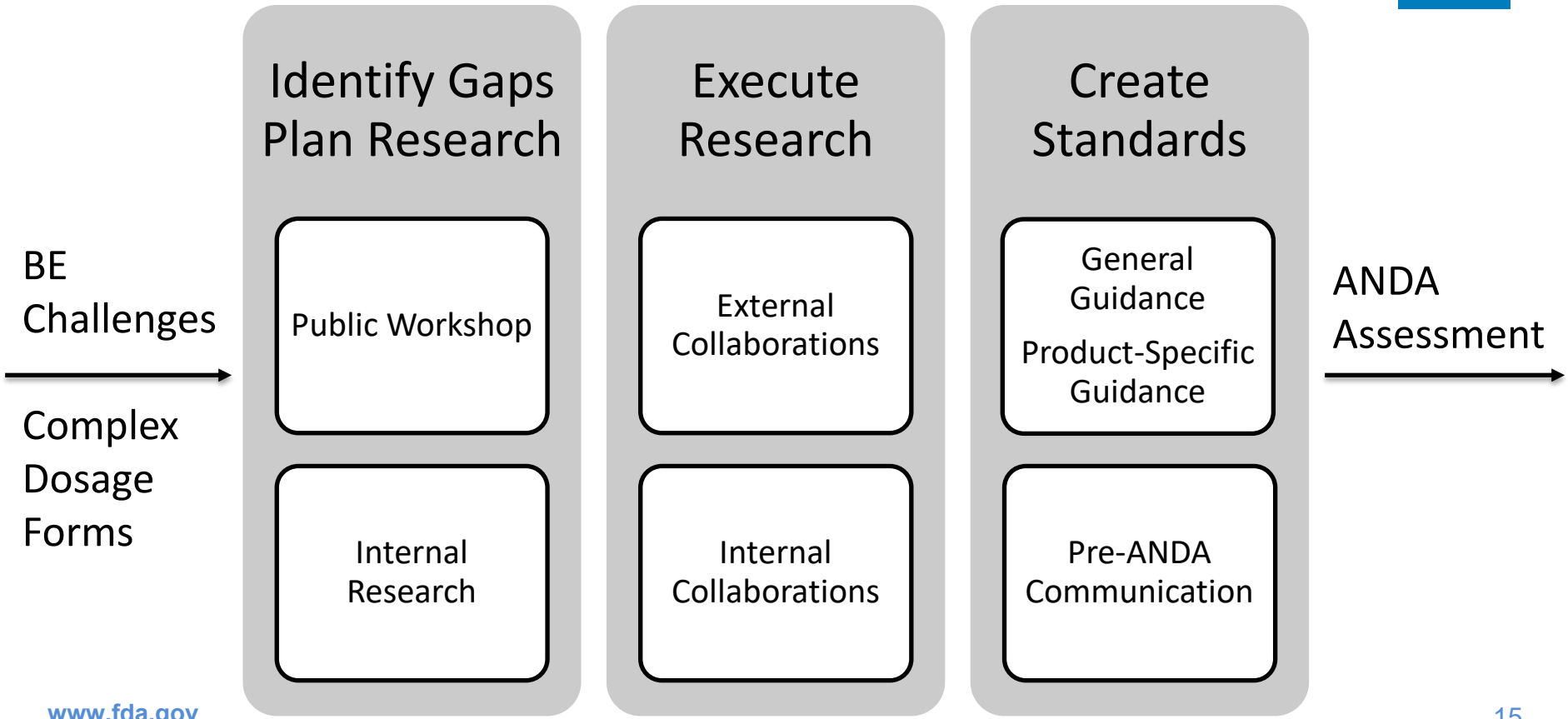
First-time Generic Drug Approvals 2022 -
Most Relevant to Dermatology (out of 90 total)

ANDA #	Generic Name	ANDA Applicant	Brand Name	ANDA Approval Date	ANDA Indication
212710	Penciclovir Cream 1%	Teva Pharma	Denavir	11/9/2022	Recurrent herpes labialis
215433	Tazarotene Gel 0.05%	Cosette Pharma	Tazorac	9/13/2022	Plaque psoriasis
208768	Posaconazole Injection	Par Sterile	Noxafil	5/25/2022	Prophylaxis of invasive Aspergillus and Candida
215398	Bexarotene Gel	Amneal Pharma	Targretin	4/27/2022	Cutaneous lesions of CTCL
214596 212424	Phytonadione Injectable Emulsion	Cipla	AquaMEP HYTON	4/22/2022	Coagulation disorders caused by Vitamin K deficiency

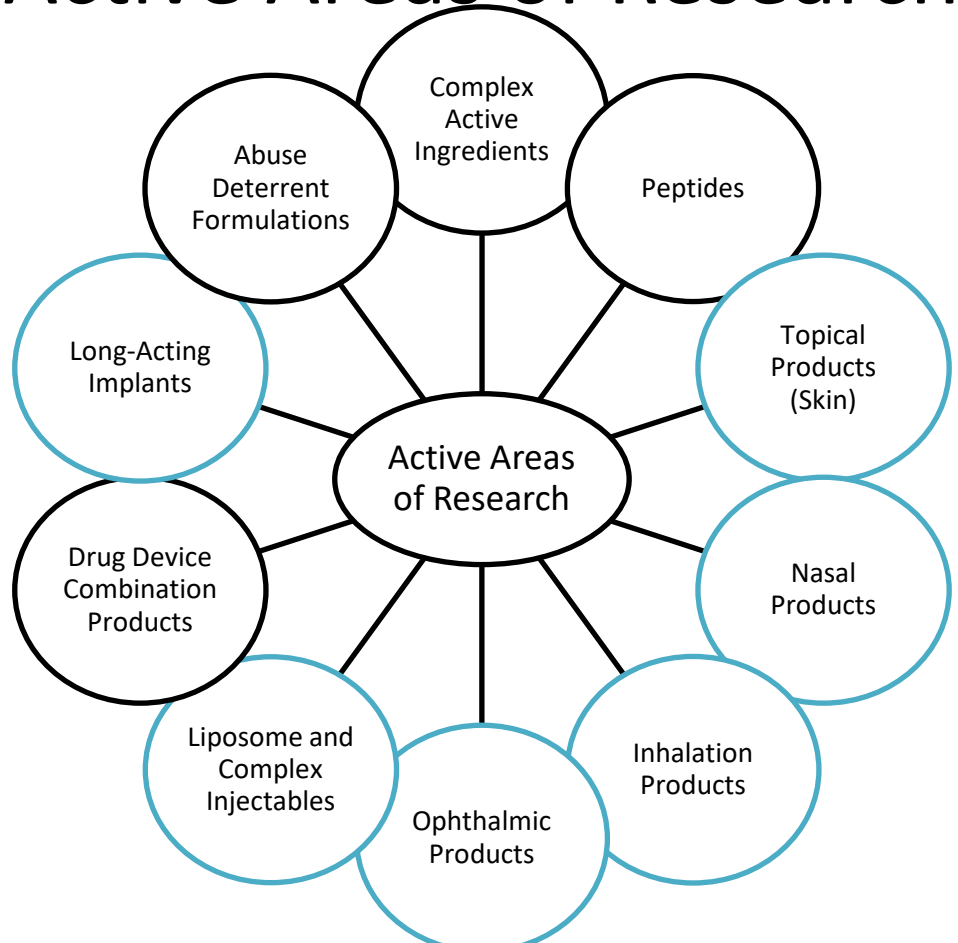
“Complex” Locally Acting Drug Products



GDUFA Science and Research Program



Active Areas of Research



Topical Drug Products (Skin)

Cutaneous Pharmacokinetics (PK)

- Microdialysis (dMD) and Open Flow Microperfusion (dOFM) directly measure the in vivo rate and extent of drug BA at/near the site of action in the skin

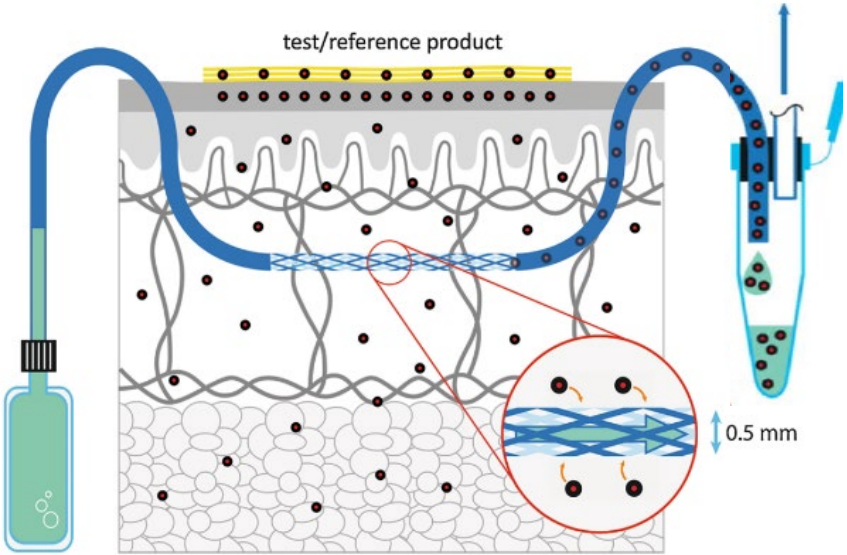
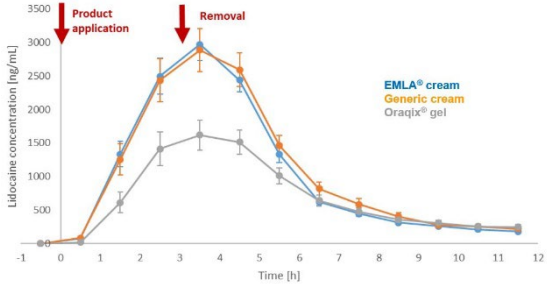
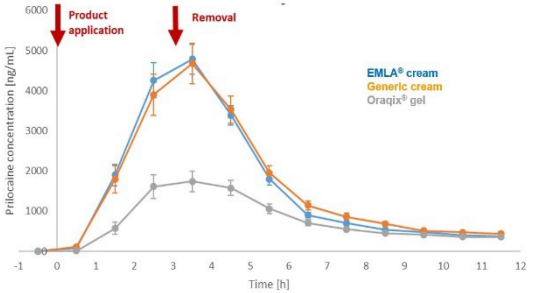


Image provided courtesy of Dr. Frank Sinner, Joanneum Research

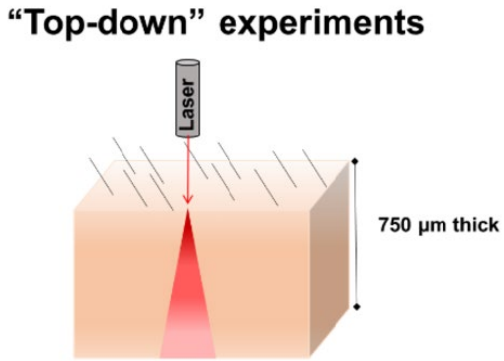


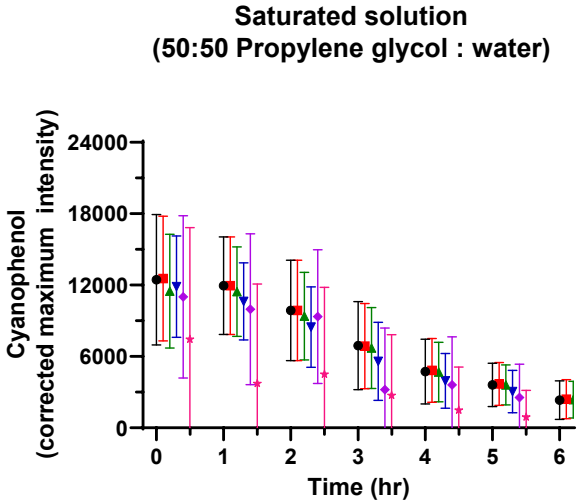


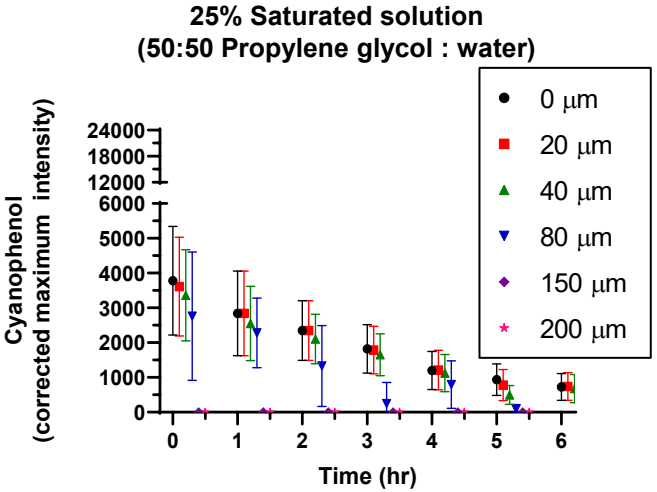
Dr. Frank Sinner provided with FDA funding for award U01-FD005861

Cutaneous PK

Confocal and Simulated Raman Spectroscopy can directly measure the rate and extent of drug bioavailability at/near the site of action in the skin.



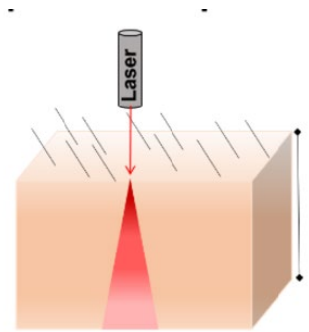


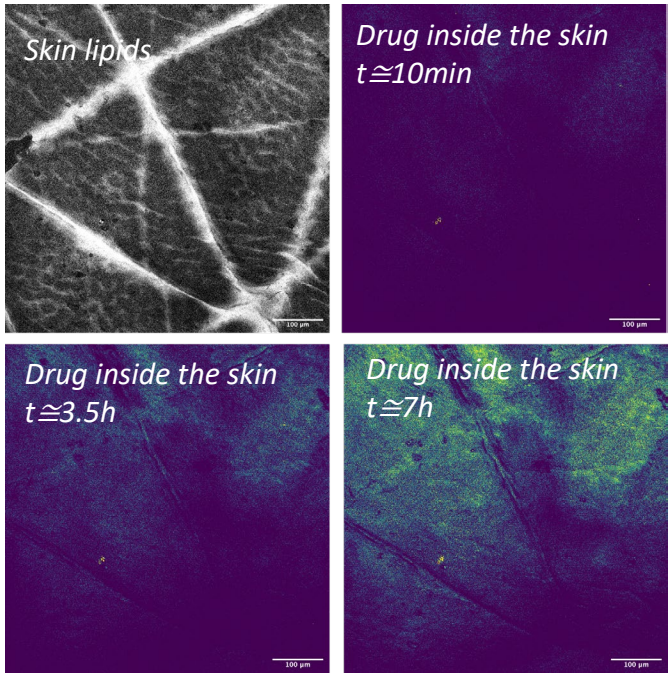


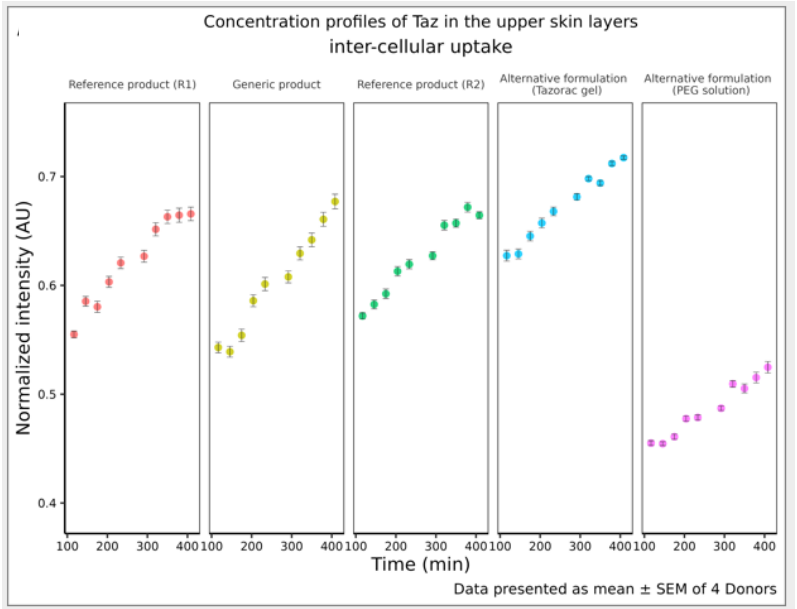
Dr. Richard Guy provided with FDA funding for award U01FD0006533

Cutaneous PK

Confocal and Simulated Raman Spectroscopy can directly measure the rate and extent of drug BA at/near the site of action in the skin.

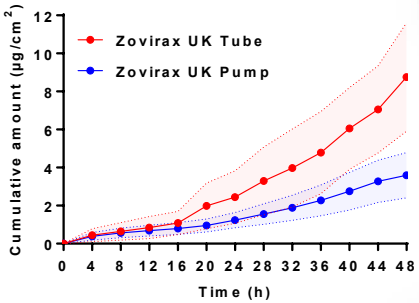






Dr. Conor Evans provided with FDA funding for award U01FD0006698

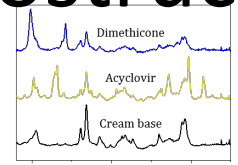
Understanding Product Microstructure

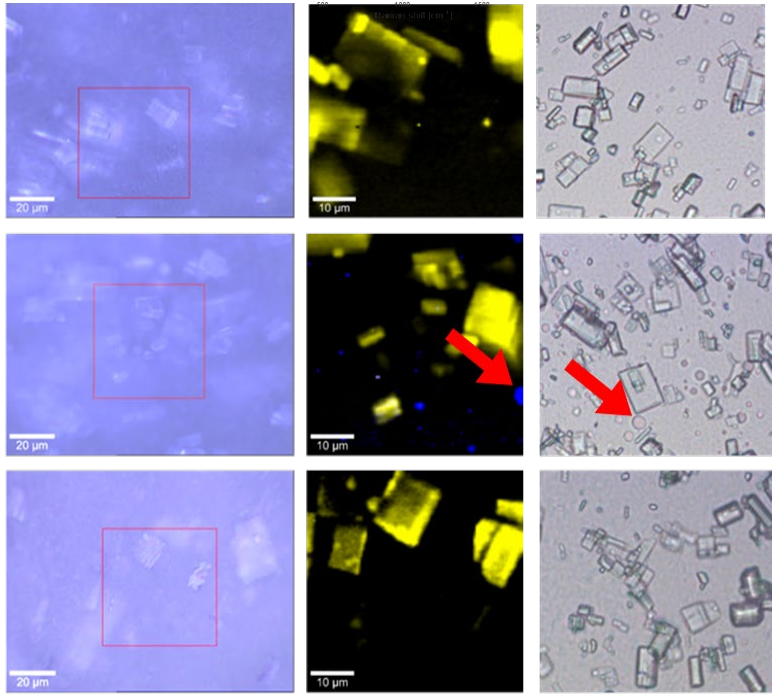


Zovirax® UK
Tube

Zovirax® UK
Pump

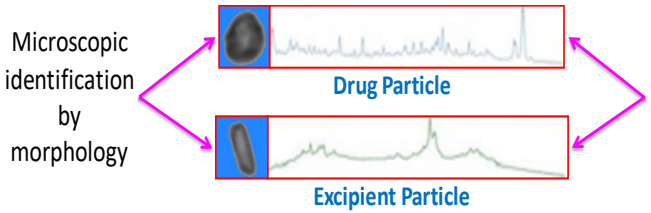
Zovirax® UK
Pump
(from inside container)

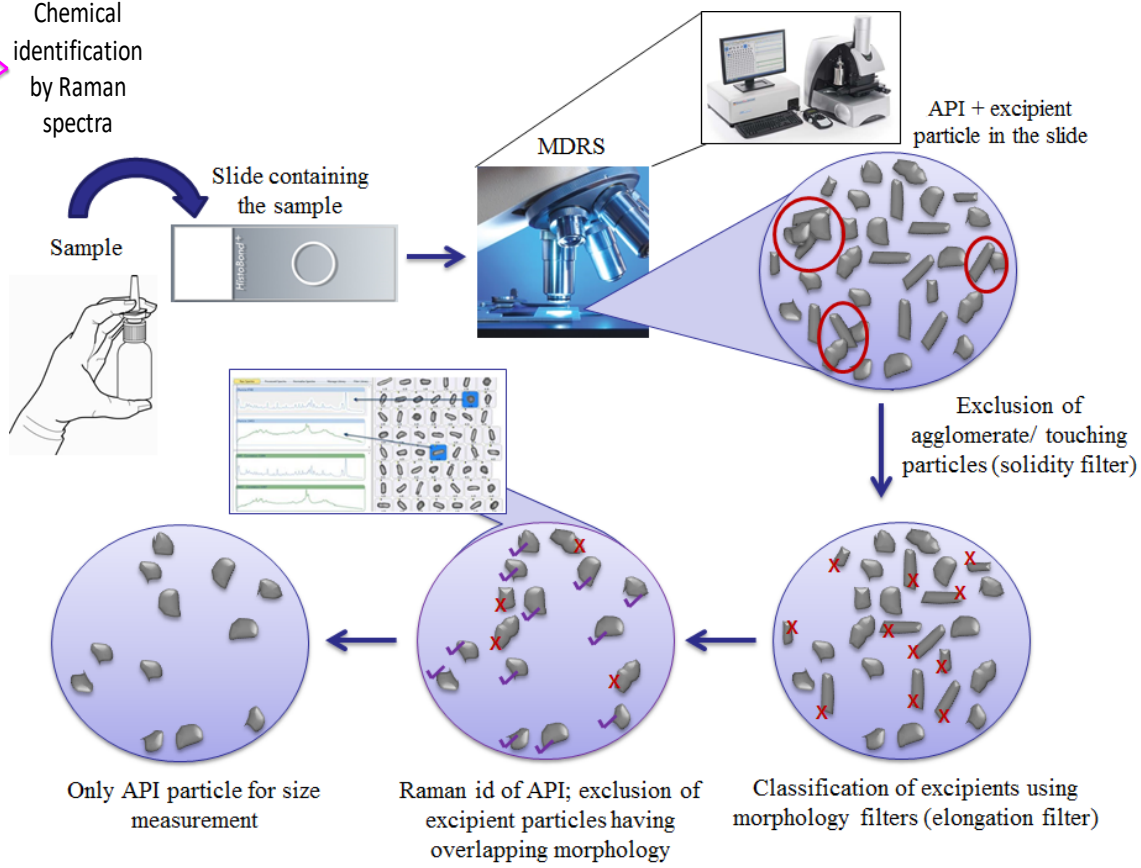




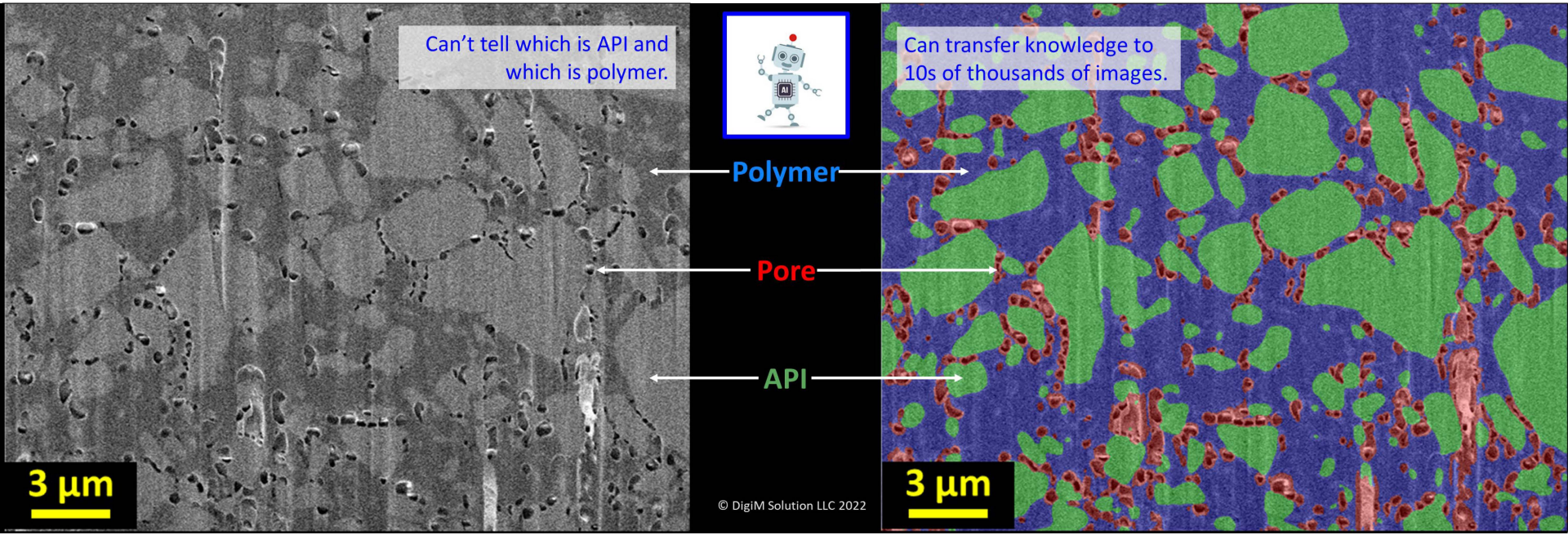
Prof. Michael Roberts provided with FDA funding for award U01-FD005226

Morphologically-Directed Raman Spectroscopy





Imaging and Artificial Intelligence



Dr. Shawn Zhang (DigiM) provided with FDA funding for award Contract # 75F40119C10157

DEIA and Regulatory Dermatology

- Numerous opportunities to have impact on diversity as FDA regulator
- Leadership at the reviewer level
- Continued efforts to increase agency and public awareness
- Diverse efforts with variable impact

Indoor Tanning/Skin Cancer Prevention

- CDRH regulates indoor tanning beds/booths
- Regulated as Class 1 devices until June 2014, when they were reclassified to Class 2
- Received comments favorable for reclassification from diverse groups, including American Academy of Dermatology, American Academy of Pediatrics, National Alliance for Hispanic Health, various state health entities.

Loprox Shampoo Labeling (revised 2012)

14 CLINICAL STUDIES

In two randomized, double-blind clinical trials, subjects 16 years and older with seborrheic dermatitis of the scalp applied LOPROX Shampoo or its vehicle twice weekly for 4 weeks. Subjects who were immunocompromised, those with psoriasis or atopic dermatitis, women of childbearing potential not using adequate contraception, and pregnant or lactating women were excluded from the clinical trials. An evaluation of the overall status of the seborrheic dermatitis, the presence and severity of erythema or inflammation, and scaling, was made at week 4, using a scale of 0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = pronounced, and 5 = severe. Effective treatment was defined as achieving a score of 0 (or a score of 1 if the baseline score was ≥ 3) simultaneously for status of the seborrheic dermatitis, erythema or inflammation, and scaling at Week 4. Ciclopirox shampoo was shown to be statistically significantly more effective than vehicle in both trials. Efficacy results for the two trials are presented in Table 1 below.

Table 1. Effective Treatment Rates at Week 4 in Trials 1 and 2

	Ciclopirox Shampoo	Vehicle
Study 1	220/380 (58%)	60/192 (31%)
Study 2	65/250 (26%)	32/249 (13%)

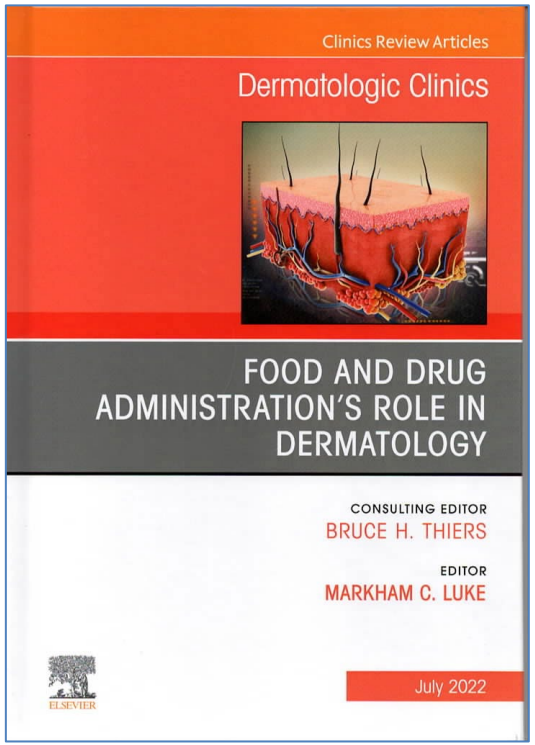
Efficacy for African American subjects was not demonstrated, although only 53 African American subjects were enrolled in the two pivotal trials.

Diversity in Dermatology Clinical Studies

Chen V, Akhtar S, Zheng C, Kumaresan V, Nouri K. Assessment of changes in diversity in dermatology clinical trials between 2010-2015 and 2015-2020: a systematic review. *JAMA Dermatol*. Published January 26, 2022:

"The results of this systematic review suggest that while reporting of racial and ethnic data has become more transparent from the 2010-2015 period to the 2015-2020 period," the authors concluded, "inclusion of representative patient populations (particularly in psoriasis studies) has not statistically significantly changed."

July 2022 Dermatologic Clinics



Insightful articles on:

- The History of Dermatology at FDA
- FDA and Dermatologic Drug Development
- Postmarket Assessment for Dermatology Drugs and Cutaneous Adverse Reactions
- How does FDA Approve Generic Drugs
- Dermatology Drugs for Children
- Regulation of Medical Devices for Dermatology
- Regulation of Cosmetics in the United States
- Cutaneous Pharmacokinetic Approaches
- Measuring What Matters to Patients in Dermatology Drugs

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