FDA's role in regulating products for dermatology, including drugs, biologics, devices, and cosmetics – with a special focus on generic drugs

Markham C. Luke, MD PhD FAAD
Director, Division of Therapeutic Performance,
Office of Research and Standards (ORS)
Office of Generic Drugs (OGD) CDER | U.S. FDA
Society for Investigative Dermatology 2025 Annual Meeting

Disclaimers

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

Any representation of brand name drugs in this talk are for purposes of scientific discussion and specific comparison.

FDA Campus

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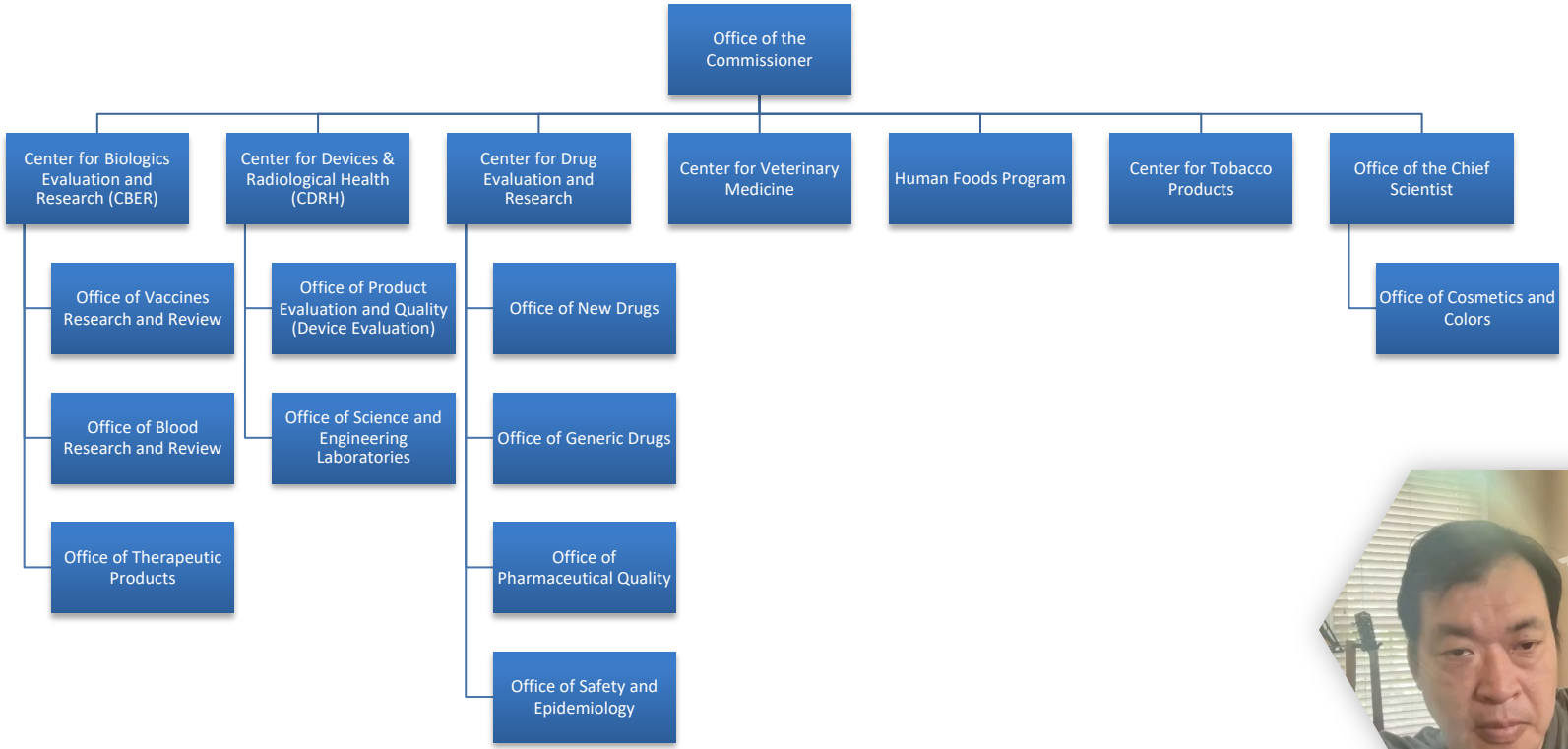
FDA Organization Chart (Abbreviated for Relevance to Dermatology)



FDA Centers

Dermatology Relevant:

- **Center for Drug Evaluation and Research (CDER)**
  - Office of New Drugs (OND) – small and large molecules
    - 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)**

- Office of Cosmetics and Colors (now in Office of Chief Scientist) post 2024 reorganization of Foods

Stages of Medical Product Development

1. Pre-Clinical Development – Conceptualization, Bench testing, Models (including animal models)
2. Clinical Exploratory Stage – first in human and feasibility/pilot studies, iterative learning and product development, dose ranging
3. Pivotal Stage – definitive study(ies) to support the safety and effectiveness evaluation of the medical product
4. Regulatory Evaluation – risk assessment, manufacturing quality
5. Post-approval Stage – includes studies intended to better understand the long-term effectiveness and safety, including rarer adverse events, use of real-world evidence
6. Product Lifecycle – Additional iterations and increased acce

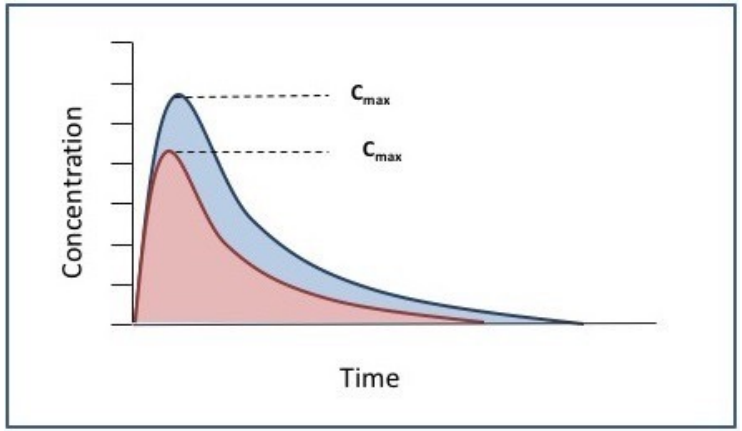
The Promise of Generic Drugs

- 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) liste
  Generic drug products can be substituted for the reference listed dru

www.fda.gov

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

How are Most 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 – pharmacokinetics or PK)

www.fda.gov

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

What are Complex Generic Products?

- **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 engagement

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

GDUFA Regulatory Science and Product-Specific Guidances (PSGs)

- GDUFA provides resources to allow FDA to perform and fund research to advance generic drug regulatory science and decision-making
  - Goal: Access to generics in all product categories
  - 90+ on-going projects
  - Recent focus on complex drug products

- Research provides new tools for FDA and industry to evaluate generic drug equivalence, to enable more efficient development of generic drugs and thus improve access
- Results from GDUFA research manifest in our PSGs as recommendations for new alternative approaches to demonstrate bioequivalence

PSGs for Complex Drug Products

- **There are over 2,000 published PSGs.**
- **These guidance documents have helped provide public access to current thinking on bioequivalence (BE) approaches for our regulated drugs.**
- **The PSGs helped industry in reducing the need for submitting controlled correspondence requests to FDA, allowing better utilization of FDA and industry generic drug development resources.**
- **In recent years, approximately 40% of published PSGs have been for complex products.**
  - BE for some complex products have historically utilized comparative clinical endpoint BE studies. PSGs would provide outlines of the recommended study protocols.
  - As science evolves, PSGs become the conduit for alternative approaches.
  - These approaches are outlined for new PSGs and as revisions to current published PSGs.

GDUFA Science and Research Program

Bio-equivalence Challenges

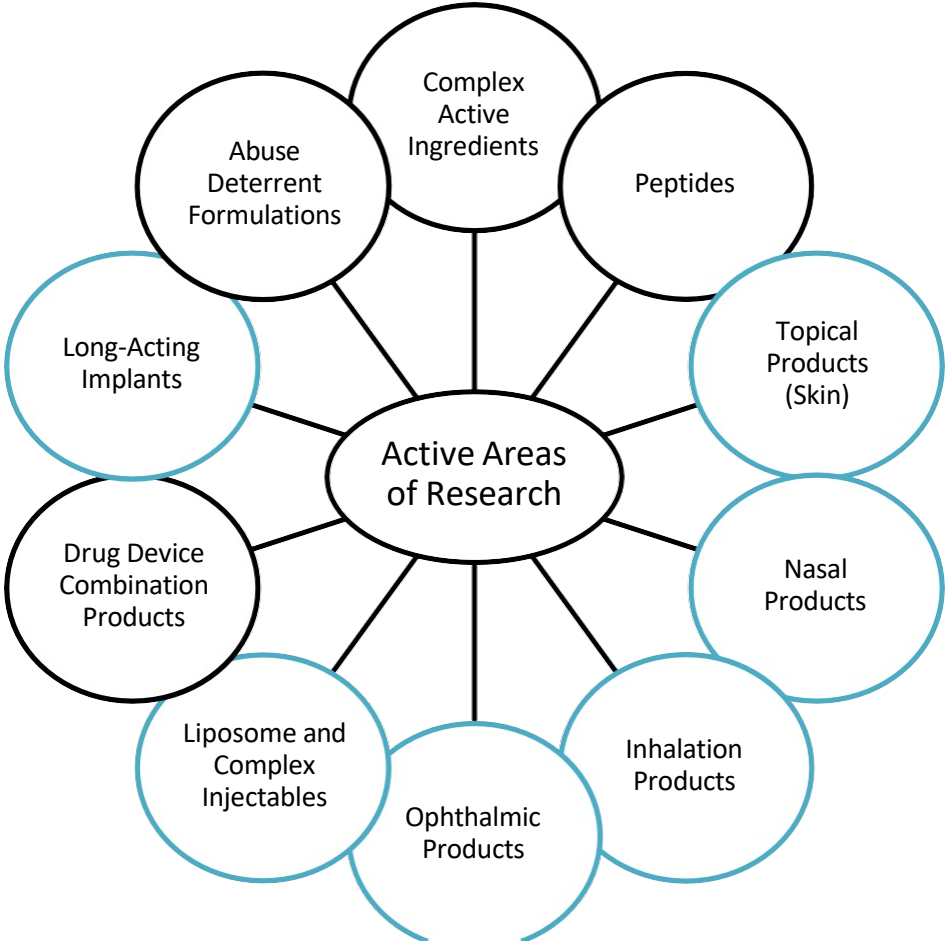
Complex Dosage Forms

Identify Gaps Plan Research	Execute Research	Create Standards
Public Workshop	External Collaborations	General Guidance Product-Specific Guidance
Internal Research	Internal Collaborations	Pre-ANDA Communication

ANDA Assessment

www.fda.gov

Active Areas of Research



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Advances in Cutaneous Pharmacokinetics

- Vasocontrictor or skin blanching assay for corticosteroid strength/penetration (McKenzie & Stoughton)
- Systemic PK correlation with local action
- Tape Stripping
- In Vitro techniques – in vitro release testing (IVRT) and in vitro permeation testing (IVPT)
- In vivo Microdialysis and Dermal Open-Flow Microperfusion (dOFM)
- Confocal Raman Spectroscopy techniques – stimulated Raman scattering microscopy
- Future techniques including in vivo, in situ, real-time microbiosensor

Cutaneous Pharmacokinetics (PK)

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

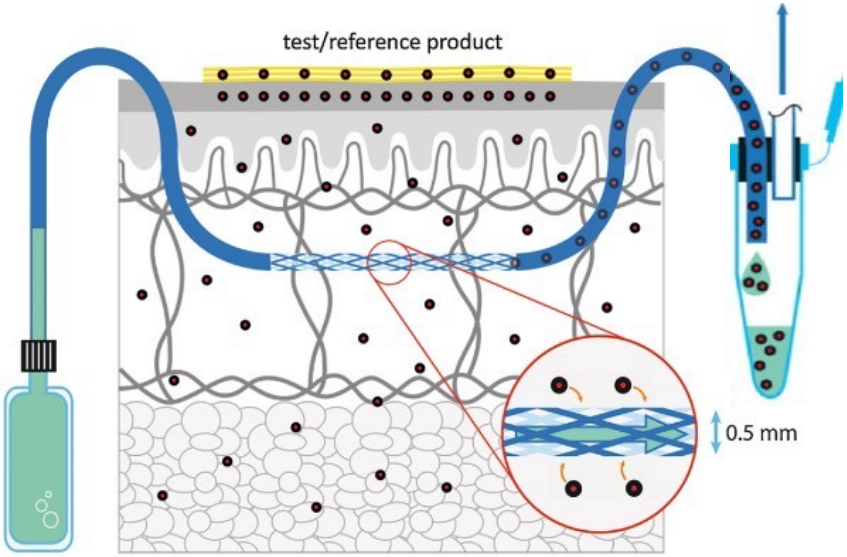
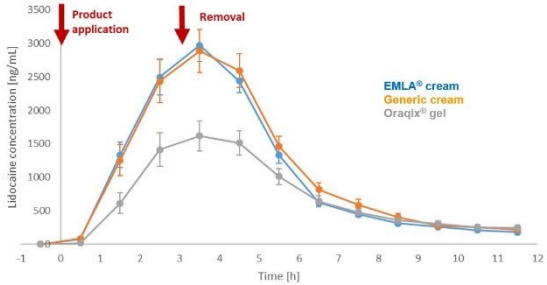
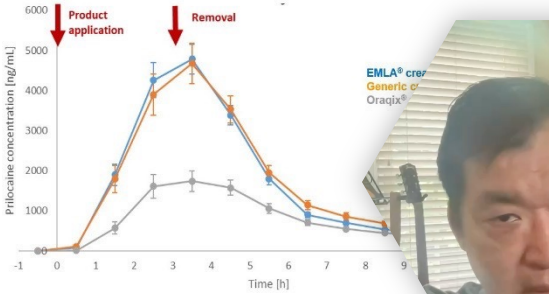
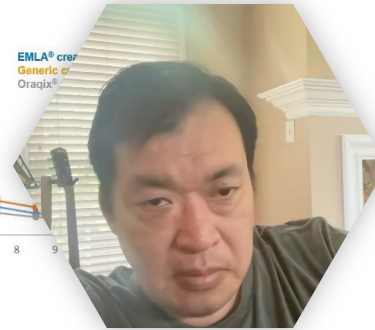


Image provided courtesy of Dr. Frank Sinner, Joanneum Research







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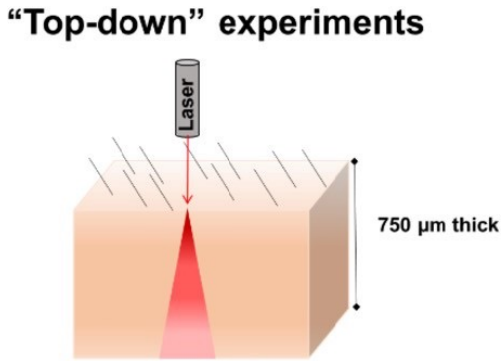
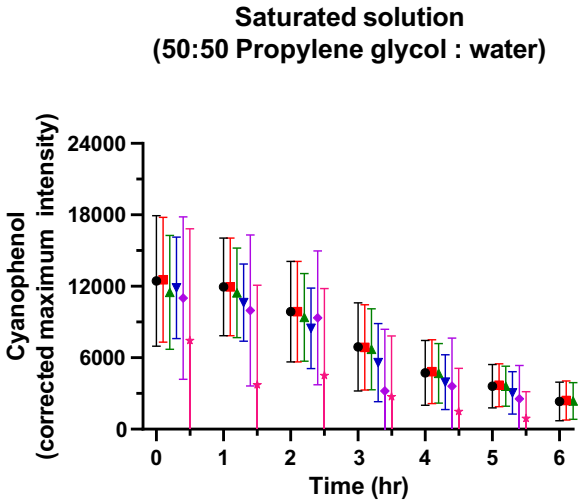
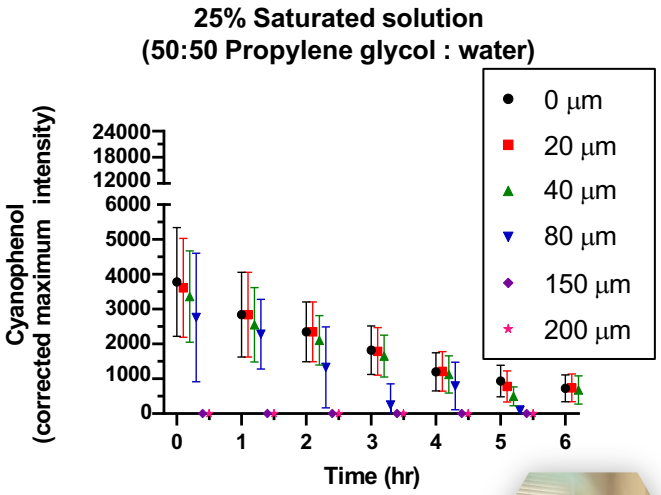
Dr. Frank Sinner provided with FDA funding for award U01-FD005861

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.







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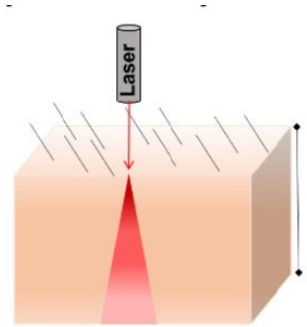
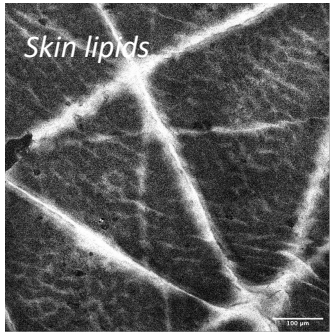
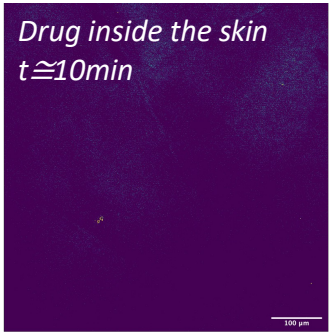
Dr. Richard Guy provided with FDA funding for award U01FD0006533

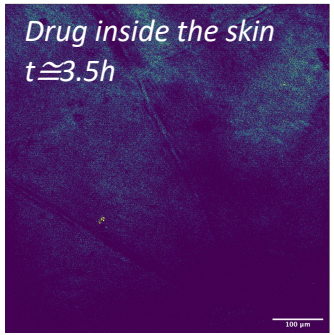
Cutaneous PK

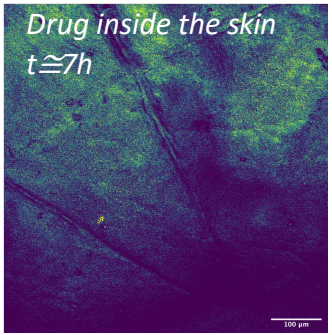
Confocal and Simulated Raman Spectroscopy can directly measure the rate and extent of drug BA at/near the site of action in the skin.

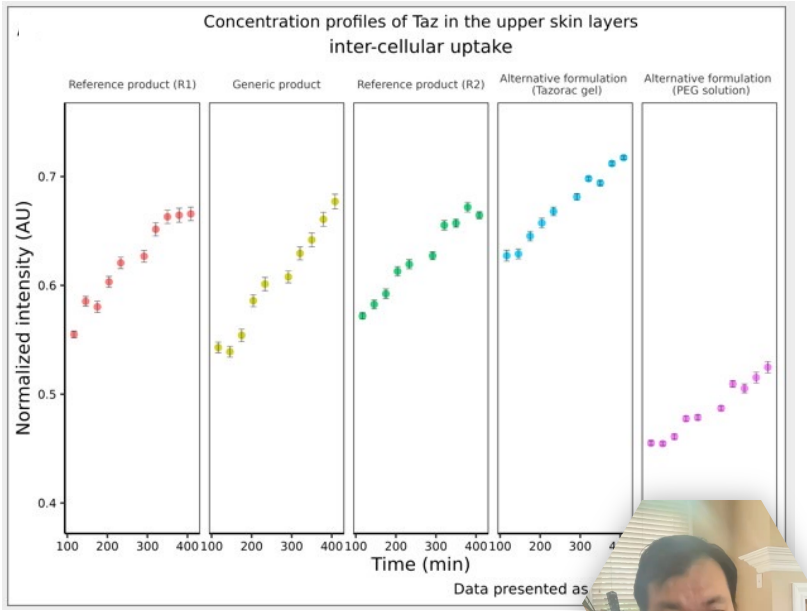












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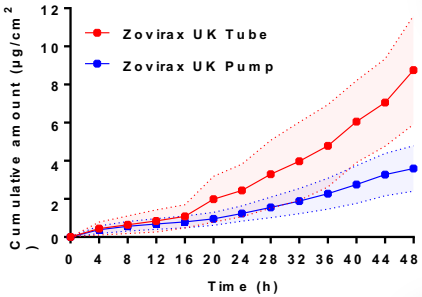
BA: bioavailability

Dr. Conor Evans provided with FDA funding for award U01FD0006698

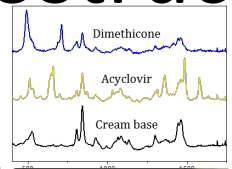
Understanding Product Microstructure

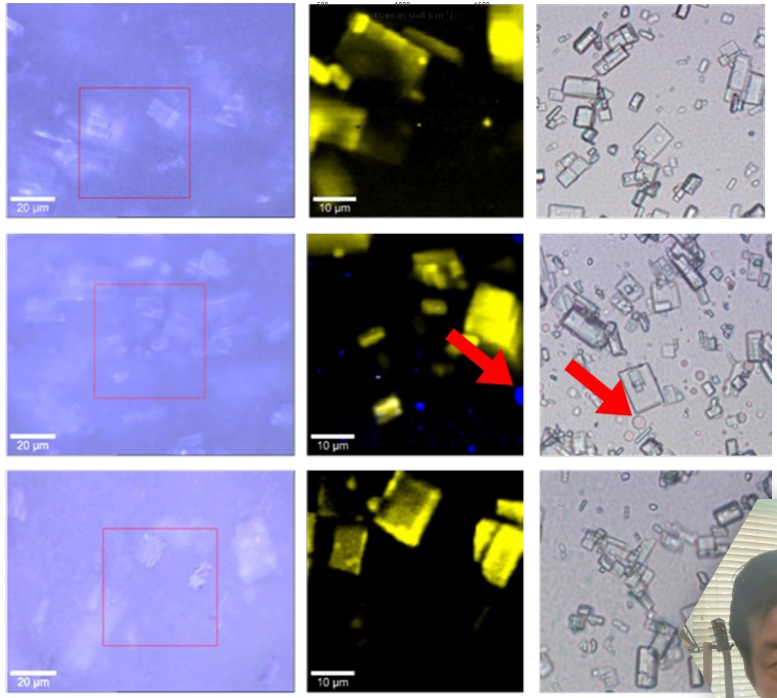


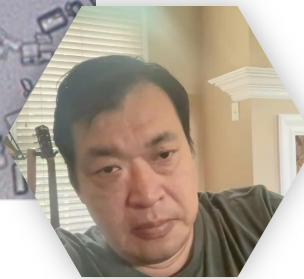
Zovirax® UK
Tube

Zovirax® UK
Pump

Zovirax® UK
Pump
(from inside container)







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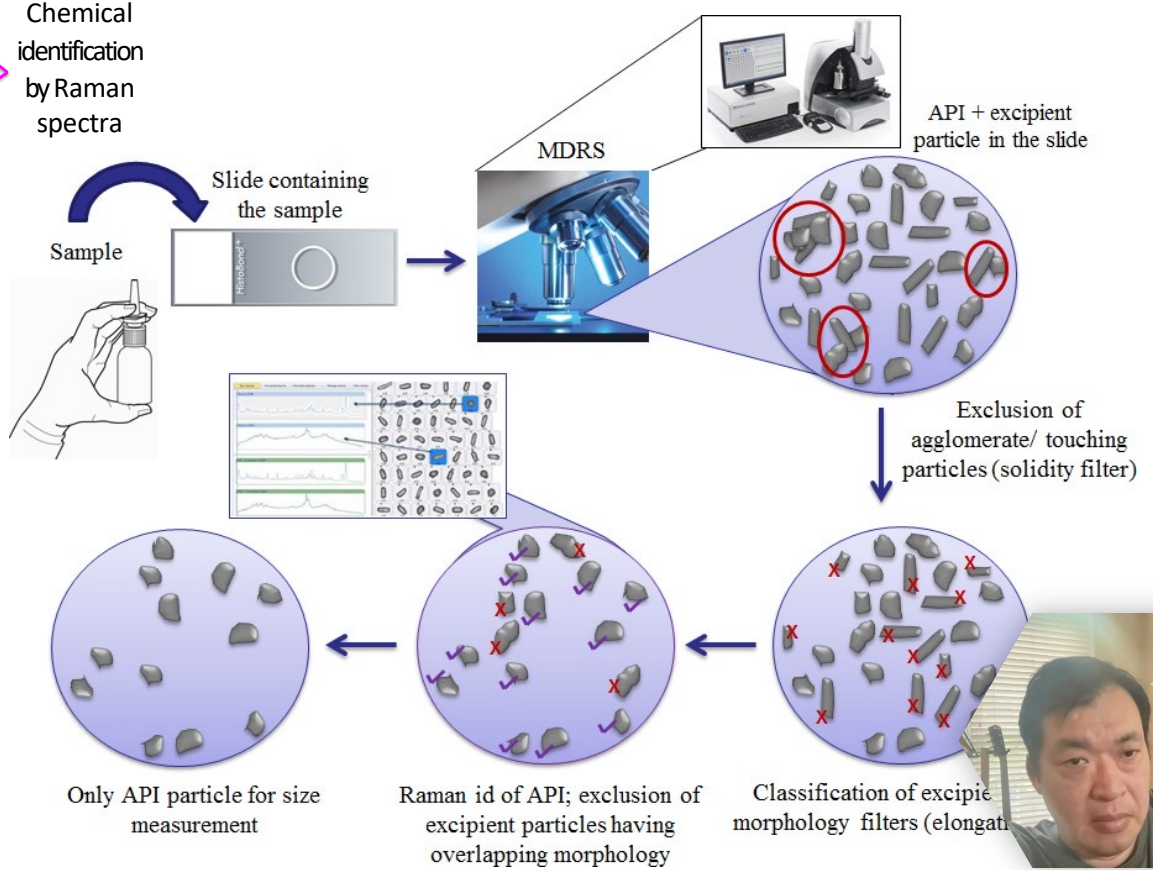
Prof. Michael Roberts provided with FDA funding for award U01-FD005226

Morphologically-Directed Raman Spectroscopy



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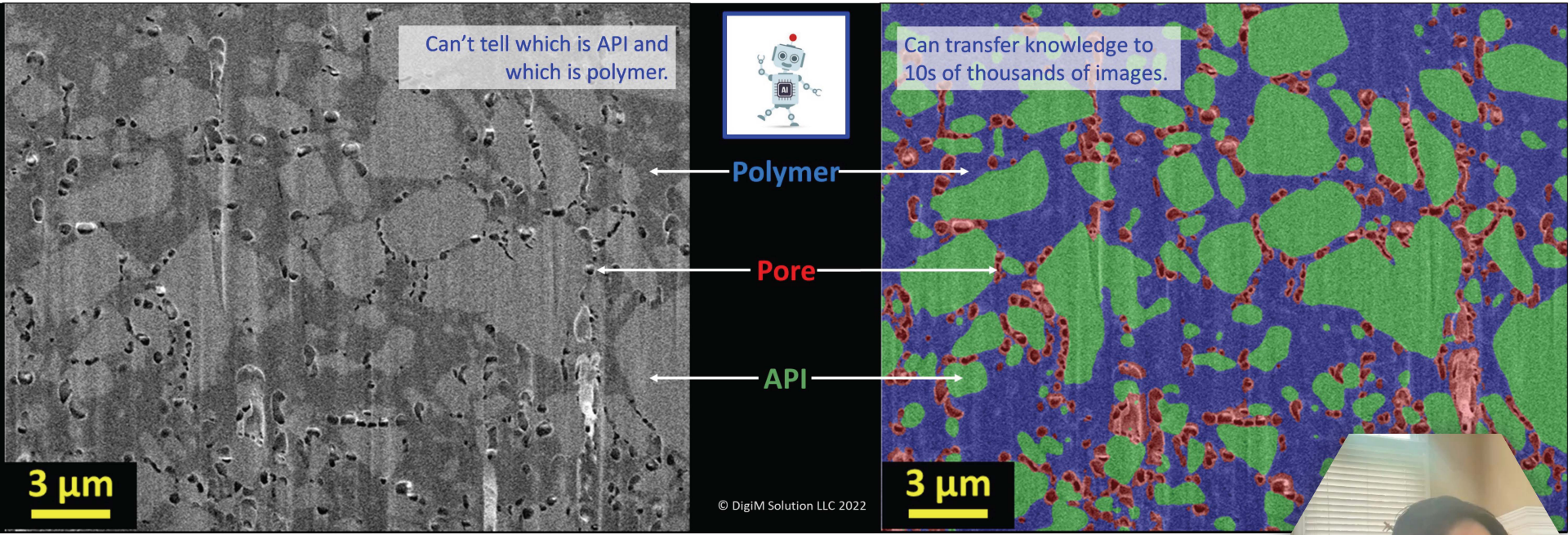
Imaging and Artificial Intelligence



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

FDA HQ Building, White Oak

www.fda.gov

What is a Medical Device?

Defined by the Food Drug & Cosmetic Act as an **instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent**, or other similar or related article, including a component part, or accessory which is:

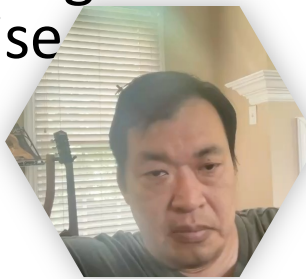
- intended for use in the **diagnosis of disease** or other conditions, or in the **cure, mitigation, treatment, or prevention of disease**
- intended to **affect the structure or any function** of the human body

What is a Medical Device?

Unlike a drug, a medical device to achieve its primary purpose:

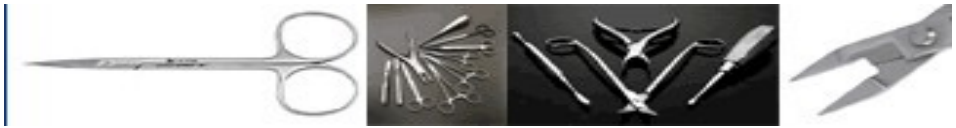
- **does not rely on chemical action** within or on the human body
- is **not dependent upon being metabolized**

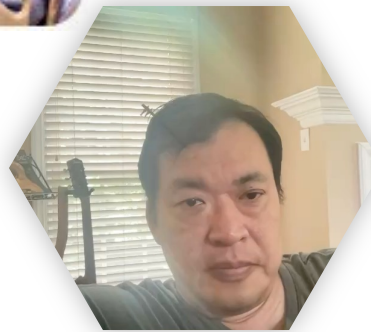
Combination products can be device/drug or device/biologics that are either physically linked or used together and raise unique regulatory issues.



Risk-Based Classification of Medical Devices

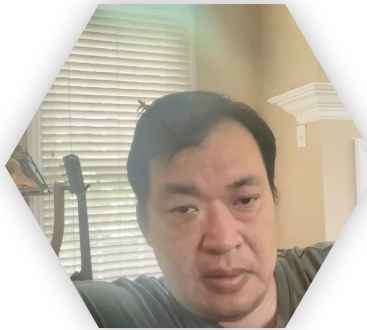
- Class I: simple, lower risk devices
  - Subject to “General Controls”
    - Registration and Listing, Quality System, Adverse Event Reporting, Prohibitions against misbranding and adulteration
  - Most exempt from premarket review





Risk-Based Classification of Medical Devices

- Class II: more complex, higher risk
  - Subject to General Controls PLUS Special Controls
  - Most require Premarket Notification [510(k)]
  - Regulatory standard is “Substantial Equivalence”
  - Most cleared based on preclinical and animal testing (10% require clinical)



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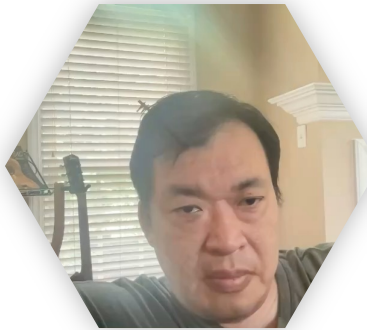
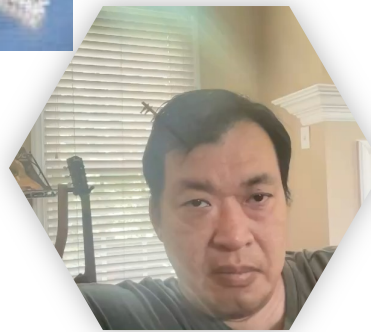
Substantial Equivalence (SE)

- 510(k) submissions compare new devices to “predicate” marketed devices
- A decision flowsheet results in a binary determination of SE vs. NSE
  - Indication and Intended Clinical Effect/Use
  - Technological Characteristics (Design/Material)
  - New types of Safety/Effectiveness Concerns
  - Performance Data (including clinical)



Risk-Based Classification of Medical Devices

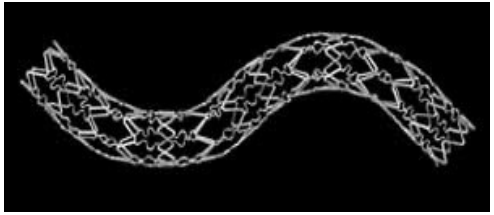
- Class III: most complex, highest risk
  - Bench + Animal + Clinical
  - Premarket Application [PMA]
  - Regulatory standard is “reasonable assurance of safety and effectiveness”
  - May include post-approval study requirements



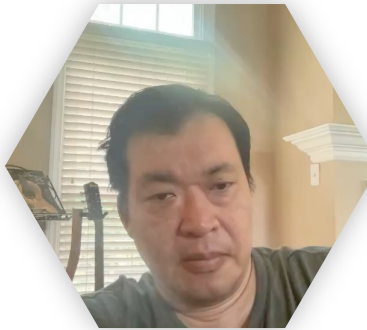
De Novo Applications

- Added in 1997 under FDAMA as an alternate pathway to classify novel devices of low to moderate risk that had automatically been placed in Class III after receiving an NSE determination for a 510(k).
- Under FDASIA, two pathways for de novo classification: (1) NSE first – then request risk-based classification, or (2) to submit a de novo classification request to FDA directly without first being required to submit a 510(k) for a low to moderate risk device.
- Devices that are classified through the de novo process may be marketed and used as predicates for future 510(k) submissions.

Combination Products



- Include device/drug and device/biologic products that are:
  - physically linked; or
  - packaged together (e.g., drug and device products); or
  - packaged separately but required to be used together.
- Raise unique regulatory and scientific issues



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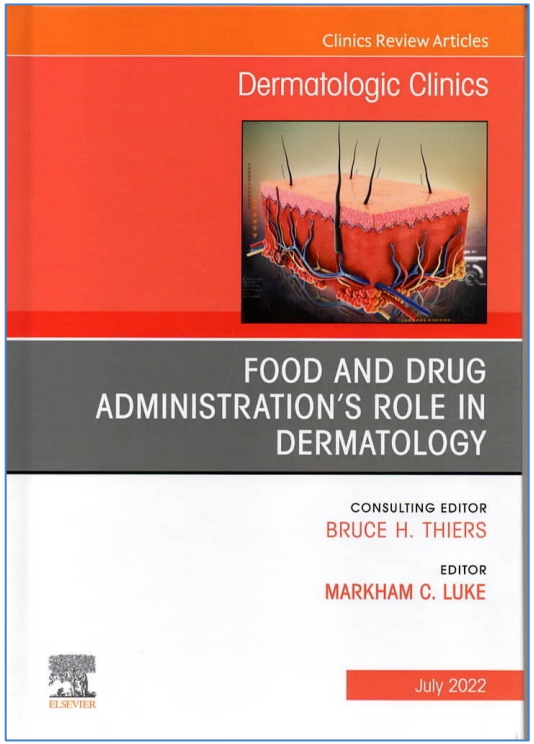
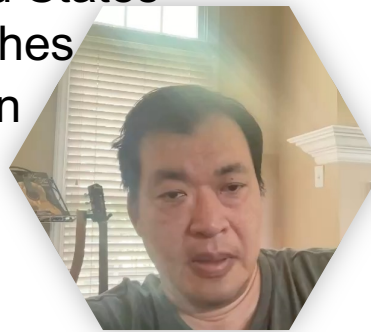


Insightful articles on:

- 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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2022 Dermatologic Clinics Vol 40

- Collaborative project with FDA's History Office (Vanessa L. Burrows, PhD)
- We wanted to explore some of the early to recent history of FDA, its regulation of dermatology relevant products and its public health-minded dermatologists

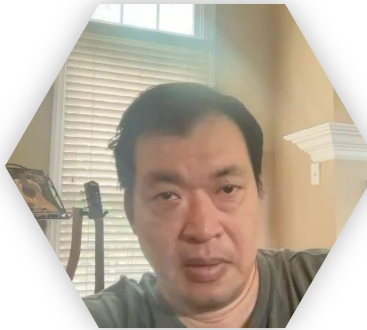

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Table 1
Major legislative milestones that impacted the regulation of dermatology therapy

Law	Year	Regulatory Impact
Biologics Control Act	1902	Required federal licensure of biologics manufacturers and products
Federal Food and Drugs Act (aka, Pure Food and Drugs Act)	1906	Banned marketing of adulterated or misbranded food or drugs; required adherence to drug standards
Federal Food, Drug, and Cosmetic Act	1938	Mandated evidence of safety before marketing drugs; brought cosmetics and medical devices under FDA's authority; created the color certification program
Durham-Humphrey Amendments	1951	Required prescription from medical professional for certain dangerous or habit-forming drugs
1962 Drug Amendments (aka, Kefauver-Harris Amendments)	1962	In addition to safety, required drugs provide substantial evidence of efficacy from sound clinical studies before marketing
Medical Device Amendments	1976	Created risk-based classification system for medical devices, requiring premarket approval for riskiest (Class III) devices and development of performance standards for less risky products
Drug Price Competition and Patent Term Restoration Act (aka., Hatch-Waxman Amendments)	1984	Incentivized development of generic drugs by allowing the use of Abbreviated New Drug Applications relying on evidence of bioequivalence to pioneer products; authorized exclusivity and patent term extension for pioneer products
Prescription Drug User Fee Act	1992	Authorized the collection of user fees to review New Drug Applications
Medical Device User Fee Amendments	2002	Authorized the collection of user fees to review medical device applications, register establishments, or list marketed products
Generic Drug User Fee Amendments	2012	Authorized the collection of user fees to review Abbreviated New Drug Applications

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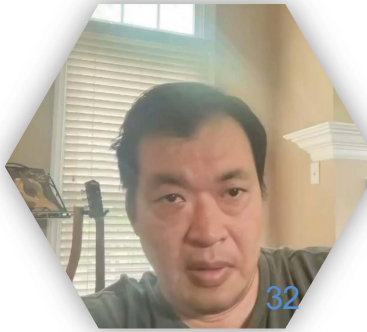

Table 2
Board-certified dermatologists who were managers at FDA

Name	Managerial Roles	Years
Dr Clarence Carnot Evans	Dermatology Branch Chief	1987–1992?
Dr Jonathan K. Wilkin	Division Director, DDDDP	1994–2005
Dr Susan Walker	Dermatology Team Leader, DDDDP	1997–2002
	Division Director, Nutritional Supplements	2003–2007
	Division Director, DDDDP	2007–2011
Dr Martin Okun	Dermatology Team Leader, DDDDP	1998–2000
Dr Markham C. Luke	Dermatology Team Leader, DDDDP	2001–2008
	Deputy Office Director, ODE, CDRH	2008–2016
	Acting Director, Cosmetics	2012–2013
	Division Director, Therapeutic Performance of Generic Drugs	2016-present
Dr Jill Lindstrom	Dermatology Team Leader, DDDDP	2004–2010
	Deputy Division Director, DDDDP	2010–2019
RADM Dr Boris Lushniak	Assistant Commissioner, Director, Emergency Preparedness (subsequently became Acting Surgeon General for the United States)	2005–2010
Dr Elektra J. Papadopoulos	Associate Office Director, New Drugs and Deputy Director, Clinical Outcomes Assessments	2009-2021

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Fig. 6. Clarence Carnot Evans. *Courtesy of* FDA History Office Still Image Collections.

Fig. 7. Drs. Jonathan Wilkin, Mohamed Al'Osh and I

Table 3
Dermatologists who have worked full-time at FDA

Name	FDA Center(s)	Years
Dr Lawrence B. McCaleb	Division of Drugs	1939–1942
Dr Clarence Carnot Evans	Bureau of Medicine CDER	1963–1992?
Dr Phyllis Huene	Bureau of Medicine CDER	1964–2005
Herbert Golomb	Bureau of Medicine	1963-?
Donald Mitchell	Bureau of Medicine	1963-?
Walter Edmundson	Bureau of Medicine	1963-?
Glenn Hays	Bureau of Medicine	c. Late-1960s
Wilson Powell	Bureau of Medicine	c. Late-1960s
John B. Sanders	Bureau of Medicine	c. Late-1960s
Leonard Trilling	Bureau of Medicine	c. Late-1960s
Dr Ramsey Labib	CDER	1990–2002
Dr Ella Toombs	CDER	1989–2002
Dr Brenda Vaughan	CDER	1993–2011
Dr Lois LaGrenade	CDER	1997–2019
Dr Denise Cook	CDER	1995–2022
Dr Jonathan K. Wilkin	CDER	1994–2005
Dr Susan Walker	CDER, CFSAN	1996–2011
Dr Kathy A. O'Connell	CDER, CBER	1996–2014
Dr Martin Okun	CDER	1997–2001
Dr Markham C. Luke	CDER, CDRH, CFSAN	1998-present
Dr Brenda Carr	CDER	2000-present
Dr Elektra Papadopoulos	CBER, CDER	2001-2021
Dr Jill Lindstrom	CDER	2002–2019
Dr Patricia Brown	CDER	2005-present
Dr Jane Leidtka	CDER	2006–2020
Dr Boris Lushniak	OC	2004–2010
Dr Kenneth Katz	CDER	2006–2007
Dr Melinda McCord	CDER	2009-present
Dr Laura Marquart	CDRH	2013-present
Dr Schlomit Halachmi	CDRH	2013-present
Dr Roslyn E. Epps	CDER	2015-present
Dr Melissa Reyes	CDER	2016-present
Dr Felisa Lewis	CDER	2020-present
Dr Mary Kim	CDER	2021-present

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Fig. 8. Drs. Brenda Vaughan, Elektra Papadopoulos and Jill Lindstrom.

Pictoral History: Problem Products

Fig. 1. LashLure and Electreat. *Courtesy of* FDA History Office, Legacy Artifact Collection.

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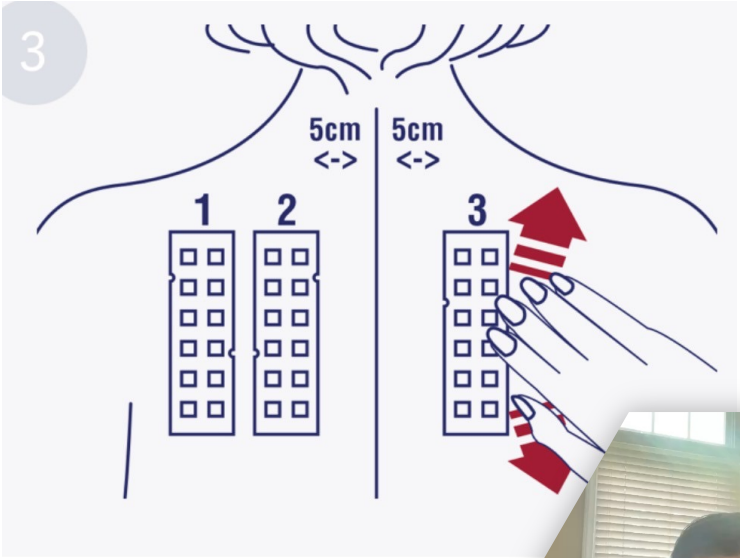
Pictoral history: Irritant and Contact Dermatology

Fig. 3. Draize test. *Courtesy of* FDA History Office, Photograph Collection.



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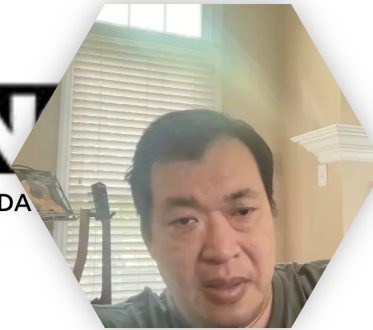
Pictoral history: Corticosteroids and Retinoids

Fig. 4. Terra-Cotril hydrocortisone ointment. *Courtesy of* National Museum of American History, Smithsonian Institution.

Fig. 5. Accutane warning. *Courtesy of* FDA fice Still Image Collections.



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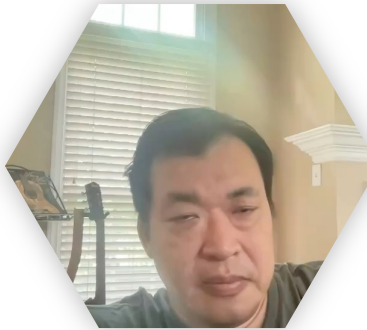
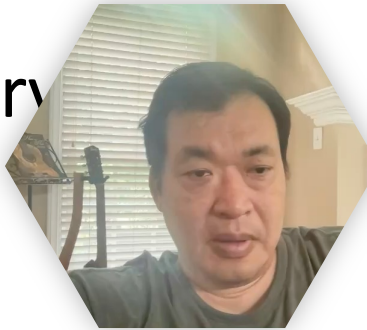
Dermatology/FDA Regulatory Landmarks



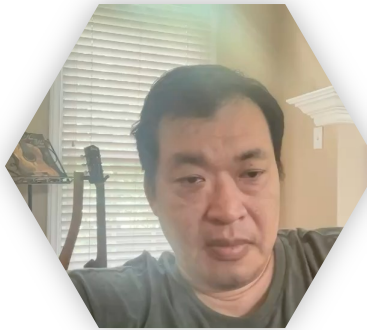
22 years since Biologic Drugs Migration

- In 2003-4, biologic drugs were migrated from CBER to CDER. This includes drugs like botulinum toxin.
- Since then, great strides have been made in the regulation of biologic drugs, including the advent of biosimilars.
- Biosimilars, under user fee provisions, have advanced with regard to their own regulatory science and research program.



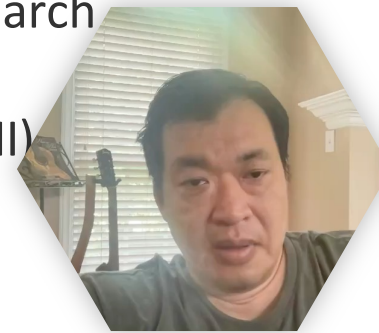
Hatch Waxman Act - 41st Anniversary

- September 24, 1984 – Drug Price Competition and Patent Term Restoration Act was signed into law
- Established the modern system of generic drug regulation in the United States
- Provisions for exclusivity for certain new drugs and first generics



Over 12 years with 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)

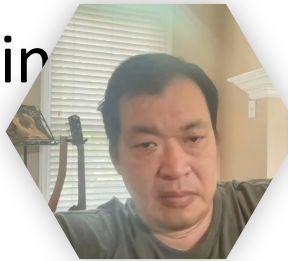


www.fda.gov

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

11th Anniversary for Indoor Tanning Bed Reclassification

- Indoor tanning beds/booths are regulated by CDRH.
- Regulated as Class 1 – low risk - devices until June 2014, when they were reclassified to Class 2 – higher risk.
- As part of the reclassification, indoor tanning beds have a boxed warning regarding safety and recommendations not to used by children.
- Notable reduction in the use of UV indoor tanning, in favor of spray tanning booths.



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Summative Conclusion

- The recent history of evidence-based dermatology and the drugs and tools used for treatment and diagnosis by dermatologists are intertwined with the history of product regulation at the FDA
- Many at FDA have played an important role in shaping the landscape of treatments and diagnostics over the years

- FDA regulation of medical products involves a mix of legal, scientific, and risk assessment

Acknowledgements

My staff and colleagues at FDA throughout the years
My supervisors, mentors, and collaborators
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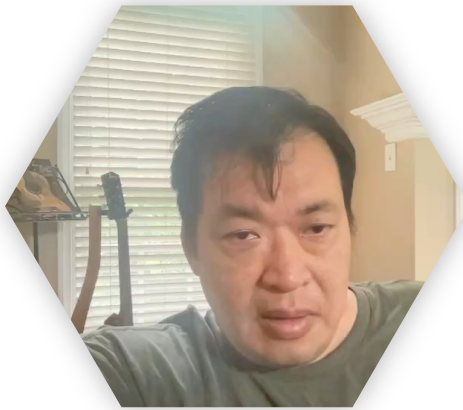

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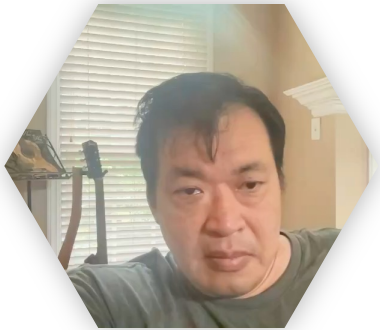
Thank You



markham.luke@fda.hhs.gov

Markham Luke, MD PhD
Director, Division of Therapeutic Performance
Office of Research and Standards (ORS), Office of Generic Drugs (OGD)
CDER | U.S. FDA