U.S. FOOD & DRUG ADMINISTRATION

Regulatory Utility of Mechanistic Modeling to Support Alternative Bioequivalence Approaches

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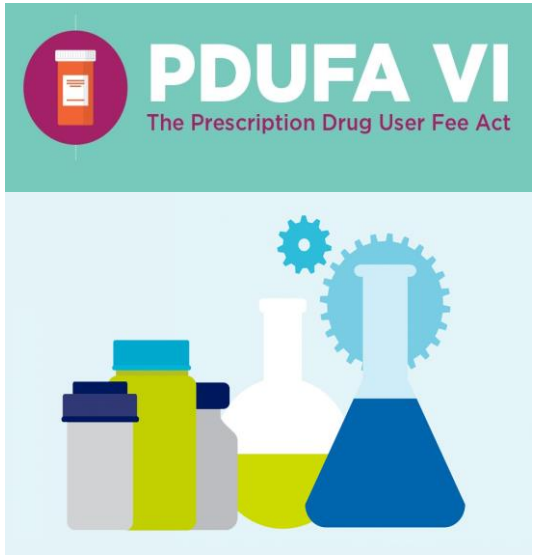
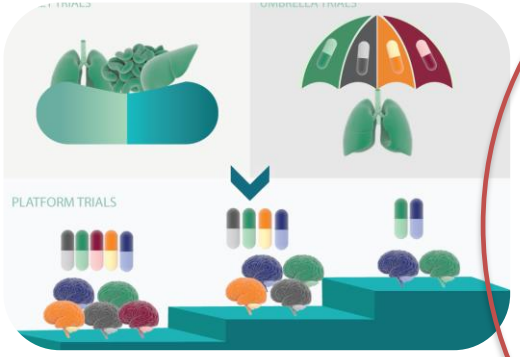
The Center for Research on Complex Generics (CRCG) facilitates research collaborations t
increase access to safe and effective generic drugs.

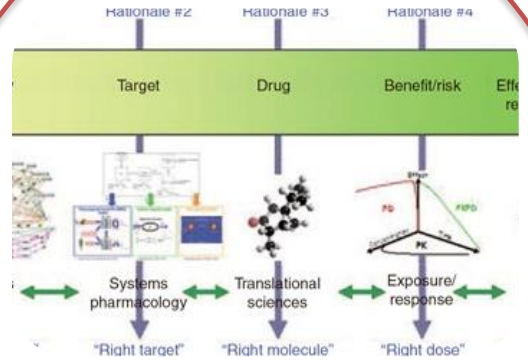
Building Partnerships to Advance Science

PDUFA VI: Regulatory Decision Tools





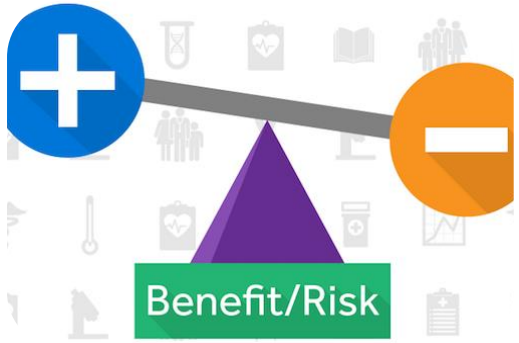
Complex Innovative Trial Designs



Model-informed Drug Development

Biomarker Qualification

Real World Evidence



Benefit/Risk Assessment

Patient Voice

Model-Informed Drug Development

- "Development and application of pharmaco-statistical models of drug efficacy and safety from preclinical and clinical data to improve drug development knowledge management and decision-making" (Lalonde)

Indication	MBDD approach adopted	Efficiencies gained over historical designs and analysis
Thromboembolism[a]	Omit phase IIa, model-based dose–response relationship, adaptive phase IIb design	2,750 Fewer patients, 1 year shorter study duration
Hot flashes	Model-based dose–response relationship	1,000 Fewer patients
Fibromyalgia	Prior data supplementation, model-based dose–response relationship, sequential design	760 Fewer patients, 1 year shorter study duration
Type 2 diabetes	Prior data supplementation, model-based dose–response relationship	120 Fewer patients, 1 year shorter study duration
Gastroesophageal reflux	Model-based dose–response relationship	1,025 Fewer patients
Rheumatoid arthritis	Model-based dose–response relationship	437 Fewer patients, increased probability of success
Global anxiety disorder	Omit phase IIb	260 Fewer patients, 1 year shorter study duration
Lower urinary tract symptoms	Meta-analysis	Increased probability of success
Urinary incontinence	Meta-analysis	Increased probability of success

MBDD, model-based drug development.

- FDA identified MIDD as an important pathway for lowering drug attrition and dealing with regulatory uncertainty

Lalonde 2007 [PMID 17522597] | Milligan 2013 [PMID 23588322]

Drug Development Tools: Fit-for-Purpose Initiative

Background

The Fit-for-Purpose (FFP) Initiative provides a pathway for regulatory acceptance of dynamic tools for use in drug development programs. Due to the evolving nature of these types of drug development tools (DDTs) and the inability to provide formal qualification, a designation of 'fit-for-purpose' (FFP) has been established. A DDT is deemed FFP based on the acceptance of the proposed tool following a thorough evaluation of the information provided. The FFP determination is made publicly available in an effort to facilitate greater utilization of these tools in drug development programs.

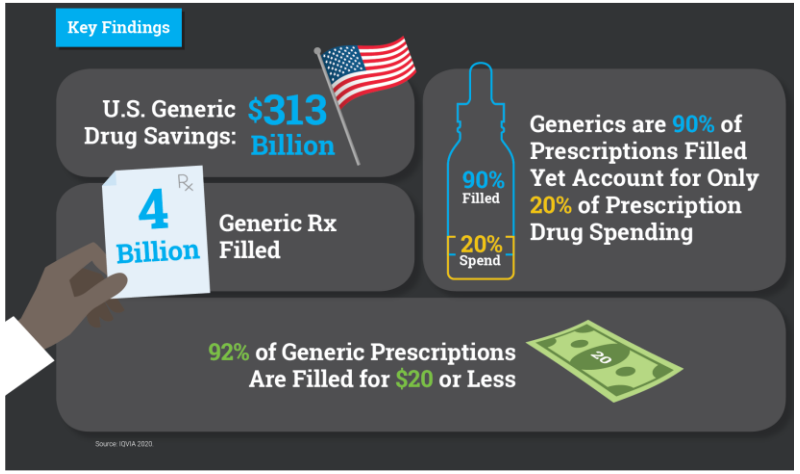
https://www.fda.gov/drugs/development-approval-process-drugs/drug-development-tools-fit-purpose-initiative

Generic Drugs in the United States

Generic Drugs:

- **90%** of prescriptions
- **20%** of prescription drug spending

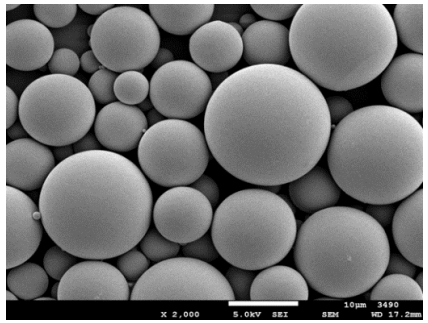
Overall Drug Products



Orally inhaled drug products (OIDP)

First Generic for OIDP (approved Jan 30, 2019)

Poly-(lactic-co-glycolic acid) (PLGA) microspheres Long-acting injectable products



No Generics

~30% are **Complex Products**
Per GDUFA II Commitment Letter Definition*

Topical drug products with generics available < 40%

Ophthalmic products with generics available < 50%

https://accessiblemeds.org/sites/default/files/2020-09/AAM-2020-Generics-Biosimilars-Access-Savings-Report-US-Web.pdf
GDUFA: Generic Drug User Fee Amendments
* https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf

Thank you!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