FY2018 Generic Drug Regulatory Science Initiatives Public Workshop

FDA Research Update on the FY18 Initiatives

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FY2018 GDUFA Priority Areas
15 priority areas under 4 broad categories

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https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm
Outline for Updates on Each Priority Area

• FDA Internal Research
• FY2017 Grants/Contracts
  – Ongoing Grants and Contracts Funded in FY2017
  – New FY2017 Contracts Awarded
    • No new grant was awarded in FY2017
• Potential FY2018 Grants/Contracts
• Outcomes 2017-2018 (May 2017- April 2018)
  – Public Workshops
  – Publications
  – Guidances
    • General guidances
    • Product-specific guidances (PSGs)
  – Notable ANDA Approvals
1. Complex active ingredients, formulations, or dosage forms

(1) Improve advanced analytics for characterization of chemical compositions, molecular structures and distributions in complex active ingredients

(2) Improve particle size, shape and surface characterization to support demonstration of therapeutic equivalence of suspended and colloidal drug products

(3) Establish predictive in silico, in vitro and animal studies to evaluate immunogenicity risk of formulation or impurity differences in generic products

(4) Develop predictive in vitro bioequivalence (BE) methods for long-acting injectables

(5) Develop better methods for evaluating abuse deterrence of generic solid oral opioid products, including in vitro alternatives to in vivo nasal studies

https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm
(1) Improve advanced analytics for characterization of chemical compositions, molecular structures and distributions in complex active ingredients

- FDA Internal Research
  - Characterization of complex active pharmaceutical ingredients (APIs)
    - Polymeric drugs, e.g., patiromer
    - Synthetic oligonucleotides
    - Peptides
      - Detecting and quantifying D-isomers in peptide drug products
  - Characterization of polymeric excipient critical quality attributes (CQAs): Polydimethylsiloxane (PDMS)

- Ongoing Grants and Contracts Funded in FY2017
  - Pentosan polysulfate in urine
(1) Improve advanced analytics for characterization of chemical compositions, molecular structures and distributions in complex active ingredients

• Outcomes 2017-2018
  – Guidances:
    • General guidance (draft): “ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin” (10/2017)
    • PSG: Sucralfate oral suspension (10/2017)
  – Notable ANDA approvals:
    • Glatiramer acetate for injection, 40 mg/mL (10/2017)-first generics
    • Sevelamer carbonate tablets (7/2017)-first generics
    • Sevelamer carbonate powder for suspension (6/2017)-first generics
(2) Improve particle size, shape and surface characterization to support demonstration of therapeutic equivalence of suspended and colloidal drug products

- **FDA Internal Research**
  - Quantifying albumin structural changes due to manufacture process and corresponding changes in binding affinity to paclitaxel
  - Evaluating accuracy, precision and reproducibility of new particle analysis methods for measuring the size and concentration of liposomal and emulsion drug products
  - Examining if/how particle concentration measurement can be used to evaluate sameness of complex suspension and liposome formulations
  - Developing nanoparticle tracking in nanofluidic slits to simultaneously measure the CQAs (e.g., concentration, size, and composition) of liposomal formulations.
  - Cryo-electron microscopy (cryo-EM) for morphological characterization of complex nano-drug products to improve the review of in vitro bioequivalence studies
  - Particle size characterization methods for API in suspension-based aqueous nasal spray products using Morphologically-Directed Directed Raman Spectroscopy (MDRS)
  - New methods on equivalence testing of complex particle size distribution profiles using Earth Mover’s Distance (EMD)

- **Outcomes 2017-2018**
  - Public workshops:
    - “Demonstrating Equivalence of Generic Complex Drug Substances and Formulations” (Oct 6, 2017)
    - “New Insights for Product Development and Bioequivalence Assessments of Generic Orally Inhaled and Nasal Drug Products” (Jan 9, 2018)
(2) Improve particle size, shape and surface characterization to support demonstration of therapeutic equivalence of suspended and colloidal drug products

- Outcomes 2017-2018 (Cont’d)
  - Publications:
  - Guidances (PSGs):
    - Barium sulfate oral suspension (02/2018)
    - Bupivacaine liposomal injection (02/2018)
    - Soybean oil injection (02/2018)
  - Notable ANDA approvals:
    - Doxorubicin liposomal injection (05/2017)-second approved generic
(3) Establish predictive in silico, in vitro and animal studies to evaluate immunogenicity risk of formulation or impurity differences in generic products

• FDA Internal Research
  – Immunogenicity assessment and impurity profiling
    • Peptides
    • Oligonucleotides

• Potential FY2018 Grants/Contracts
  – Evaluating immunogenicity risk of generic peptide drugs using non-clinical assays
(3) Establish predictive in silico, in vitro and animal studies to evaluate immunogenicity risk of formulation or impurity differences in generic products

• Outcomes 2017-2018
  – Guidance:
    • General guidance (draft): “ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin” (10/2017)
(4) Develop predictive in vitro bioequivalence (BE) methods for long-acting injectables

- **FDA Internal Research**
  - In vitro BE for suspension injectables

- **Ongoing Grants and Contracts Funded in FY2017**
  - Four grants and two contracts on long-acting injectable (LAI) modeling, poly(lactic-co-glycolic acid) (PLGA)-peptide interactions, and PLGA characterization

- **New FY2017 Contract**
  - “In vitro in vivo correlation of the long-acting injectable suspensions to improve scientific approaches to evaluate generic drugs”
    - Awarded to the University of Connecticut (#HHSF223201710135C)
  - “Development of analysis technique for structural characterization of star-shaped polyesters used for drug delivery”
    - Awarded to Akina Inc (#HHSF223201710123C)

- **Potential FY2018 Grants/Contracts**
  - Influence of raw materials, manufacturing variables, and storage conditions on bioequivalence of large peptides and potential peptide PLGA interactions
  - Impact of polymer source variations on parenteral microsphere drug product performance
(4) Develop predictive in vitro bioequivalence (BE) methods for long-acting injectables

• Outcomes 2017-2018
  – Publications:
  – Guidance:
    • PSG: Leuprolide acetate intramuscular injectable depot (02/2018)
(5) Develop better methods for evaluating abuse deterrence of generic solid oral opioid products, including in vitro alternatives to in vivo nasal studies

• FDA Internal Research
  – Lab-based, 16 active projects covering 9 key areas
    • Technical profiles of reference listed drugs (RLDs)
    • Determination of syringeability and injectability
    • In vitro manipulation and extraction studies
    • Nasal powder characterization
    • Nasal regional deposition model
    • Chewing IVIVC model
  – Quantitative analysis
    • IVIVC development of opioid products using in vitro chewing method and PBPK modeling
    • Advanced PK modeling of opioid following nasal insufflation of physically manipulated products (3-D computation fluid dynamics (CFD) model, regional deposition, dissolution/diffusion studies)
    • Pharmacokinetic/pharmacodynamic (PK/PD) relationship of abuse deterrent (AD) opioid products

• Ongoing Grants and Contracts Funded in FY2017
  – Contract on nasal PK study of opioids following insufflation of physically manipulated products (OXYCONTIN)
    • Study was completed. Preliminary PK results were obtained
Develop better methods for evaluating abuse deterrence of generic solid oral opioid products, including in vitro alternatives to in vivo nasal studies

Potential FY2018 Grants/Contracts
- Nasal PK/PD studies with oral agonist/antagonist combination products
- Oral chewing PK/PD studies with oral opioid products

Outcomes 2017-2018
- Publications:
- Guidances:
  - General guidance (final): “General principles for evaluating the abuse deterrence of generic solid oral opioid drug products” (Nov 2017)
2. Complex routes of delivery

(6) Improve Physiologically Based Pharmacokinetic (PBPK) models of drug absorption via complex routes of delivery (e.g., nasal, inhalation, dermal, ophthalmic)

(7) Expand characterization-based bioequivalence (BE) methods across all topical dermatological products

(8) Expand characterization-based BE methods across all ophthalmic products

(9) Develop more efficient alternatives to the use of forced expiratory volume in one second (FEV1) comparative clinical endpoint BE studies for inhaled corticosteroids

(10) Develop alternatives to comparative clinical endpoint BE studies for locally-acting nasal products

https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm
(6) Improve Physiologically Based Pharmacokinetic (PBPK) models of drug absorption via complex routes of delivery (e.g., nasal, inhalation, dermal, ophthalmic)

• FDA Internal Research
  – Topical: Physics-based modeling predictions of evaporation, spreading, and penetrability for non-Q1/Q2 solution product
  – Ophthalmic: PBPK-based assessment of impact of Q3 differences on local bioavailability/bioequivalence for 3 different suspension products; tear film break-up time and local bioavailability modeling of an emulsion product
  – Inhalation: Upper and lower human airway deposition predictions of solution pMDIs and “soft mist inhalers”
  – Nasal: Local and systemic delivery predictions of nasally insufflated abuse deterrent formulation
  – Locally-acting drug products physiochemical and pharmacokinetic knowledgebase

• Ongoing Grants and Contracts Funded in FY2017
  – 3 Grants for CFD-based modeling of lung deposition
  – 1 Grant for CFD and PBPK model for nasal products
  – 2 Grants to advance ophthalmic PBPK modeling
  – 2 Grants to advance topical/transdermal PBPK modeling
(6) Improve Physiologically Based Pharmacokinetic (PBPK) models of drug absorption via complex routes of delivery (e.g., nasal, inhalation, dermal, ophthalmic)

- **Potential FY2018 Grants/Contracts**
  - Formulation drug product quality attributes in dermal physiologically-based pharmacokinetic models for topical dermatological drug products and transdermal delivery systems
  - Characterize skin physiology parameters utilized in dermal physiologically-based pharmacokinetic model development across different skin disease states
  - CFD and discrete element modeling (DEM) approach for predictions of dry powder inhaler (DPI) drug delivery
  - Three-dimensional approach for modeling nasal mucociliary clearance via CFD
  - Potential contract/BAAs to support continued development of CFD and/or PBPK models for products with complex routes of delivery
  - Contract to order in vitro and animal studies to support internal research efforts
(6) Improve Physiologically Based Pharmacokinetic (PBPK) models of drug absorption via complex routes of delivery (e.g., nasal, inhalation, dermal, ophthalmic)

- Outcomes 2017-2018
  - Publications:
    - Pak J, et al., Computational modeling of drug transport across the in vitro cornea. *Computers in biology and medicine*. 2018 Jan 1;92:139-146
  - Upcoming public workshop:
    - PBPK modeling for locally-acting products (March 13, 2019, ASCPT Pre-Conference, Washington DC)
(7) Expand characterization-based bioequivalence (BE) methods across all topical dermatological products

**FDA Internal Research**
- Development of novel bio-relevant in vitro skin permeation tests (IVPT) using in-line flow through diffusion cells
- Manufacture of AT-rated topical ointment formulations for in vitro release test (IVRT) method validation

**Ongoing Grants and Contracts Funded in FY2017**
- 1 Contract to expand characterization-based BE methods across petrolatum-based topical ointments, including AT-coded ointments
- 3 Grants to advance in vitro cutaneous pharmacokinetic BE methods (IVPT studies) and expand characterization-based BE methods across all topical dermatological products
- 2 Grants to develop in vivo cutaneous pharmacokinetic BE methods (dermal microdialysis/microperfusion clinical studies) to expand the availability of novel, efficient BE methods across all topical dermatological products, including non-Q1/Q2 generics
(7) Expand characterization-based bioequivalence (BE) methods across all topical dermatological products

• Potential FY2018 Grants/Contracts
  – Bioequivalence of Topical Products: Evaluating the Cutaneous Pharmacokinetics of Topical Drug Products Using Non-Invasive Techniques
  – Bioequivalence of Topical Products: Elucidating the Thermodynamic and Functional Characteristics of Compositionally Different Topical Formulations
  – Establish a correlation between local and systemic drug concentrations leveraging dermal open-flow microperfusion (dOFM) data

• Outcomes 2017-2018
  – Publications:
Outcomes 2017-2018 (Cont’d)

Notable Guidances (PSGs):
Each includes a novel BE approach developed based on GDUFA Research

- Bimatoprost Topical Solution, 0.03% (02/2018)
- Crisaborole Topical Ointment, 2% (02/2018)
- Dapsone Topical Gel, 5% (rev 10/2017)
- Dapsone Topical Gel, 7.5% (10/2017)
- Docosanol Topical Cream, 10% (10/2017)
- Ivermectin Topical Cream, 1% (10/2017)
- Silver Sulfadiazine Topical Cream, 1% (07/2017)

Notable ANDA Approvals:
4 more generics approved for Acyclovir Topical Ointment, 5% (8 Total)
- All ANDAs approved based upon a characterization-based BE method
4 more first generics approved (all with PSGs)
- Estradiol Vaginal Cream USP, 0.01% (12/2017)
- Butenafine Hydrochloride Cream, 1% (11/2017)
- Hydrocortisone Butyrate Lotion, 0.1% (11/2017)
- Dapsone Gel, 5% (10/2017)
(8) Expand characterization-based BE methods across all ophthalmic products

- **FDA Internal Research**
  - Asymmetric flow field flow fractionation measurement of cyclosporine ophthalmic emulsion
  - Unit dose content testing and particle size/size distribution testing of
    - ciprofloxacin ophthalmic ointment
    - dexamethasone ophthalmic suspension
  - Evaluating physicochemical testing of non-Q2 ophthalmic solution products
  - Evaluating rheological properties of in-situ forming ophthalmic gels: impact of excipient grade and diluent media composition
  - Animal model ocular bio-distribution studies: impact of formulation viscosity and particle size
  - Assessment of in vitro release testing methods for ophthalmic emulsion products

- **Ongoing Grants and Contracts Funded in FY2017**
  - Contract on pulsatile microdialysis for in vitro release of ophthalmic emulsions
Expand characterization-based BE methods across all ophthalmic products

**Potential FY2018 Grants/Contracts**
- In vitro studies (tissue-based assays) for topical products (ophthalmic)

**Outcomes 2017-2018**
- Publications:
  - Bao Q. et al., In vitro and ex vivo correlation of drug release from ophthalmic ointments. *J Control Release* 2018 Apr 28;276:93-101
- Guidances (PSGs that incorporated in vitro BE approaches supported by research):
  - Fluorometholone Ophthalmic Suspension (10/2017)
  - Loteprednol Etabonate Ophthalmic Suspension (02/2018)
(9) Develop more efficient alternatives to the use of forced expiratory volume in one second (FEV1) comparative clinical endpoint BE studies for inhaled corticosteroids

- **FDA Internal Research**
  - Biorelevant methods for assessing quality and performance of inhalation products
    - Realistic mouth-throat for deposition

- **Ongoing Grants and Contracts Funded in FY2017**
  - 1 Contract for PK study on dry powder inhaler (DPI)
    - The PK study on DPI was completed
  - 1 Grant for PK study on metered dose inhaler (MDI)

- **New FY2017 Contracts**
  - “Investigating the microstructure of dry powder inhalers using orthogonal analytical approaches”
    - Awarded to the University of Bath (#HHSF223201710116C)

- **Potential FY2018 Grants/Contracts**
  - CFD and discrete element modeling (DEM) approach for predictions of dry powder inhaler (DPI) drug delivery
  - Impact of differences in aerodynamic particle size distribution (APSD) and device resistance on CFD predictions of dry powder inhaler drug delivery
  - Development of empirical models and in vitro methods for prediction of batch to batch variability of dry powder inhaler formulations
  - Characteristic tracheobronchial models of adult female and male chronic obstructive pulmonary (COPD) patients for CFD analysis
(9) Develop more efficient alternatives to the use of forced expiratory volume in one second (FEV1) comparative clinical endpoint BE studies for inhaled corticosteroids

- **Outcomes 2017-2018**
  - Public workshop: “New Insights for Product Development and Bioequivalence Assessments of Generic Orally Inhaled and Nasal Drug Products” (Jan 9, 2018)
  - Publications:
  - Guidances: 6 new PSGs
    - Glycopyrrolate Powder (07/2017)
    - Tiotropium Bromide Powder for Inhalation (10/2017)
    - Fluticasone Propionate Powder for Inhalation (10/2017)
    - Fluticasone Propionate Inhalation Aerosol (10/2017)
    - Mometasone Furoate Powder for Inhalation (10/2017)
    - Salmeterol Xinafoate Powder for Inhalation (10/2017)
(10) Develop alternatives to comparative clinical endpoint BE studies for locally-acting nasal products

- **FDA Internal Research**
  - Particle size characterization methods for API in suspension-based aqueous nasal spray products using MDRS (also under (2))
  - Meta-analysis of in vitro BE data submitted in the ANDA applications for nasal products

- **Ongoing Grants and Contracts Funded in FY2017**
  - Contract for nasal PK study

- **New FY2017 Contracts**
  - “Investigating orthogonal analytical approaches to demonstrate bioequivalence of nasal suspension formulations”
    - Awarded to the University of Bath (#HHSF223201710163C)
Develop alternatives to comparative clinical endpoint BE studies for locally-acting nasal products

• Potential FY2018 Grants/Contracts
  – Improving in vitro tests for clinical relevance (nasal models)
  – Three dimensional approach for modeling of mucociliary clearance via CFD

• Outcomes 2017-2018
  – Public workshop: “New Insights for Product Development and Bioequivalence Assessments of Generic Orally Inhaled and Nasal Drug Products” (Jan 9, 2018)
  – Guidances: 2 new PSGs
    • Azelastine Hydrochloride Spray, metered (05/2017, RLD: NDA 20114)
    • Azelastine Hydrochloride Spray, metered (10/2017, RLD: NDA 22203)
  – Notable ANDA Approvals
    • Azelastine Hydrochloride and Fluticasone Propionate Nasal Spray, 137mcg/50mcg (4/2017)
3. Complex drug-device combinations

(11) Evaluate the impact of identified differences in the user-interface on the substitutability of generic drug-device combination products

https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm
Evaluate the impact of identified differences in the user-interface on the substitutability of generic drug-device combination products

• New FY2017 Contracts
  – “Patient’s perception of dry powder inhaler airflow resistance”
    • Awarded to Imperial College of Science and Technology (#HHSF223201710072C)

• Potential FY2018 Grants/Contracts
  – Patients’ perceptions to device substitution

• Outcomes 2017-2018
  – Publications:
  – Upcoming public workshop:
    • DIA-FDA Complex Generic Drug-Device Combination Product workshop (Oct 9-10, 2018, Silver Spring, MD)
4. Tools and methodologies for BE and substitutability evaluation

(12) Improve quantitative pharmacology and bioequivalence trial simulation to optimize design of BE studies for complex generic drug products

(13) Integrate predictive dissolution, PBPK and PK/Pharmacodynamic (PD) models for decision making about generic drug bioequivalence standards

(14) Expand the scientific understanding of the role of excipients in generic drug products to support the expansion of the Biopharmaceutics Classification System of Class 3 bio-waivers to non-Q2 (quantitatively inequivalent) formulations

(15) Develop methods that will allow FDA to leverage large data sets (such as bioequivalence study submissions, electronic health records, substitution and utilization patterns and drug safety and quality data) for decisions related to generic drug approval and post-market surveillance of generic drug substitution

https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm
(12) Improve quantitative pharmacology and bioequivalence trial simulation to optimize design of BE studies for complex generic drug products

- **FDA Internal Research**
  - Quantitative analysis of PK/PD relationship of abuse-deterrent opioid products
  - Clinical trial simulation on comparative clinical endpoint BE studies for locally acting drug products
  - Use of PK/PD modelling and simulation for assessment of post-market risk

- **Ongoing Grants and Contracts Funded in FY2017**
  - Contract for BE methods for PK using sparse sampling
  - Pharmacometric modeling and simulation for a generic drug substitutability evaluation and post-marketing risk assessment
  - Pharmacometric modeling and simulation and statistical analysis for LAI microsphere products

- **New FY2017 Contracts**
  - “Evaluation and development of model-based bioequivalence analysis strategies”
    - Awarded to Uppsala University (#HHSF223201710015C)

- **Potential FY2018 Grants/Contracts**
  - Bioequivalence evaluation of nanoparticulate and molecular medicines
  - Developing PBPK/PD models for IUDs to evaluation alternative BE approaches
  - Alternate BE study design for long acting products
(12) Improve quantitative pharmacology and bioequivalence trial simulation to optimize design of BE studies for complex generic drug products

• Outcomes 2017-2018
  – Publications: 7 manuscripts
    Examples:
    • Li et al., Risk-Based Bioequivalence Recommendations for Antiepileptic Drugs, *Current Neurology Neuroscience Reports*. 2017; 17: 82
  – Guidances: 46 PSGs
    Examples:
    • Ivermectin topical cream (10/2017)
    • Naloxone nasal spray (4/2017)
  – Notable ANDA Approvals: 29 related ANDA approvals
    • Brimonidine topical gel (tentative approval in 07/2017)
(13) Integrate predictive dissolution, PBPK and PK/Pharmacodynamic (PD) models for decision making about generic drug bioequivalence standards

• **FDA Internal Research**
  – PBPK modeling and simulations to (1) assess impact of dissolution profiles on PK and BE, (2) assess a chewing device for abuse deterrence assessment, (3) identify the drug interaction mechanism of nifedipine ER and a proton pump inhibitor, omeprazole, and (4) identify the rate-limiting step for Omega-3 ethyl ester intestinal absorption
  – Multivariate similarity testing for multi-batch dissolution profiles

• **Ongoing Grants and Contracts Funded in FY2017**
  – Grants on supersaturation models, in vivo predictive dissolution methodology, wireless analysis device to measure in vivo drug dissolution, PK study on IVIVC for amorphous dispersions, PK study on PPI interactions, contract for MRI measurements of GI water content, grants for PK/PD studies on metoprolol and methylphenidate

• **New FY2017 Contracts**
  – “Phase behavior and transformation kinetics of a poorly water soluble weakly basic drug upon transit from low to high pH conditions”
    • Awarded to Purdue University (#HHSF223201710137C)

• **Potential FY2018 Grants/Contracts**
  – Development of a virtual bioequivalence trial simulation platform that integrates population pharmacokinetic modeling algorithms into physiologically-based pharmacokinetic models
  – Evaluation of relative bioavailability of pediatric products
  – Establishment of alternative bioequivalence evaluation methodology by integrating sequential design and Bayesian methodology
Integrate predictive dissolution, PBPK and PK/Pharmacodynamic (PD) models for decision making about generic drug bioequivalence standards

Outcomes 2017-2018

- Publications: 9 manuscripts
  
  Examples:
  
  
  
  
  

- Notable ANDA Approvals:
  
  - Prasugrel hydrochloride tablets (7/2017)
(14) Expand the scientific understanding of the role of excipients in generic drug products to support the expansion of the Biopharmaceutics Classification System of Class 3 bio-waivers to non-Q2 (quantitatively inequivalent) formulations

• FDA Internal Research
  – Bi-phasic dissolution systems
  – Impact of excipients on drug solubility, passive permeability, and intestinal metabolism and transport
  – A database on commonly observed excipients in IR products for BCS Class III drug substances

• Ongoing Grants and Contracts Funded in FY2017
  – Effect of excipients on intestinal drug transporters
(14) Expand the scientific understanding of the role of excipients in generic drug products to support the expansion of the Biopharmaceutics Classification System of Class 3 bio-waivers to non-Q2 (quantitatively inequivalent) formulations

• Outcomes 2017-2018
  – Publications:
  – Guidances:
    • ICH harmonization discussion on-going
Develop methods that will allow FDA to leverage large data sets (such as bioequivalence study submissions, electronic health records, substitution and utilization patterns and drug safety and quality data) for decisions related to generic drug approval and post-market surveillance of generic drug substitution

- **FDA Internal Research**
  - Machine learning/neural network analysis to predict the association between kinase targets and adverse reactions
  - Big data analytics for post-marketing signal detection

- **Ongoing Grants and Contracts Funded in FY2017**
  - Grant on use of pharmacometrics for post-market surveillance

- **Potential FY2018 Grants/Contracts**
  - Generic utilization and substitution of thyroid agents
  - Machine learning for IVIVC PK and PD analysis
(15) Develop methods that will allow FDA to leverage large data sets (such as bioequivalence study submissions, electronic health records, substitution and utilization patterns and drug safety and quality data) for decisions related to generic drug approval and post-market surveillance of generic drug substitution

- **Outcomes 2017-2018**
  - Publications:
    - Liu Q, et al., The adoption of generic immunosuppressant medications in kidney, liver, and heart transplantation among recipients in Colorado or nationally with Medicare part D. *Am J Transplant.* 2018 Mar 31 [Epub ahead of print]
    - Dasai RJ, et al., Differences in rates of switchbacks after switching from branded to authorized generic and branded to generic drug products: cohort study. *BMJ.* 2018 Apr 3;361:k1180. doi: 10.1136/bmj.k1180
Research Outcomes Summary
(May 2017-April 2018)

Public Workshops
5

Publications
29 in FY2017
19 in 2018

Guidances
General: 3
PSGs: 229
(60 for complex, 26%
48 new, 11 rev, 1 final)

First Generics Approvals
(4/2017-3/2018)
80
(18 complex, 23%)
15 of 18 (83%) had PSGs
Future Workshops in 2018 and 2019

• CDER Small Business and Industry Assistance (SBIA) Regulatory Education for Industry (REdI): Complex Generic Product Development Workshop (September 12-13, 2018)

• Drug Information Association (DIA)/FDA Generic Drug-Device Combination Products Workshop (October 9-10, 2018)

• PBPK Modeling for Locally-Acting Products (March 13, 2019)

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GDUFA Science and Research Website

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Public Workshops
May 2017-April 2018

- May 19, 2017: Oral Absorption Modeling and Simulation for Formulation Development and Bioequivalence Evaluation Workshop
- October 2-3, 2017: Leveraging Quantitative Methods and Modeling to Modernize Generic Drug Development and Review
- October 6th, 2017: Demonstrating Equivalence of Generic Complex Drug Substances and Formulations
- October 20th, 2017: Topical Dermatological Generic Drug Products: Overcoming Barriers to Development and Improving Patient Access
- January 9th, 2018: New Insights for Product Development and Bioequivalence Assessments of Generic Orally Inhaled and Nasal Drug Products

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