GDUFA Regulatory Science Update

Robert Lionberger, Ph.D.
Director
Office of Research and Standards
Office of Generic Drugs
Center for Drug Evaluation and Research, FDA

GDUFA Regulatory Science Public Meeting May 20, 2016

GDUFA Regulatory Science Update

- Yearly List of Research Priorities with Stakeholder Input (Public Meetings, Docket)
- FY 2016 Priorities
  - Post-market Evaluation of Generic Drugs
  - Equivalence of Complex Products
  - Equivalence of Locally Acting Products
  - Therapeutic Equivalence Evaluation and Standards
  - Computational and Analytical Tools
- Implementation
  - FDA is engaging with leading pharmaceutical and clinical scientists from across the world to ensure that the regulatory review of generic drugs is based on the best available science.
  - ~100 ongoing external research collaborations (contracts and grants)
    - 10x more resources than pre-GDUFA
  - ORISE research fellows in FDA (OGD and labs)
  - ORS (Office of Research and Standards) staff connects **research** results to new **standards** (via guidance, controls, review consults, petition response)

GDUFA Regulatory Science Scale Up

OGD Funded GDUFA Science

	Contracts/Grants ($$) and ORISE	New Contracts/ Grants	Cumulative Funds Under Management	Cumulative External Projects Under Management
FY2016	~$20M	~15	$90M	105
FY2015	$26.8M	25	$72M	95
FY2014	$22.8M	35	$54M	76
FY2013	$20.9M	29	$31M	41
FY2012	$3.6M	4		15
FY2011	$2.2M	3		12
FY2010	$3.1M	5		9

FY 2016 numbers are estimates

GDUFA Regulatory Science Impact

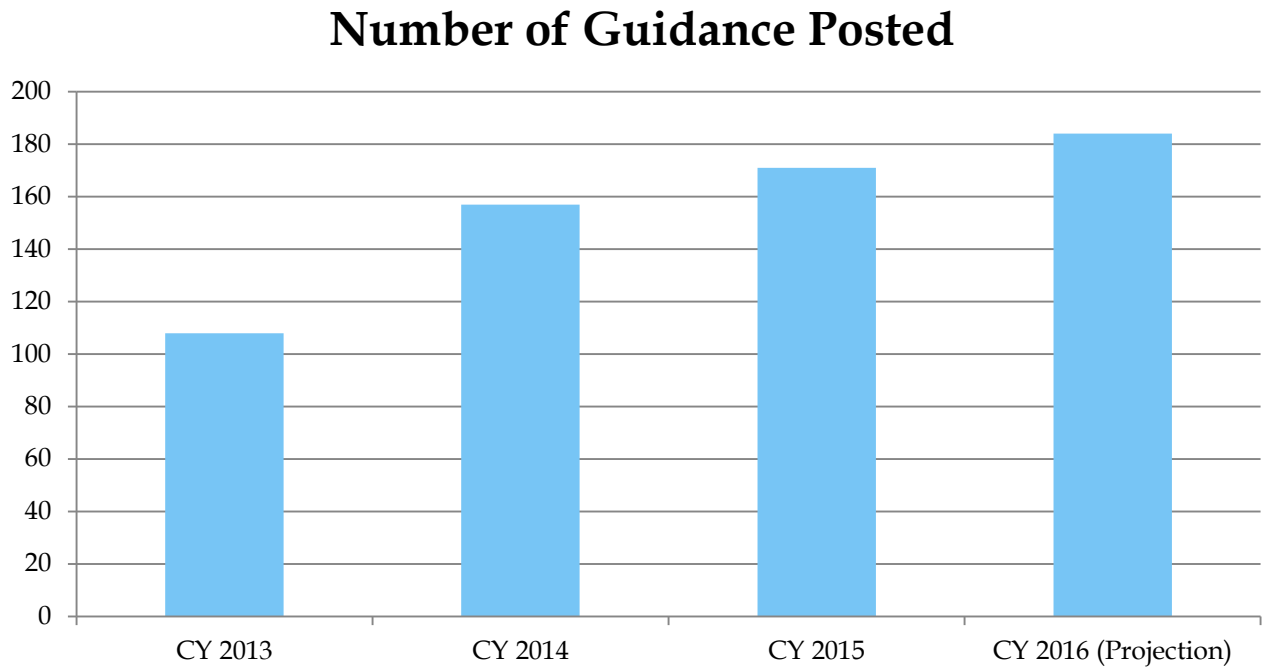
- Generic Access in all Product Categories
- Confidence in Generic Drug Substitution
- Better Tools for Development and Review

Success of Generics

Non-Discounted Spending and Dispensing by Product Type					
Spending US$Bn	**2011**	**2012**	**2013**	**2014**	**2015**
Total U.S. Market	**328.3**	**317.8**	**331.5**	**378.6**	**424.8**
Brands	74.5%	71.7%	71.0%	72.1%	73.3%
Unbranded Generics	13.6%	16.1%	16.9%	16.9%	16.0%
Branded Generics	11.9%	12.2%	12.1%	11.0%	10.7%
Dispensed prescriptions Mn	**2011**	**2012**	**2013**	**2014**	**2015**
Total U.S. Market	**4,014**	**4,155**	**4,236**	**4,325**	**4,368**
Brands	20.2%	15.9%	13.6%	12.3%	11.3%
Unbranded Generics	72.7%	77.7%	80.5%	82.1%	83.4%
Branded Generics	7.1%	6.4%	5.9%	5.6%	5.3%

IMS, *Medicines Use and Spending in the U.S.* April 2016

BE guidance



- Fraction that are for complex products is growing
- New Draft Guidance
  - Ophthalmic emulsion, Otic suspension, Liposomal Injections (3), Sublingual Film, IUD: Subq nanomaterial injection, locally acting GI tablets and capsules

Generic Access in all Product Categories

- Complex Active Ingredients
  - Immunogenicity of peptide impurities, High resolution analytics, multivariate data
- Topical Dermatological Products
  - 9 grants: new in vivo data, characterization of semi-solid formulations, PBPK modeling
- Inhalation Products
  - 9 grants: dissolution, particle size and PK studies, CFD modeling, non Q1-Q2 products
- Ophthalmic Products
  - 9 grants: in vitro characterization, drug release, and drug delivery modeling
- Nasal Products
  - Use of PK studies alone for BE: in vitro, in vivo and modeling projects
- Liposomes and Nanomaterials
  - 7 grants: in vitro release, product characterization, critical manufacturing variables
- Microspheres (Long acting injectables)
  - 9 grants: material characterization, in vitro release, in vivo animal data and modeling

Confidence in Generic Drug Substitution

- Brand-to-Generic Switching Studies in Patients
  - All completing studies confirm the conclusions of the studies submitted in the ANDA
  - Change public debate about generic substitution for AED
- Post-Market Surveillance
  - Adverse Event Reports: How to interpret for generic substitution
  - Claims and EHR Data: expected substitution patterns for different therapeutic classes, how to compare outcomes and usage patterns
- Product Specific Standards
  - NTI Drugs: Tighter BE standards when needed
  - pAUC Comparisons: PK profile similarity when needed

Better Tools for Development and Review

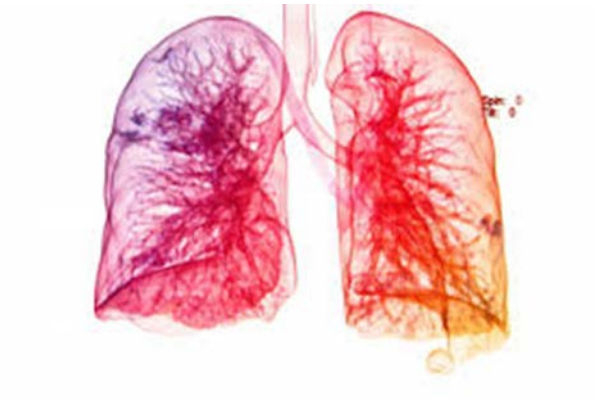
- Models of Non-systemic Absorption
  - 7 grants: PBPK for non-oral delivery
- Pharmacometrics for Generics
  - 5 grants: NTI drugs, pAUC selection, post-approval risk
- Advancing In Vitro Release
  - ~20 grants for complex or locally acting drugs have outcomes of improved drug release, product performance or dissolution methods that can accelerate generic product development
  - Solid Oral: predictive dissolution and oral absorption Models, excipient impact on absorption, pathway for generic versions of abuse-deterrent formulations
- High resolution analytics and multivariate data comparisons
  - ~20 collaborations with FDA labs

Generic Access in all Product Categories: Complex Active Ingredients

- Peptides, complex mixtures, natural source products
- Approval of ANDA for glatiramer acetate
- New Draft Guidance:
  - Conjugated Estrogens
  - Sevelamer Carbonate
  - Omega-3 products
- Guidance Agenda
  - rDNA origin reference peptides guidance pending
  - rDNA origin RLD controls are meeting GDUFA goals
- Research
  - Immunogenicity of peptide related impurities
  - High resolution analytics and multivariate data comparisons

Analyze the Pieces
Evaluate Equivalence of the Product

Generic Access in all Product Categories Inhalation Products



- Inhalation Product Research
  - Role of dissolution, particle size and PK studies
  - CFD modeling of deposition
  - Non Q1-Q2 inhalation products
- Leads to Guidance

Product-Specific Recommendations for Inhalation Products

Thirteen, as of the April 2016 posting

- Fluticasone propionate/salmeterol Xinafoate DPI (9/13)
- Albuterol MDI (9/13)
- Budesonide/formoterol fumarate MDI (6/15)
- Levalbuterol tartrate MDI (6/15)
- Formoterol fumarate DPI (9/15)
- Aclidinium bromide MDI (9/15)
- Ciclesonide MDI (1/16)
- Beclomethasone dipropionate MDI (1/16)
- Mometasone furoate/formoterol fumarate MDI (1/16)
- Fluticasone furoate/vilanterol trifenatate DPI (4/16)
- Fluticasone furoate DPI (4/16)
- Indecaterol maleate DPI (4/16)
- Mometasone furoate MDI (4/16)

Generic Access in all Product Categories
Ophthalmic Products

- Ophthalmic Products
  - Nine coordinated grants on in vitro characterizatic delivery modeling
  - Modeling and simulation tool chain: PBPK for oph
    - SimulationsPlus
    - CFD Research
  - In vitro release methods
    - University of Eastern Finland (suspension)
    - Texas A&M (emulsion)
    - University of Connecticut (ointments)
- Q3 In vitro approach for Q1 and Q2 formulations
  - Cyclosporine Emulsion (2013)
  - Difluprednate Emulsion (2016)
- Other Guidance
  - 10 ophthalmic suspension guidances
  - Research on study designs for aqueous humor PK
  - Q3 approaches

Generic Access in all Product Categories Nasal Products

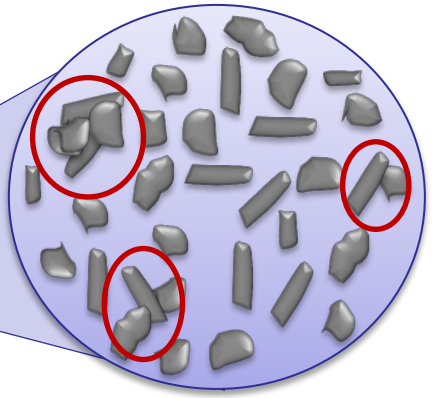
- Nasal Products
  - Use of PK studies alone for BE: in vitro, in vivo and modeling projects
- Innovative Technology
  - MDRS particle sizing
  - Instrument first available in 2012
  - ANDA approval in 2016 supported by this technology

API + excipient particle in the slide

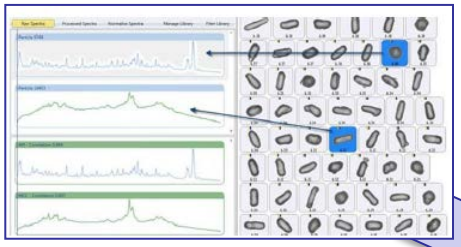
MDRS

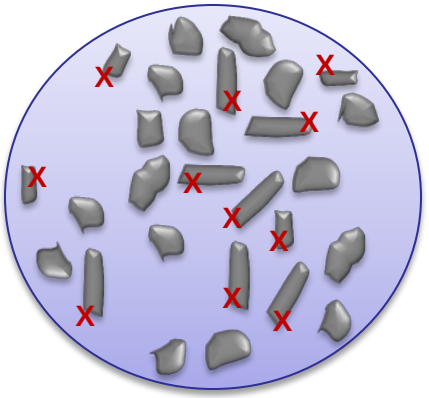
Slide containing the sample

Sample

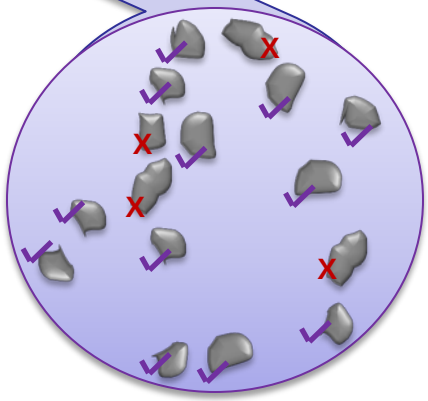


Exclusion of agglomerate/ touching particles (solidity filter)

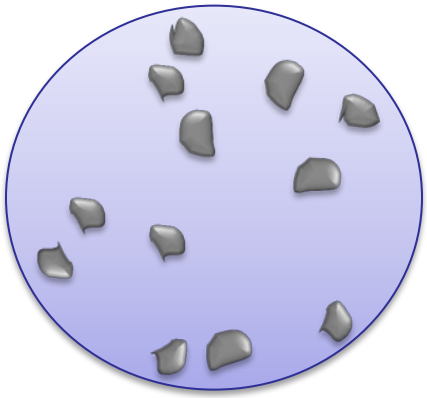




Classification of excipients using morphology filters (elongation filter)



Raman id of API; exclusion of excipient particles having overlapping morphology



Only API particle for size measurement

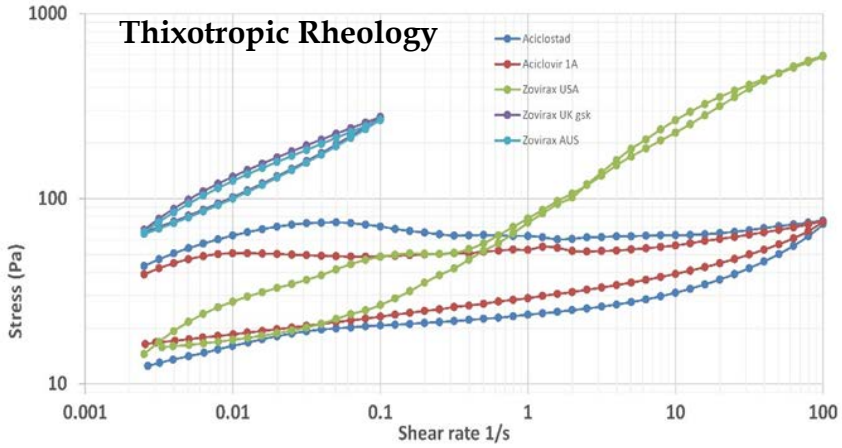
Generic Access in all Product Categories
Topical Dermatological Products

- Topical Dermatological Products
  - Six coordinated grants (international: US, Europe, Australia) that include
    - New in vivo data
    - Manufacturing of semi-solid formulations
    - Characterization of semi-solid formulations
    - New PBPK modeling approaches
  - Advanced Q3 Equivalence

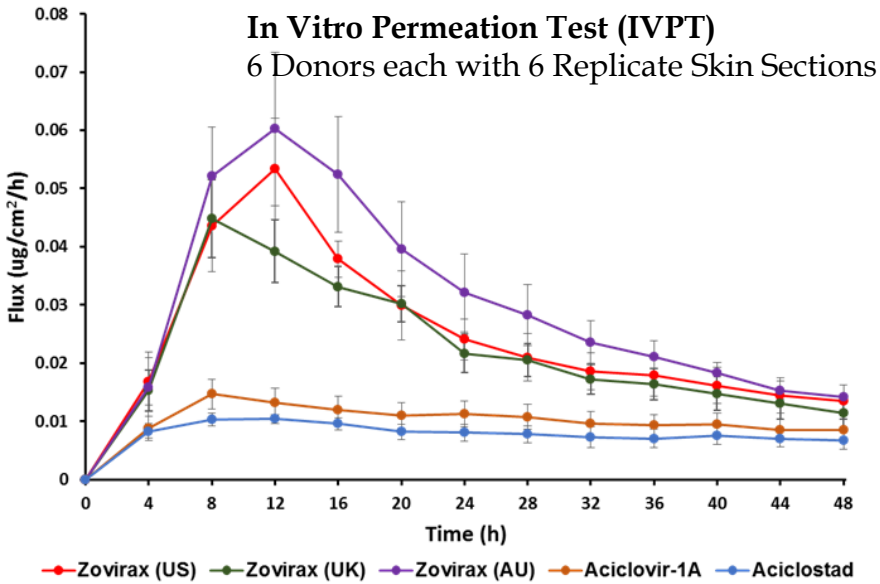
Topical Drug Products [3]
Clinical endpoint BE studies helped make generics available for only **~23.9%** of RLDs
In vivo vasoconstrictor BE studies helped make generic glucocorticoids available for another **~13.8%** of RLDs
Total % of topical products with generics ➔ **37.7%**

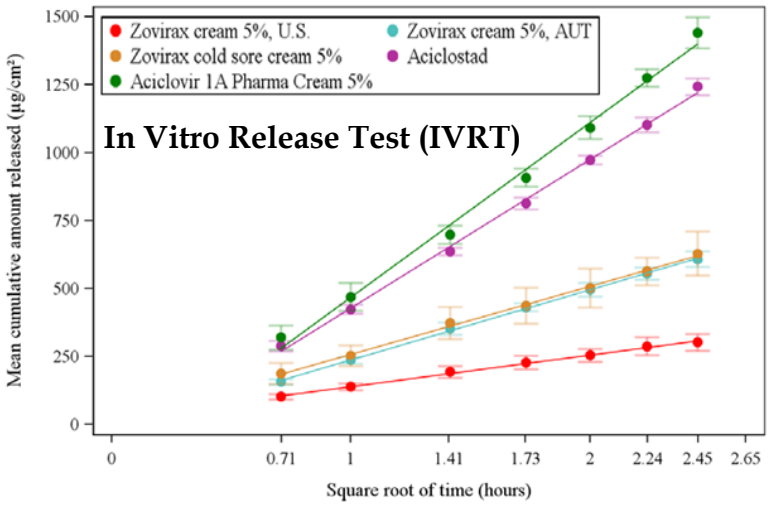
Q3 Testing: Acyclovir 5% Creams

	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 alcohol	Cetyl alcohol	Cetyl alcohol
	SLS	SLS	SLS	[redacted]	
	Poloxamer 407	Poloxamer 407	Poloxamer 407		
	[redacted]	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



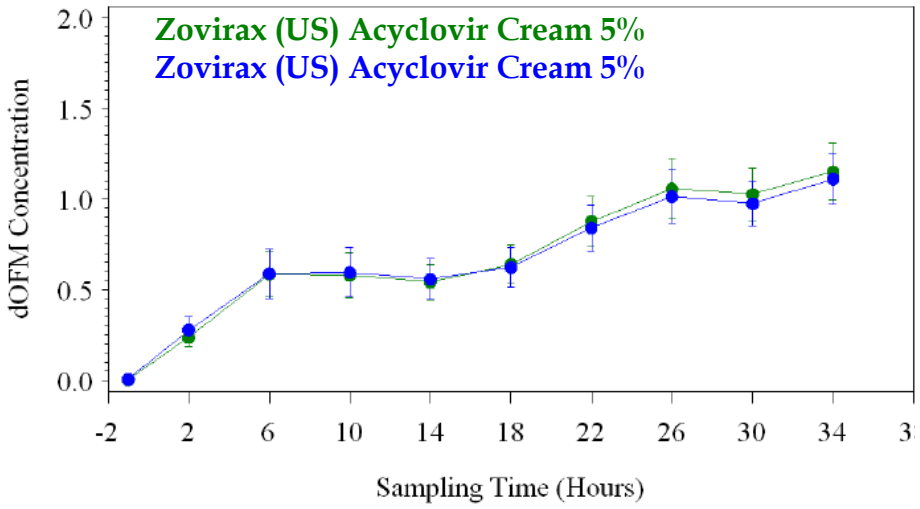
In Vitro Permeation Test (IVPT)
6 Donors each with 6 Replicate Skin Sections

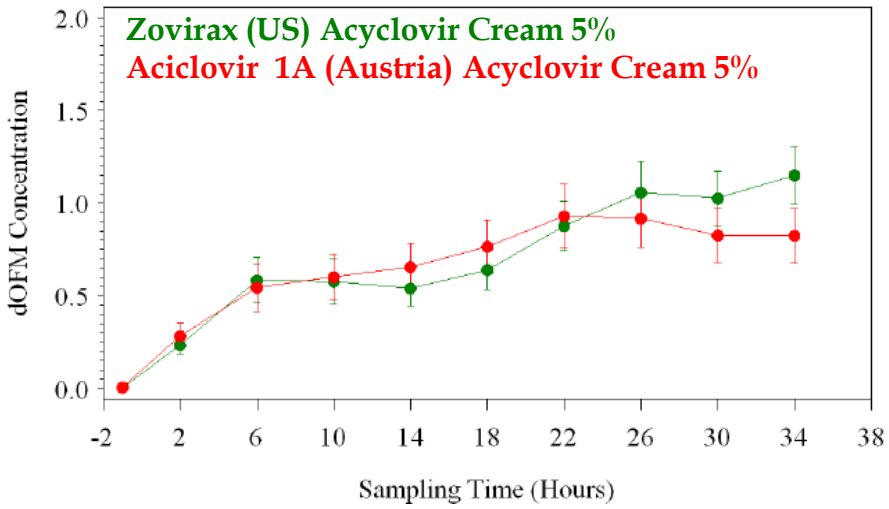




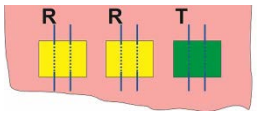
In Vivo dOFM: (dermal Open Flow Microperfusion)

Dermal Pharmacokinetics by dOFM (20 subjects)





Outcome variable	$CI_{90\%}$
log(AUC0-36h)	[-0.148 ; 0.162] or [86.2 % ; 117.5 %]
log(C_{max})	[-0.155 ; 0.190] or [85.7 % ; 120.9%]

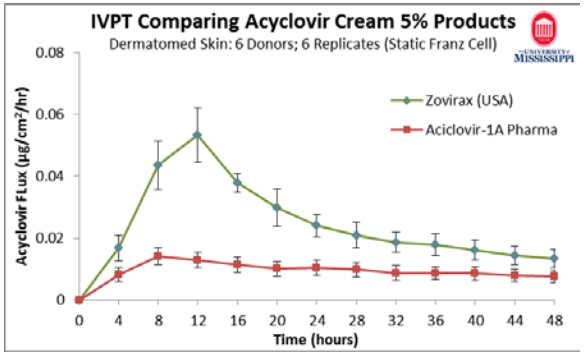


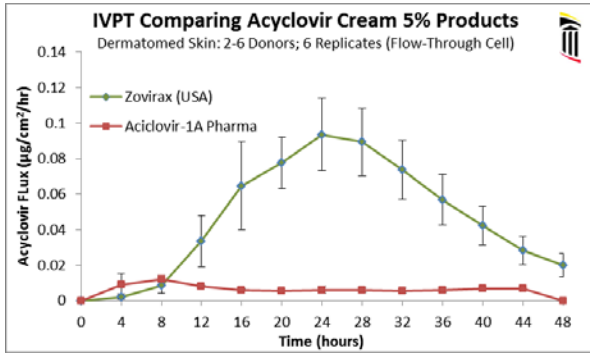
JOANNEUM RESEARCH HEALTH

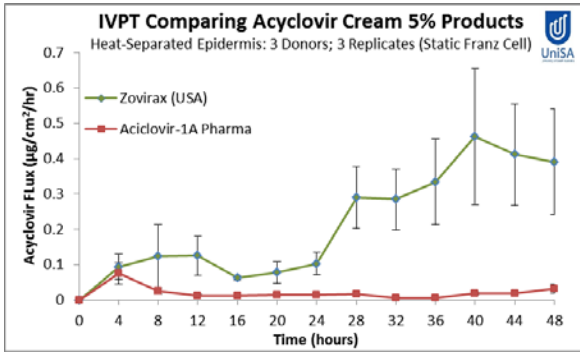
Outcome variable	$CI_{90\%}$
log(AUC0-36h)	[-0.369 ; 0.050] or [69.1 % ; 105.2 %]
log(C_{max})	[-0.498 ; 0.022] or [60.8 % ; 102.2%]

Scaled Average BE: Acyclovir Cream 5% IVPT

- **Negative Controls** for BE: Aciclovir-1A® vs. Zovirax® US







Aciclovir-1A® (T) vs. **Zovirax® US (R)**

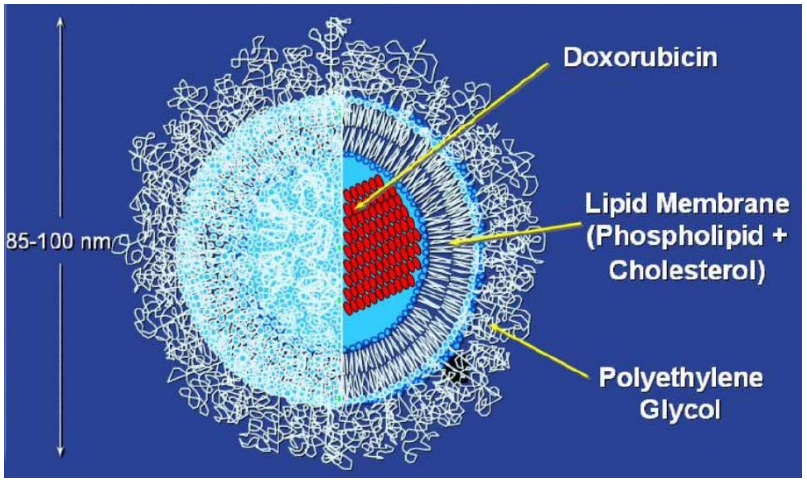
IVPT PK Endpoint	Maximum Flux **(Jmax)**	Total Bioavailability **(AUC)**
Point Estimate	0.2902	0.3661
Σ Within Reference	0.5747	0.4193
SABE [0.80, 1.25]	2.3828 (Non-BE)	1.8843 (Non-BE)
SABE [0.75, 1.33]	2.2138 (Non-BE)	1.7932 (Non-BE)
N for [0.80, 1.25]	8	20
N for [0.75, 1.33]	6	12

Aciclovir-1A® (T) vs. **Zovirax® US (R)**

IVPT PK Endpoint	Maximum Flux **(Jmax)**	Total Bioavailability **(AUC)**
Point Estimate	0.1722	0.1042
Σ Within Reference	0.5214	0.5512
SABE [0.80, 1.25]	4.4326 (Non-BE)	7.2356 (Non-BE)
SABE [0.75, 1.33]	4.2964 (Non-BE)	7.0832 (Non-BE)
N for [0.80, 1.25]	6	8
N for [0.75, 1.33]	4	6

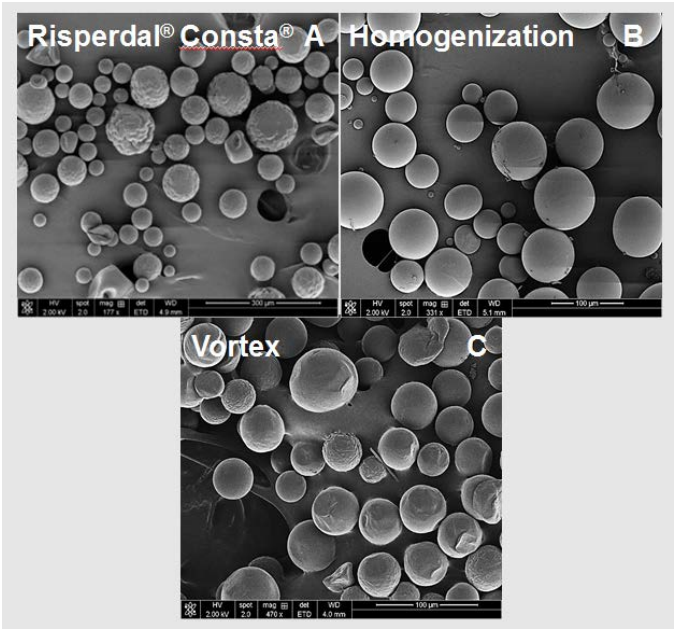
Generic Access in all Product Categories Liposomes and Nanomaterials

- 7 grants on in vitro release, product characterization and linkage to critical manufacturing variables
- Guidance on Liposomal Injections (3), Subq nanomaterial injection, Ferumoxytol, Sodium ferric gluconate



Generic Access in all Product Categories Microspheres and LAI

- 9 grants related to material characterization, in vitro release, in vivo animal data and modeling
- Guidance for Risperidone and Naltrexone IM injection



Generic Access in all Product Categories Complex Drug-Device Combinations

- DPI, MDI, nasal spray, transdermal system, auto-injectors
- New Draft Guidance
  - multiple MDI, DPI, Nasal Spray guidance now available
  - Adhesion for transdermal systems
- Research
  - Irritation for transdermal systems
  - Patient use factors

Generic Access in all Product Categories Abuse Deterrent Formulations

- Provides a path for generic versions of abuse deterrent opioid formulations
- Relies on comparative in vitro and PK studies

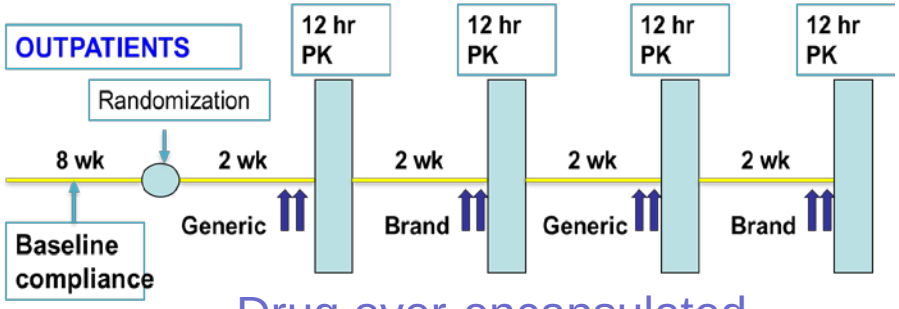
- Essential GDUFA Research
- $500,000 ADF contract with NIPTE (UMD, Purdue) issued in 2013
- ORISE Fellows and equipment in FDA's DPA and DPQR labs for testing ADF starting in 2013

Confidence in Generic Drug Substitution Brand-to-Generic Switching Studies in Patients

- All completing studies confirm the conclusions of the studies submitted in the ANDA
- Results on AED and immunosuppressants presented at medical professional societies that have been skeptical of generic substitution
  - American Epilepsy Society Annual meeting
  - American Academy of Neurology Annual meeting
  - Antiepileptic Drug and Device Trials XIII Annual meeting
  - American Transplant Congress meeting

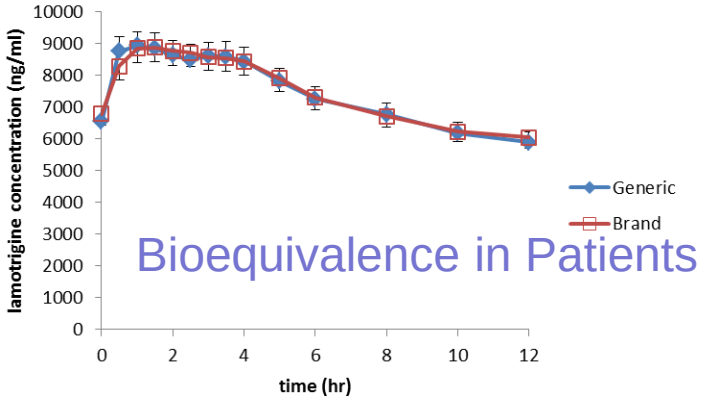
Brand vs Generic lamotrigine Bioequivalence in Epilepsy Patients (BEEP Study)

Study Design



Drug over-encapsulated

Primary Outcome



Bioequivalence in Patients

Patient Demographics

Sex	Male N=20	Female N=15	N=35
Age Range (Mean years)	19-66 (44)	20-63 (39)	19-66 (42)
Epilepsy			
Focal	17	10	27
Generalized	3	5	8
AED concomitant			
Valproic acid (inhibitor)	3	0	3
Inducer	3	3	6
Smoking (inducer)	1	2	3
Comorbid conditions			
None	9	4	13
One or more	11	11	22

Generic Brittle Patients

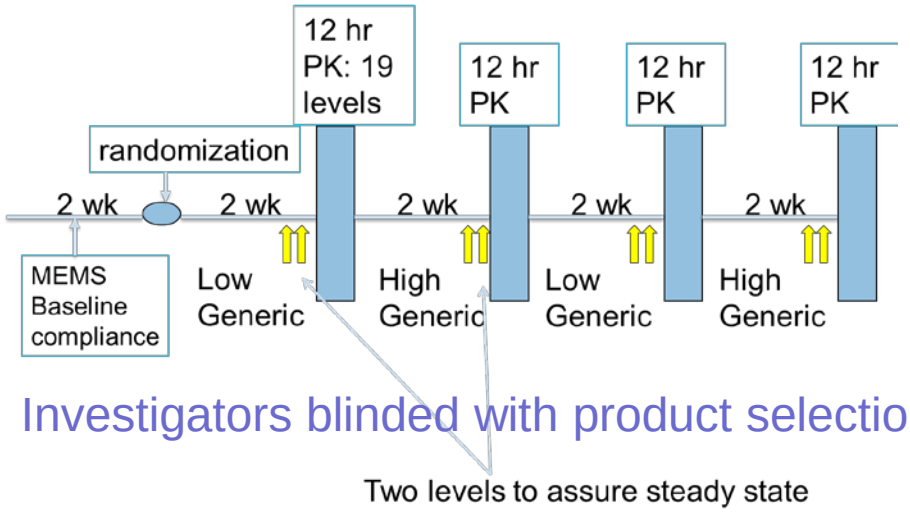
	Generic to Brand GMR(CI)
AUC	99.4% (97.23-101.61%)
Cmax	101.6% (98.79-104.51%)

Secondary Outcome

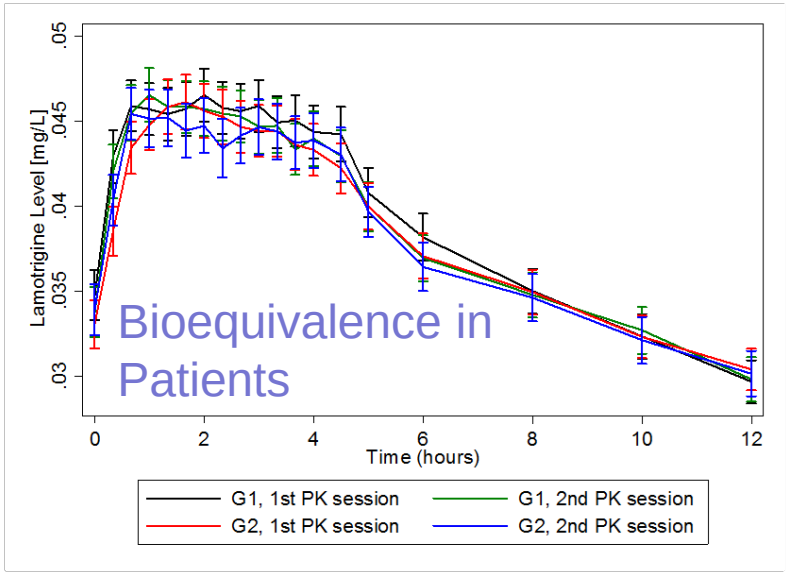
Secondary analysis of seizure control and dose-related adverse events support BE

Generic vs Generic: Multiple Dose Study Design

Study Design



Primary Outcome



Patient Demographics

	Sequence 1 (n=14)	Sequence 2 (n=19)
Age, years	42·7 (31·2–55·9)	49·4 (32·6–52·6)
Previous history of sensitivity to drug product switches	1 (7%)	3 (16%)
Seizure exacerbations	1 (7%)	2 (11%)
Increased adverse events	0	1 (5%)

Secondary Outcome

- No loss of seizure control

- No unexpected adverse effects and standardized side effect measure scores were not different between generics

Epilepsia
Official Journal of the International League Against Epilepsy

FULL-LENGTH ORIGINAL RESEARCH

Generic lamotrigine versus brand-name Lamictal bioequivalence in patients with epilepsy: A field test of the FDA bioequivalence standard

*Tricia Y. Ting, †Wenlei Jiang, †Robert Lionberger, ‡Jessica Wong, ‡Jace W. Jones, ‡Maureen A. Kane, *Allan Krumholz, †Robert Temple, and ‡James E. Polli

Epilepsia, 56(9):1415–1424, 2015
doi: 10.1111/epi.13095

Dr. Tricia Y. Ting is an epileptologist and associate professor of neurology at University of Maryland.

SUMMARY

Objective: To test the current U.S. Food and Drug Administration (FDA) bioequivalence standard in a comparison of generic and brand-name drug pharmacokinetic (PK) performance in "generic-brittle" patients with epilepsy under clinical use conditions.

Methods: This randomized, double-blind, multiple-dose, steady-state, fully replicated bioequivalence study compared generic lamotrigine to brand-name Lamictal in "generic-brittle" patients with epilepsy (n = 34) who were already taking lamotrigine. Patients were repeatedly switched between masked Lamictal and generic lamotrigine. Intensive PK blood sampling at the end of each 2-week treatment period yielded two 12-h PK profiles for brand-name and generic forms for each patient. Steady-state area under the curve (AUC), peak plasma concentration (C_{max}), and minimum plasma concentration (C_{min}) data were subjected to conventional average bioequivalence (ABE) analysis, reference-scaled ABE analysis, and within-subject variability (WSV) comparisons. In addition, generic-versus-brand comparisons in individual patients were performed. Secondary clinical outcomes included seizure frequency and adverse events.

Results: Generic demonstrated bioequivalence to brand. The 90% confidence intervals of the mean for steady-state AUC, C_{max}, and C_{min} for generic-versus-brand were 97.2–101.6%, 98.8–104.5%, and 93.4–101.0%, respectively. The WSV of generic and brand were also similar. Individual patient PK ratios for generic-versus-brand were similar but not identical, in part because brand-versus-brand profiles were not identical, even though subjects were rechallenged with the same product. Few subjects had seizure exacerbations or tolerability issues with product switching. One subject, however, reported 267 focal motor seizures, primarily on generic, although his brand and generic PK profiles were practically identical.

Significance: Some neurologists question whether bioequivalence in healthy volunteers ensures therapeutic equivalence of brand and generic antiepileptic drugs in patients with epilepsy, who may be at increased risk for problems with brand-to-generic switching. Bioequivalence results in "generic-brittle" patients with epilepsy under clinical conditions support the soundness of the FDA bioequivalence standards. Adverse events on generic were not related to the small, allowable PK differences between generic and brand.

KEY WORDS: Bioequivalence, Switchability, Lamotrigine, Generic-brittle, Narrow therapeutic index.

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*Department of Neurology, University of Maryland, Baltimore, Maryland, U.S.A.; †Food and Drug Administration, White Oak, Maryland, U.S.A.; and ‡Department of Pharmaceutical Sciences, University of Maryland, Baltimore, Maryland, U.S.A.
Address correspondence to James E. Polli, Department of Pharmaceutical Sciences, University of Maryland, 20 Penn Street, Baltimore, MD 21201, U.S.A. E-mail: jpolli@rx.umaryland.edu

EPILEPSY CURRENTS

Current Literature
In Clinical Science

Generic Substitution of AEDs: Is it Time to Put This Issue to Rest?

by Barry E. Gidal, PharmD

Epilepsy Currents, Vol. 16, No. 1 (January/February) 2016 pp. 18–20

"Clearly, this well designed study represents a major step forward in addressing the epilepsy community's concerns and provides valuable insight regarding AED PK variability."

"While encouraging, these observations do require confirmation in other patient populations. This issue of individual outliers certainly merits further study."

"Final data analysis from the EQUIGEN study group (EQUIvalence among GENeric AEDs) is near completion and should help further clarify this issue."

Generic-to-generic lamotrigine switches in people with epilepsy: the randomised controlled EQUIGEN trial

Michael D Privitera, Timothy E Welty, Barry E Gidal, Francisco J Diaz, Ron Krebill, Jerzy P Szaflarski, Barbara A Dworetzky, John R Pollard, Edmund J Elder Jr, Wenlei Jiang, Xiaohui Jiang, Michel Berg

Summary

Background Patients and clinicians share concerns that generic drug substitution might lead to loss of efficacy or emergence of adverse events. In this trial, we assessed US Food and Drug Administration (FDA) bioequivalence standards by studying the effects of switching between two disparate generic immediate-release lamotrigine products in patients with epilepsy.

Lancet Neurol 2016; 15: 365–72
Published Online
February 11, 2016
http://dx.doi.org/10.1016/S1474-4422(16)00014-4

The safety of generic substitution in epilepsy

Emilio Perucca

Lancet Neurology, Feb 2016

"The EQUIGEN trial by Michael Privitera and colleagues published in *The Lancet Neurology* provides strong evidence that, at least for lamotrigine, concerns about generic substitution are largely misplaced."

"Overall, Privitera and colleagues' findings are quite reassuring, and organisations with a negative attitude to generic antiepileptic drug substitution should consider reviewing their position."

Substantial Increase about Patient Preference about Generic Drugs

Variations in Patients' Perceptions and Use of Generic Drugs: Results of a National Survey

Aaron S. Kesselheim, M.D., J.D., M.P.H.[1,3], Joshua J. Gagne, Pharm.D., Sc.D.[1,3], Jessica M. Franklin, Ph.D.[1,3], Wesley Eddings, Ph.D.[1,3], Lisa A. Fulchino, B.A.[1,3], Jerry Avorn, M.D.[1,3], and Eric G. Campbell, Ph.D.[2,3]

J Gen Intern Med
DOI: 10.1007/s11606-016-3612-7

Do you think generic drugs	% (95 % Confidence Interval) respondents answering definitely/ probably yes
Are as effective as their brand-name versions	87 (85, 90)
Are as safe as their brand-name versions	88 (86, 91)
Have the same side effects as their brand-name versions	80 (77, 83)
Are made of the same active ingredients as their brand-name versions	84 (82, 87)
How comfortable do you feel:	% (95 % Confidence Interval) responden answering very/somewhat comfortable
Asking your doctor to write a prescription for a generic drug if one is available	94 (92, 96)
Taking a generic drug that was prescribed for you by your doctor	97 (95, 98)
If your pharmacist filled the prescription with an FDA-approved generic version of that drug when your doctor prescribed a brand-name drug	90 (87, 92)
If your health insurance company required use of an available and FDA-approved generic version of a brand-name drug that your doctor prescribed*	60 (56, 63)

2014 Survey (Kesseheim et al.)
Over 80%

2007 Survey (Shrank et al.)
Less than 40%

Non-Caucasians
- prefer brand over generic
- More skeptical of generic drug clinical equivalence

Greater Physician Confidence about Generic Drug Safety and Efficacy

Prevalence and predictors of generic drug skepticism among physicians: Results of a National Survey

Kesselheim et al.
JAMA Internal Medicine, In press

Perceptions	Respondents who strongly or somewhat agree, proportion (%(95% CI))
Generics are as effective as their corresponding brand-name versions	89 (86-91)
Generics are as safe as their corresponding brand-name versions	91 (89-93)
Do not cause more adverse effects than their corresponding brand-name versions	73 (70-76)

2014 Survey (Kesselheim et al.)
89% believes generic are as effective as the RLD

Physician perceptions about efficacy of generic drugs

2009 Survey (Shrank et al.)
Over 23% expressed negative perceptions

Further work
- Limiting interactions with pharmaceutical marketing
- Directed educational outreach

Confidence in Generic Drug Substitution Post-Market Surveillance

Adverse Event Reports

- Which ANDA?
- Potential reporting biases
- How to normalize?
- Research on authorized generics

Claims and EHR Data

- Link to NDC code
- See substitution events
- Research on expected substitution patterns for different therapeutic classes
- Researching how to compare outcomes and usage patterns

Confidence in Generic Drug Substitution Product Specific Standards

NTI Drugs

- Same BE standards for high and low risk drugs does not build confidence
- Tighter BE standards when needed

pAUC Comparisons

- PK profile differences do not build confidence
- PK profile similarity when needed
- Identify clinically meaningful time points

Better Tools for Development and Review Pharmacometrics for Generics

NTI Drugs

- Exposure response analysis for identifying NTI drugs
- Draft Guidance:
  - tacrolimus ER, phenytoin, levothyroxine, carbamazepine
- Petition Response
  - Not needed for dalfampridine

pAUC Comparisons

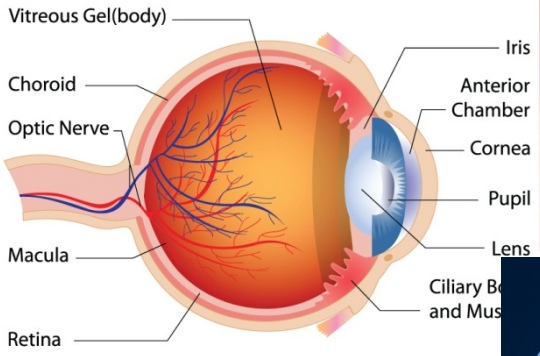
- PK/PD models to identify when pAUC for BE are needed
- Draft Guidance:
  - methylphenidate products
- Petition Response
  - No pAUC for Naproxen/Esomeprazole

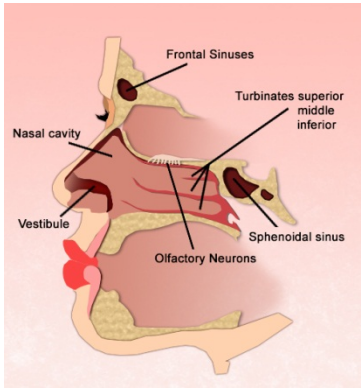
Better Tools for Development and Review
Non-systemic Absorption

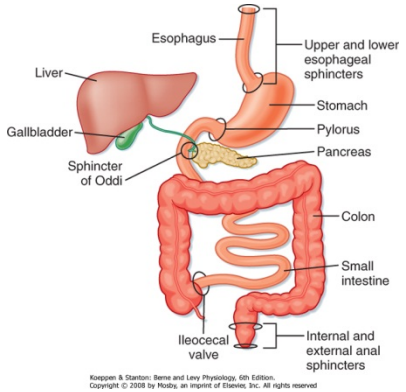
Drug substance
Formulations
In vitro performance

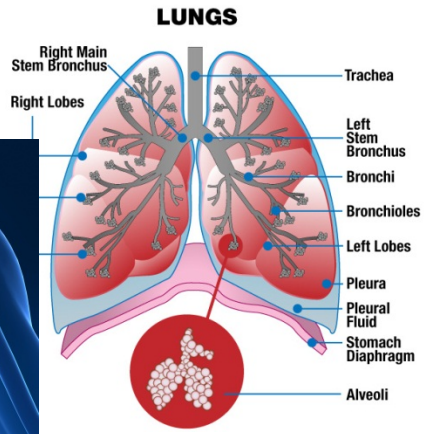
→ **Model** →

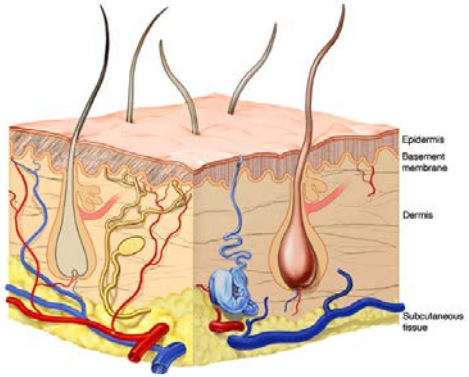
In vivo performance







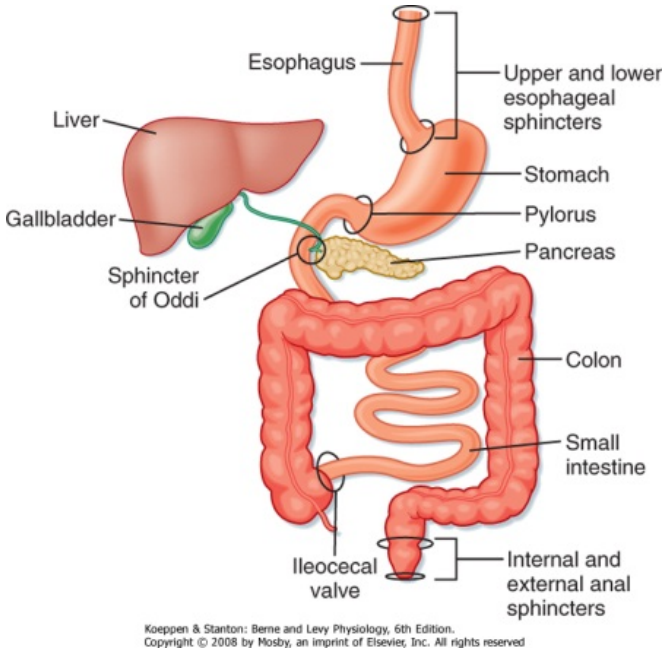




7 grants on PBPK for non-oral delivery routes

Better Tools for Development and Review Advancing In Vitro Release

- Solid Oral Dosage forms
  - Predictive Dissolution and Oral Absorption Models
  - Excipient impact on absorption
  - Pathway for generic versions of abuse-deterrent formulations
- Complex or Locally Acting Drugs
  - ~20 grants have outcomes of improved drug release, product performance or dissolution methods that can accelerate generic product development for complex or locally acting drugs



GDUFA Regulatory Science Input Requested Today

- Generic Access in all Product Categories
- Confidence in Generic Drug Substitution
- Better Tools for Development and Review

Summary

- Huge public health impact for small regulatory science investments
- Access
  - Access to $billion markets
  - Guidance on complex products
  - FDA research aids internal alignment on complex issues
- Confidence
  - FDA science supports public perceptions
- Faster Development and Review
  - Analytical tools
  - Modeling & simulation tools