“Genericize” the Complex Drug Product Landscape

Wenlei Jiang, Ph.D.
Senior Science Advisor

Office of Research and Standards
Office of Generic Drugs
Center for Drug Evaluation and Research
US FDA

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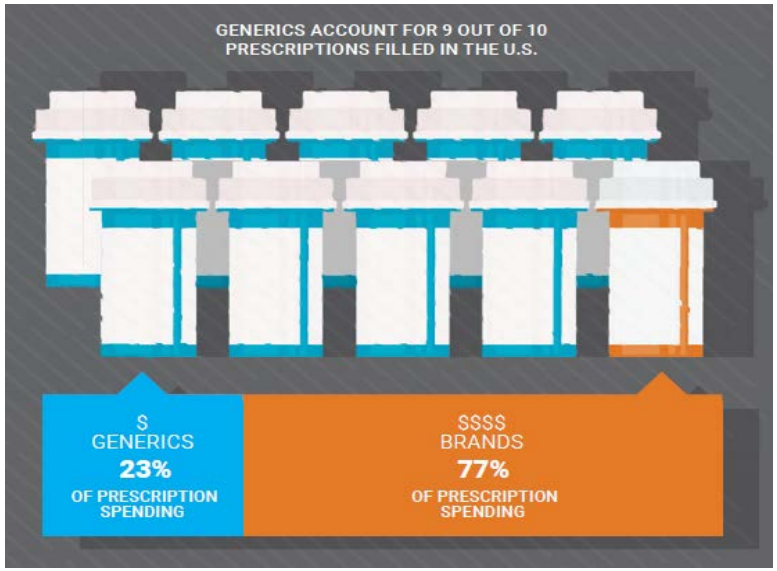
Generic Drugs in the United States

Overall Drug Products



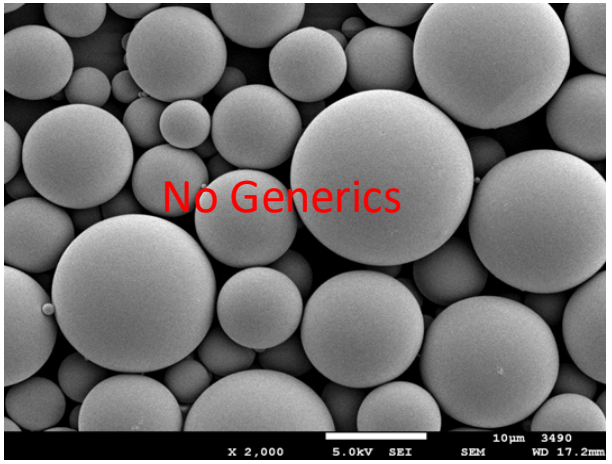
However,

Topical drug products with generics available < 40%
Ophthalmic products with generics available < 50%

Orally inhaled drug products

1 Generic

Poly-(lactic-co-glycolic acid) (PLGA) microspheres



https://accessiblemeds.org/sites/default/files/2018_aam_generic_drug_access_and_savings_report.pdf

Complex Drug Products

According to the **GDUFA II commitment letter**, complex drug products generally include products with

1) complex active pharmaceutical ingredients (APIs);
2) complex formulations;
3) complex routes of delivery;
4) complex dosage forms;
5) complex drug-device combination;
6) other products where there is complexity or uncertainty concerning the approval pathway or possible alternative approach would benefit from early scientific engagement.

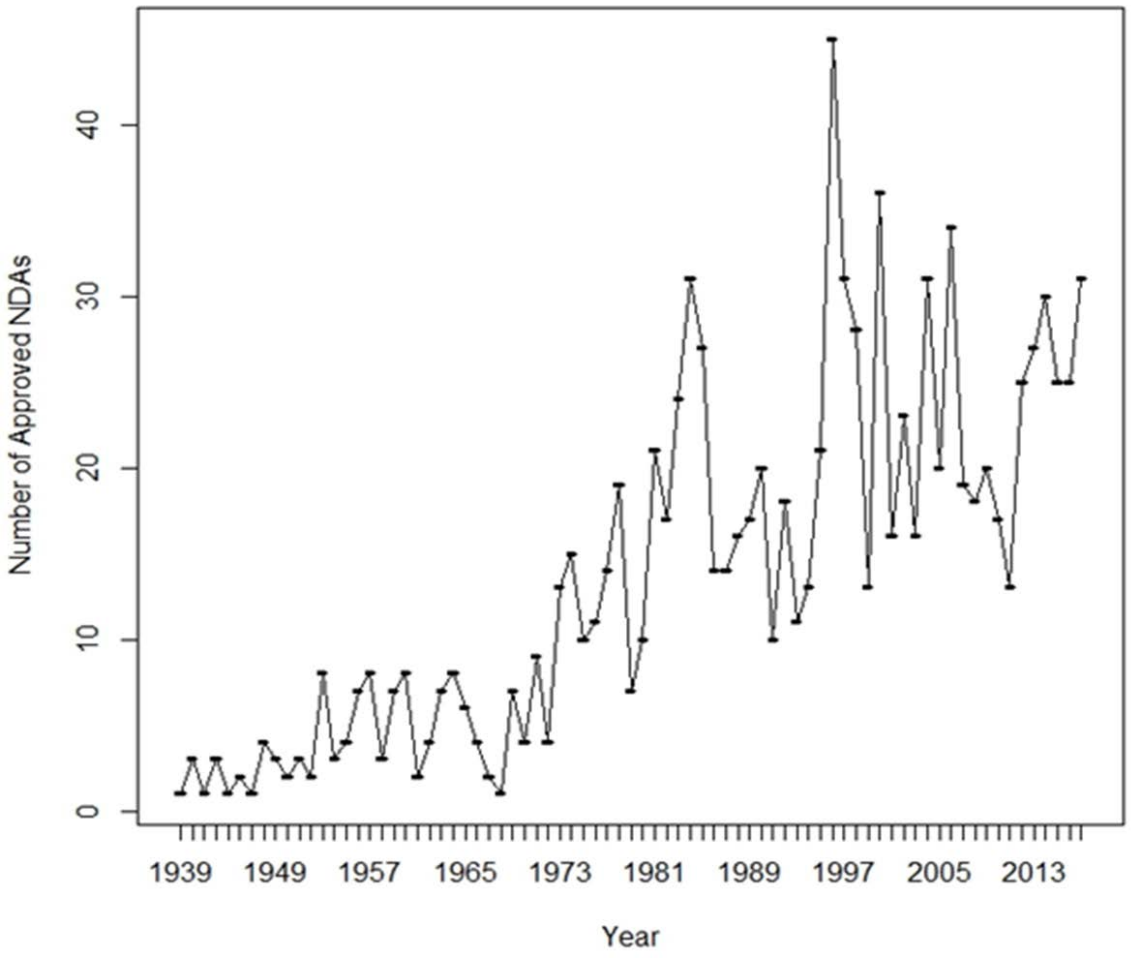
GDUFA: Generic Drug User Fee Amendments

https://www.fda.gov/downloads/forindustry/userfees/genericdruguserfees/ucm525234.pdf

Complex active pharmaceutical ingredient (API)	• Any drug product containing a complex API, regardless of administration routes and dosage forms. e.g., Conjugated Estrogen Tablet, Glatiramer Acetate Injection
Complex routes of delivery	• Any non-solution drug product with a non-systemic site of action (e.g., topical, ophthalmic, local gastrointestinal (GI) action) e.g., Cyclosporine Emulsion, Acyclovir Cream
Complex dosage forms/formulations	• Any non-oral complex formulation/dosage form product where there are often two or more discrete states of matter within the formulation e.g., Doxorubicin HCl Liposomes, Leuprolide Acetate for Depot Suspension
Complex drug-device combinations	• Where the drug constituent part is pre-loaded in a product-specific device constituent part or is specifically cross-labeled for use with a specific device, in which the device design affects drug delivery to the site of action and/or absorption e.g., Epinephrine Injection (autoinjector)
Other products	• Any solid oral opioid drug products with FDA approved labeling for that show properties (and thus gaining their labeling) to meaningfully deter drug abuse e.g., Hydrocodone Bitartrate ER Tablet

Lionberger R. Innovation for Generic Drugs: Science and Research Under the Generic Drug User Fee Amendments of 2012, Clinical Pharmacology & Therapeutics (CPT), 2019, Vol.105(4), p.878-885

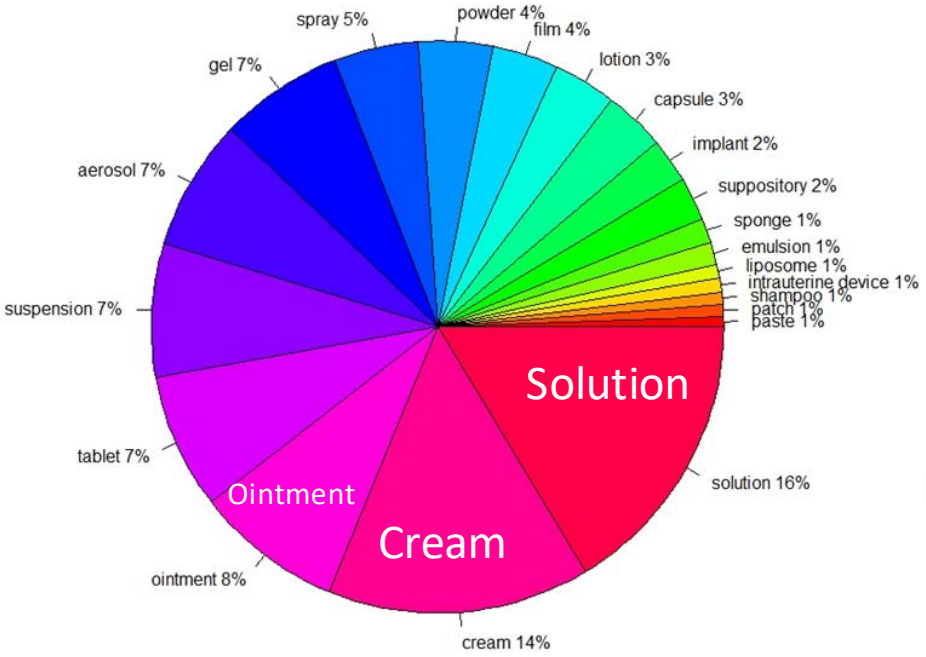
Approved New Drug Applications (NDAs) Considered as Complex Drug Products



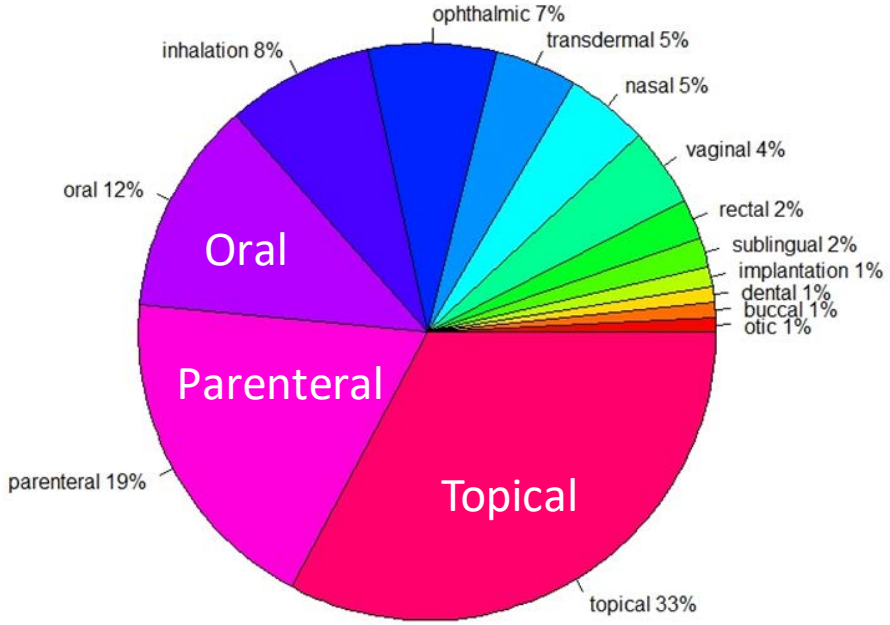
Data in this figure are up to 2017.

Distribution of Complex Drug Products Based on Dosage Forms and Administration Routes

Dosage Form



Administration Route



Data in these figures are up to 2017.

GDUFA Regulatory Research

The FDA committed to employ regulatory science initiatives for generic drugs based on 2012 GDUFA.

FY14 Research 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

FY19 Research Priorities

- Complex active ingredients, formulations, or dosage forms
- Complex routes of delivery
- Complex drug-device combinations
- Tools and methodologies for bioequivalence and substitutability evaluation

Complex Drug Products

https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/ucm567695.htm

GDUFA Regulatory Research Communications

FDA and ASCPT Co-Sponsored ASCPT 2019 Pre-conference: PBPK Modeling for the Development and Approval of Locally Acting Drug Products **NEW**

GDUFA Implementation: Bi-Annual Industry Regulatory Science Work Group Meeting Minutes **NEW**

FY 2019 Generic Drug Regulatory Science Initiatives Public Workshop (May 1, 2019) **NEW**

Collaboration Opportunities

See a listing of available grant and fellowship opportunities

Priorities & Projects

Learn more about FDA generic drug research priorities, public workshops, and awarded projects

Guidances & Reports

View FDA generic drug research publications, including product-specific guidances and annual reports

Research Publications & Resources

Browse FDA generic drug research published in scholarly journal articles, presentations, and posters

https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/ucm567695.htm

Product-Specific Guidance Development

Total number of currently published Product Specific Guidances: 1,682

Product-Specific Guidances Arranged by Active Ingredient

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

Newly Added Guidances since February 1, 2019 (22 New; 52 Revisions) updated 2/22/2019

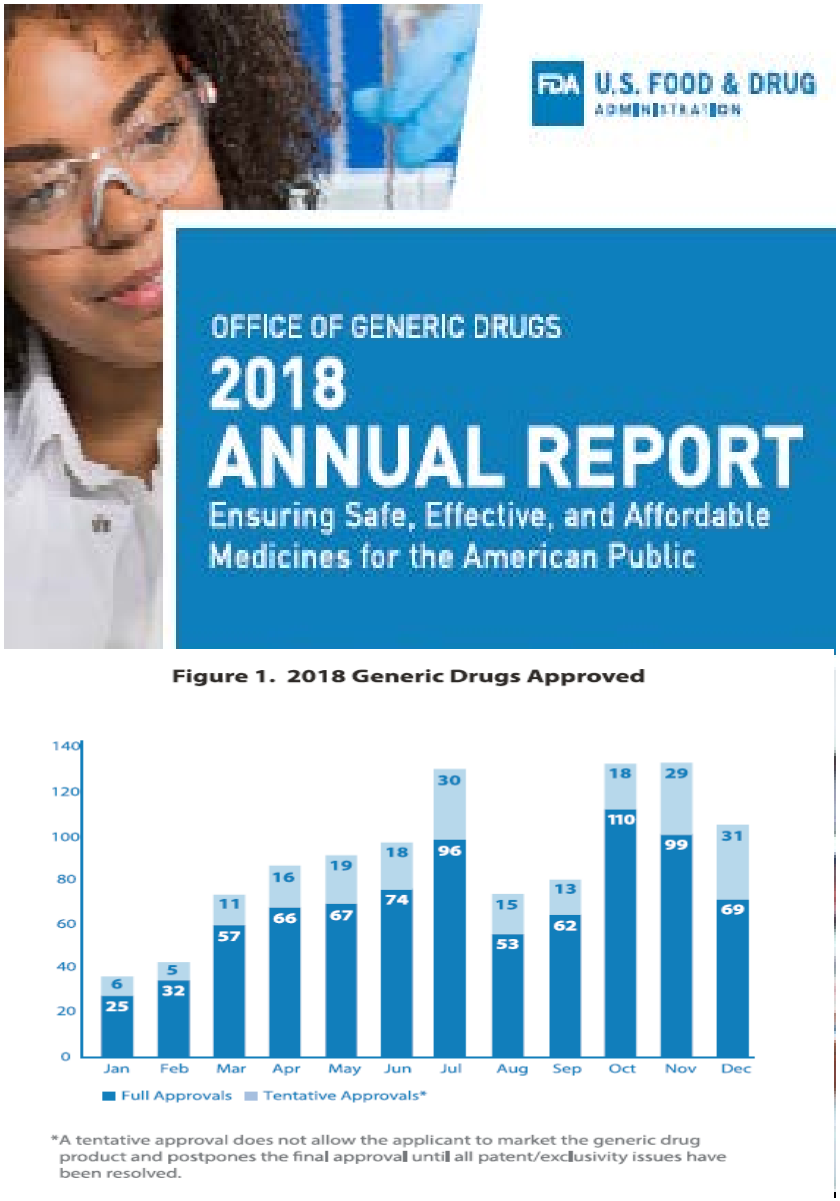
Active Ingredient (link to Specific Guidance)	Type	Route of Administration	Dosage Form	RLD Application Number (link to Orange Book)	Date Recommended
Acalabrutinib (PDF - 30KB)	Draft	Oral	Capsule	210259	2/2019
Acetaminophen; Caffeine; Dihydrocodeine bitartrate (PDF - 45KB)	Draft	Oral	Capsule	204785	2/2019
Angiotensin II acetate (PDF - 40KB)	Draft	Intravenous	Solution	209360	2/2019
Bexarotene (PDF - 56KB)	Draft	Topical	Gel	021056	2/2019

https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/ucm075207.htm

Pre-ANDA Meetings for Complex Drug Products

Meeting Type	Meeting Focus	Product Stages
Product Development Meeting	• Help ANDA applicant engage early with FDA about scientific exchange of an individual product development program, e.g. alternative bioequivalence approach	During complex generic product development stage
Pre-submission Meeting	• Discuss and explain the format and content of an ANDA to be submitted	6-12 months before ANDA submission
Mid-review-cycle meeting	• Provide the applicant an update about the application review status	During ANDA review

Improve quality of ANDA submissions and reduce the number of review cycles required to obtain ANDA approval, particularly for complex generic products



https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/ucm631710.htm

FDA News Release

FDA approves first generic Advair Diskus

For Immediate Release

January 30, 2019

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm630151.htm

FDA Statement

Statement from FDA Commissioner Scott Gottlieb, M.D., on 2019 efforts to advance the development of complex generics to improve patient access to medicines

For Immediate Release

Jan 30, 2019

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm630160.htm

Acknowledgements

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U.S. FOOD & DRUG ADMINISTRATION

Thank you!

Any Question?