FDA Public Meeting

Generic Drug User Fee Amendments (GDUFA) of 2017

07/21/2020
9:00 am – 3:00 pm

Stephen M. Hahn, MD

Commissioner of Food and Drugs, FDA

Public Meeting on the Reauthorization of the Generic Drug User Fee Amendments

Sally Choe, PhD
Director, Office of Generic Drugs
GDUFA III Public Meeting
7/21/2020

Public Health Impact of Generic Drugs During COVID-19

Provide access to:

- drugs facing increased demand and short supply
- important drugs used in ICU settings

Examples of Recent Approvals of Generic Drugs Used in the COVID-19 Response

- Albuterol
  - Inhalation Solution
  - Metered Dose Inhaler
- Azithromycin
- Cisatracurium
- Dexmedetomidine
- Heparin sodium
- Lidocaine hydrochloride
- Succinylcholine

Supporting Generic Drug Development and Assessment through **Enhanced Communications**

- Information Requests
- Discipline Review Letters
- Mid-review-cycle teleconferences
- Complete Response Letters (CRLs)
  - Post-CRL teleconferences
- Controlled correspondence ("controls")
  - Clarification of ambiguities

Supporting Generic Drug Development and Assessment through **GDUFA Policy and Procedural Documents**

- Guidances for Industry
- Product-Specific Guidances
- Manuals of Policies and Procedures

Outreach and Education to Industry

- Public meetings and workshops
- Webinars, emails, and scientific and educational articles
- Websites
  - Upcoming Product-Specific Guidances (PSGs) for Complex Drug Product Development
  - List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic
  - Patent Certifications and Suitability Petitions
  - Reference Listed Drug Access Inquiries
  - List of all approved ANDAs for drug products that received a CGT

Supporting Generic Drug Development and Assessment through GDUFA Research

- Guidance on complex generic drug products
- Internal alignment on complicated issues
- Confidence in generic substitution
- Review tool development
- Faster and smarter generic drug development and assessment

GDUFA Research Paves the Way for Complex Generic Drug Product Approval

- Albuterol sulfate inhalation aerosol for patients with asthma
- Fluticasone propionate/salmeterol inhalation powder for patients with chronic obstructive pulmonary disease
- Acyclovir cream for patients with herpes simplex virus

Pre-ANDA Program Enhances Access to Complex Generic Drug Products

GDUFA II designed the Pre-ANDA Program to:

- Better facilitate development and review of ANDAs for complex generic products
- Reduce the number of review cycles to approval
- Increase approvals of safe, high-quality, and lower-cost generic drugs

FDA's Generic Drug Program is poised and ready to take the program to the next level. We look forward to working with you!


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GDUFA & Pharmaceutical Quality at FDA:
Programs That Have Grown Up Together

Michael Kopcha, Ph.D., R.Ph.
Director
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

@QualityKop

Public Meeting on the Reauthorization of the Generic Drug User Fee Amendments (GDUFA)
July 21, 2020

Topics

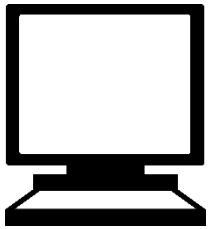
- A Lifecycle Approach to Pharmaceutical Quality
- FDA Research Informs Quality Assessment
- Innovations in FDA's Generic Drug Assessment
- Generics in the Time of COVID-19

A Lifecycle Approach to Pharmaceutical Quality

US FDA Center for Drug Evaluation and Research

Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.



Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

Drugs are no different.

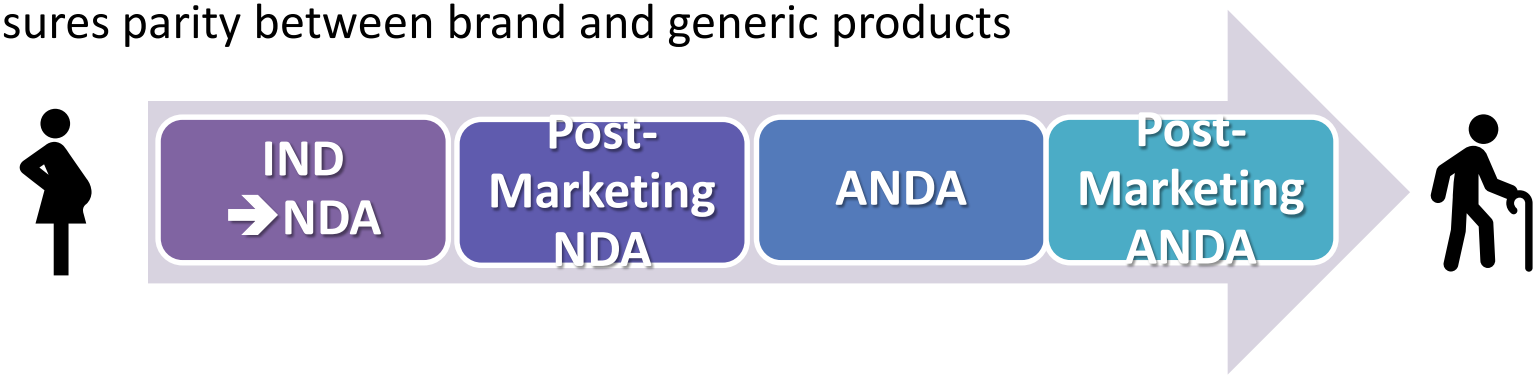

FDA
Patients expect safe and effective medicine with every dose they take

Pharmaceutical quality is

what gives patients confidence in their next dose of medicine

Quality Over the Drug Product Lifecycle

- **CDER's Office of Pharmaceutical Quality focuses on the entire drug product life**
- **We emphasize knowledge sharing across life stages**
  - Assures quality medicines are consistently available to the American public
  - Proactively works to prevent drug shortages
  - Ensures parity between brand and generic products



Lifecycle Successes Under GDUFA

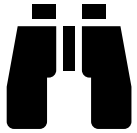
- **FDA ensures innovator drug labeling is current, complete, and complies with standards**
  - Enables the timely approval of more generic drugs
- **Integrated quality assessment brings quality discipline experts together to resolve difficult issues**
  - Results in approvals of “difficult” or complex generic drug products

FDA Research Informs Quality Assessment

US FDA Center for Drug Evaluation and Research

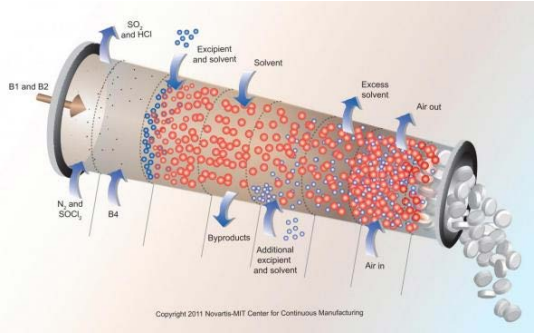
FDA's Proactive Science & Research Approach

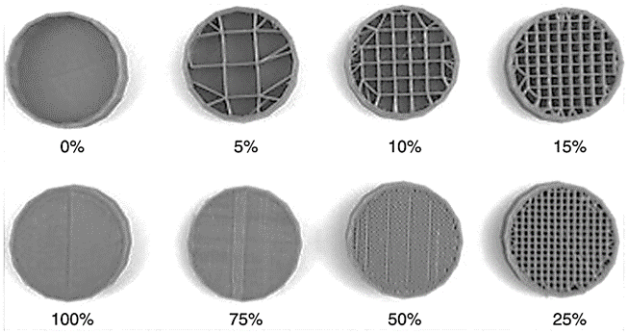
- **FDA's GDUFA science program is designed to maintain preparedness to respond**
  - Consumer complaints
  - Public health issues
- **FDA's GDUFA research program is "forward looking"**
  - New and emerging technologies for process control and advanced manufacturing
  - Advanced analytics (instrument and modelling)
  - Advances in drug design and formulation



What is Advanced Manufacturing?

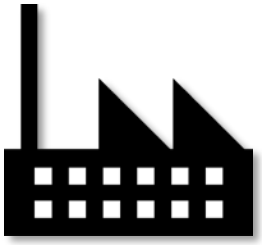
- Novel **manufacturing methods** to improve process robustness and efficiency
- Novel **dosage forms** or delivery systems to improve drug delivery and targeting
- Novel **analytical tools** to improve product quality testing, process monitoring and/or control





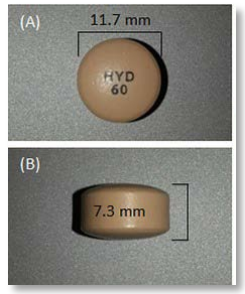
The Importance of Advanced Manufacturing for FDA & Industry

- **Addresses the underlying causes of drug shortages**
  - Mitigate or prevent future production problems
  - COVID-19: Faster commercial production w/o scale-up issues
- **Facilitates new clinical modalities**
  - Precision and individualized medicines
  - A wider range of novel dosage forms and doses
  - Convenient fixed-combination dosage forms
- **Improves manufacturing efficiency**
  - Increase process robustness
  - Lower manufacturing costs
  - Increase supply chain flexibility

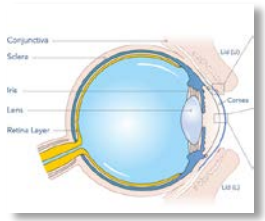


FDA Research Supports Generic Approvals

- **Abuse-deterrent formulations (ADFs) in opioid products**
  - Part of FDA's comprehensive action plan to address opioid addiction
  - Research fuels understanding of formulations for assessment of ADF technologies in applications



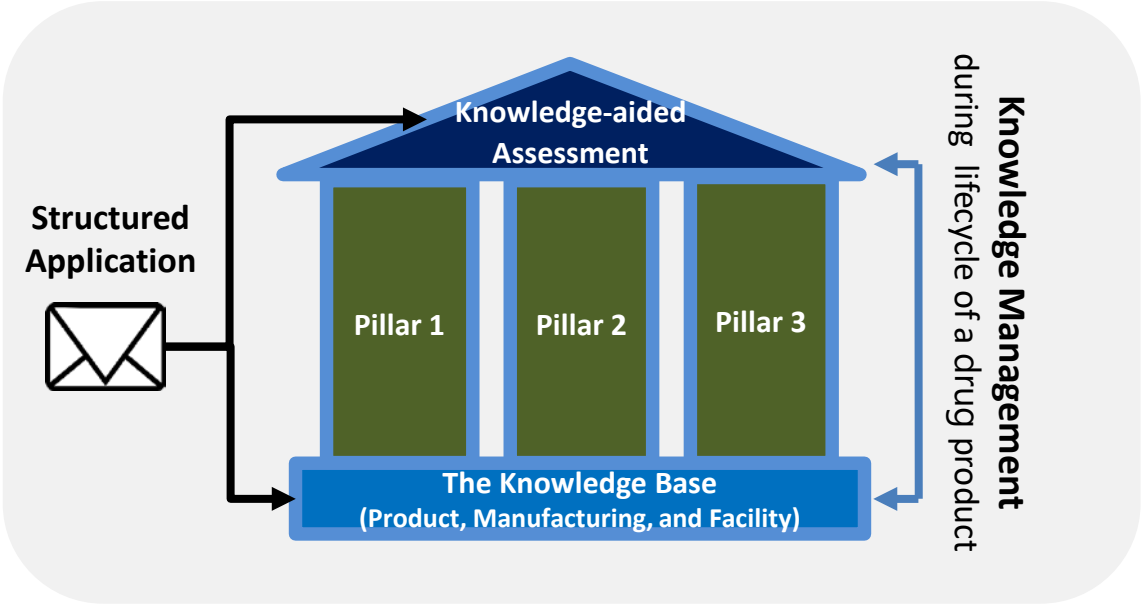
- **Locally acting ophthalmic drug products**
  - Challenging for development and assessment of bioequivalence
  - Research facilitates the development of guidances for these products



Innovations in FDA's Generic Drug Assessment

US FDA Center for Drug Evaluation and Research

KASA: The Future of Quality Assessment



A data-based platform for structured quality assessments and applications that supports knowledge management

KASA = Knowledge-aided Assessment and Structured Application

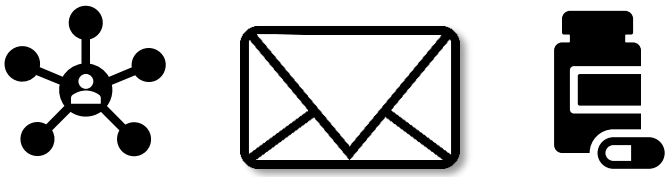
FDA's KASA System

Benefits to FDA

- Enhances consistency and objectivity of regulatory assessment
- Enables knowledge management of product, manufacturing, and facility
- Accelerates regulatory action and decision-making

FDA's KASA System

Benefits to Patients & Industry



- Clearer regulatory expectations; enhanced transparency
- Increased 1st cycle approvals (esp. generics)
- More affordable and accessible medicines

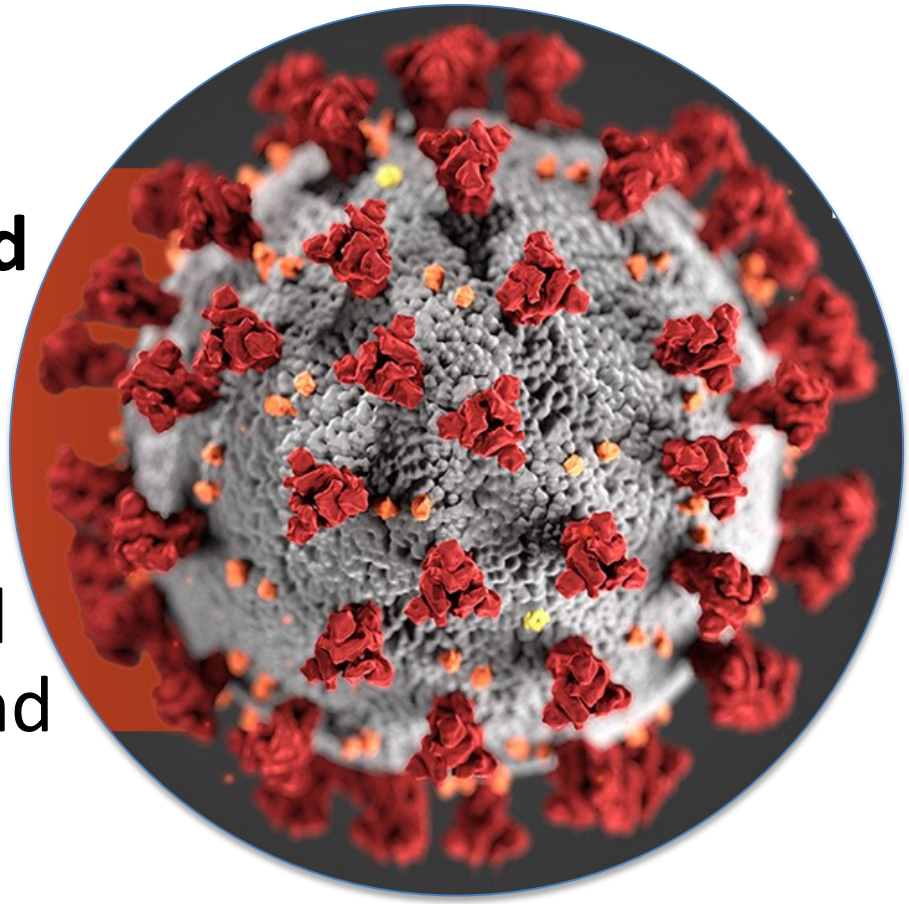
Generics in the Time of COVID-19

US FDA Center for Drug Evaluation and Research

The Era of COVID-19

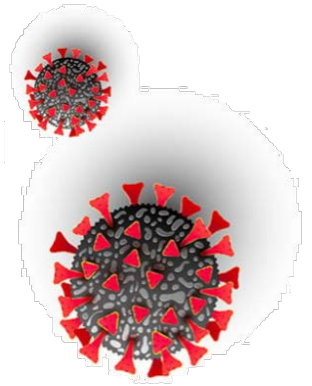
Long-existing quality issues are now magnified

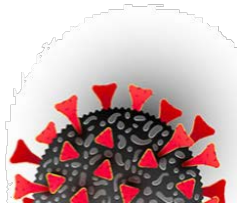
- Supply chains
- Shortages
- Decision-making based on changing science and risk



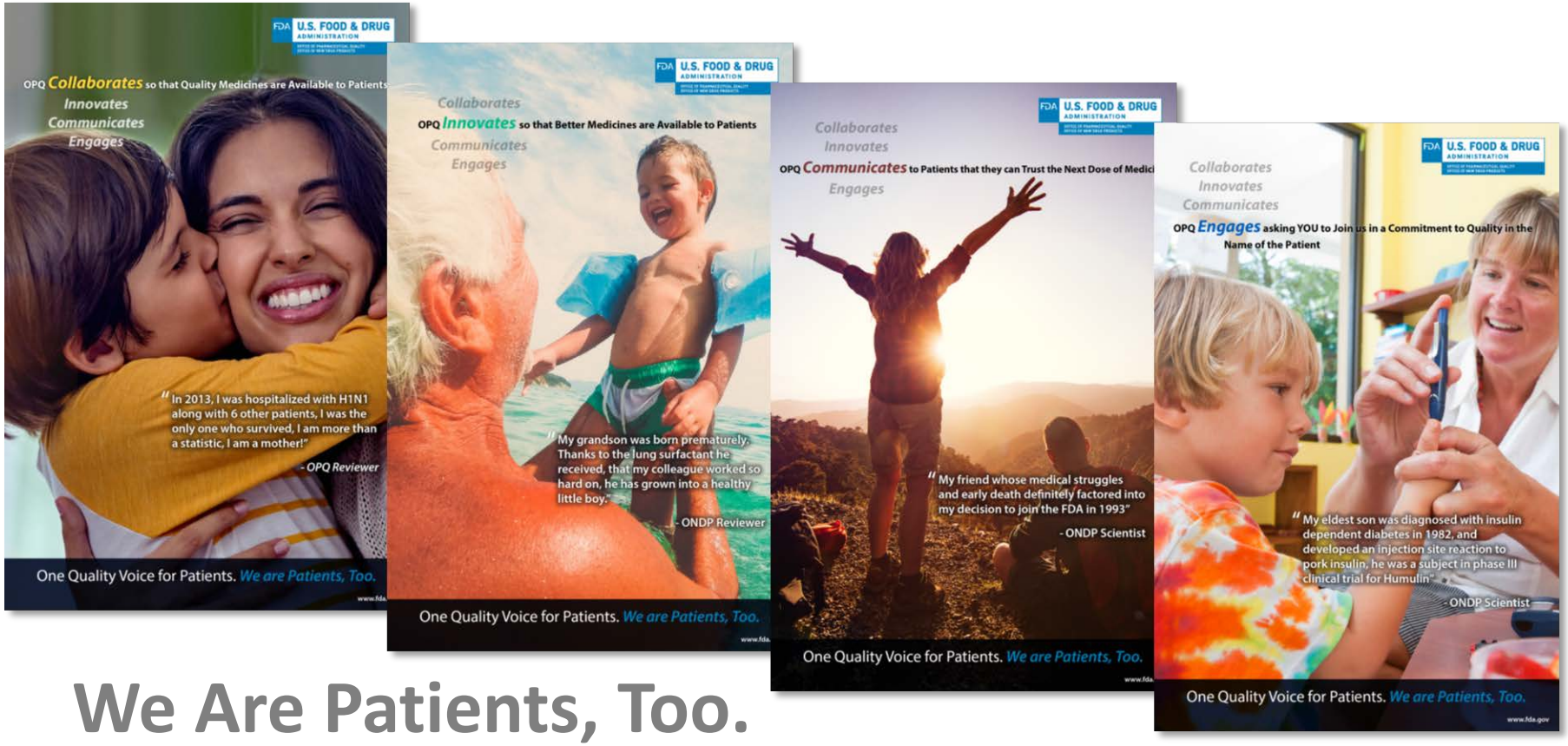
GDUFA-Enabled COVID Response: Quality-Related

- **Ensure supply chain security of critical treatments for COVID-19 patients**
  - Hundreds of quality supplement assessments expedited
  - Hundreds approved
- **Regulatory discretion granted to accelerate post-approval changes**
  - Based on risk and medical necessity, downgraded some supplements so they did not require prior approval to implement
- **Driving first-cycle quality adequacy for COVID-19-related ANDAs**
  - Issued multiple rounds of Information Requests (IRs) to increase the likelihood of an approval





One Quality Voice for Patients



We Are Patients, Too.


Let’s continue giving us all confidence in our *next* dose of generic medicine

FDA GDUFA III Q&A Panel

Jacqueline Corrigan-Curay
Director, Office of Medical Policy
FDA/CDER

Alonza Cruse
Director, Office of Pharmaceutical Quality Operations
FDA/ORA

Ashley Boam
Director, Office of Policy for Pharmaceutical Quality
FDA/CDER/OPQ

Maryll Toufanian
Director, Office of Generic Drug Policy
FDA/CDER/OGD

Edward "Ted" Sherwood
Director, Office of Regulatory Operations
FDA/CDER/OGD

Robert Lionberger
Director, Office of Research and Standards
FDA/CDER/OGD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GDUFA II: Overview of Goals and Accomplishments

Maryll W. Toufanian

GDUFA III Public Meeting

7/21/2020

GDUFA II Agreement

- GDUFA II agreement critical to facilitating faster access to generic drug products, with two major objectives:
  - reducing the number of review cycles to approval
  - increasing approvals of safe, high-quality, and lower-cost generic drugs
- The goals and commitments include:
  - new pre-ANDA program to better facilitate development and review of ANDAs for complex generic products
  - new review goals for priority ANDA submissions
  - greater accountability and reporting, a modified user-fee structure, and relief for small businesses

GDUFA II: By the Numbers

Efforts of FDA and Agency have resulted in a profound benefit to American patients:

- 2256 Approvals*
- 553 Tentative Approvals*

= The result of a tremendous effort by FDA and regulated industry

* As of 06/30/20

GDUFA II: Numbers Behind the Numbers**

- 6514 complete response letters**
- 6631 discipline review letters**
- 11323 information requests**
- 1614 drug master file (DMF) completeness assessments**
- 8450 controlled correspondence received**
- 264 pre-ANDA program meetings**
- 2376 PAS/31,833 “changes being effected” (CBE) supplements submitted+
- > 20,000 communications with applicants**

**as of 05/31/20

+ as of 01/30/20

GDUFA II: Numbers Behind the Numbers (cont.)

- 27 draft and final guidances with topics including:
  - Refuse-to-receive decisions, prior approval supplements, common deficiencies, meetings, completeness assessments, user fees, information requests and discipline review letters, tentative approval-to-full approval requests, and more
  - Scientific topics including complex dosage forms, combination products, peptides, abuse deterrence, consensus standards
  - Orange Book (+ public dockets)
- > 20 MAPPs, with topics including ANDA communications with industry, assessment activities, and pre-ANDA process

GDUFA II: Numbers Behind the Numbers (cont.)

Significant number of informational activities directly supported generic drug access

- New webpages:
  - "Upcoming Product-Specific Guidances for Complex Drug Products"
  - Overhauled Paragraph IV Certification webpage
  - Created competitive generic therapy (CGT) webpage
  - Established webpage on CREATES implementation
- 12 research and science-related public meetings
- > 25 FDA Small Business & Industry Assistance events, webinars, and podcasts on GDUFA II guidances, scientific topics, CGTs, more
- Extensive individual participation in external regulatory and scientific meetings; scientific publications
- Program commitment to global landscape, including significant investment in International Council for Harmonisation (ICH) activities

GDUFA II Goals: A Shared Mission

- Importance of generic drug access embraced by FDA and Administration in Drug Competition Action Plan
- Complements GDUFA II agreement and maximizes policy efforts to facilitate generic drug access
  - Increase transparency and efficiency in FDA assessment
  - Enhance development and review of complex product ANDAs
  - Reduce “gaming” that frustrates and delays generic approval
- Website reflects significant efforts: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan

GDUFA II: Achievement

As a result of GDUFA, we have:

- Demonstrated ability to do what it takes to meet the goals of the agreement
- A healthy generic program, with steady numbers of applications with industry and FDA
- Most predictable and transparent assessment process to date
- Thriving, strategically-positioned science and research program

= Springboard to GDUFA III

Looking Ahead

Next authorization cycle creates new opportunities to further enhance program and partnership

- With success comes responsibility
  - Increased post-approval activities that ensure continued access to safe and effective, high-quality generic drugs
  - Include manufacturing and labeling updates, safety surveillance
- Still work to be done to further enhance efficiency, transparency, and gain more first-cycle approvals
- Must be forward thinking: anticipate future generic drug submission horizon, incorporate rapidly advancing technologies, embrace creative thinking

We can all maximize the return on investment -- for the American public


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The Future of Inspections: ORA Perspective

Elizabeth Miller, Pharm.D.
Assistant Commissioner
Medical Products and Tobacco Operations
Office of Regulatory Affairs

Perspectives

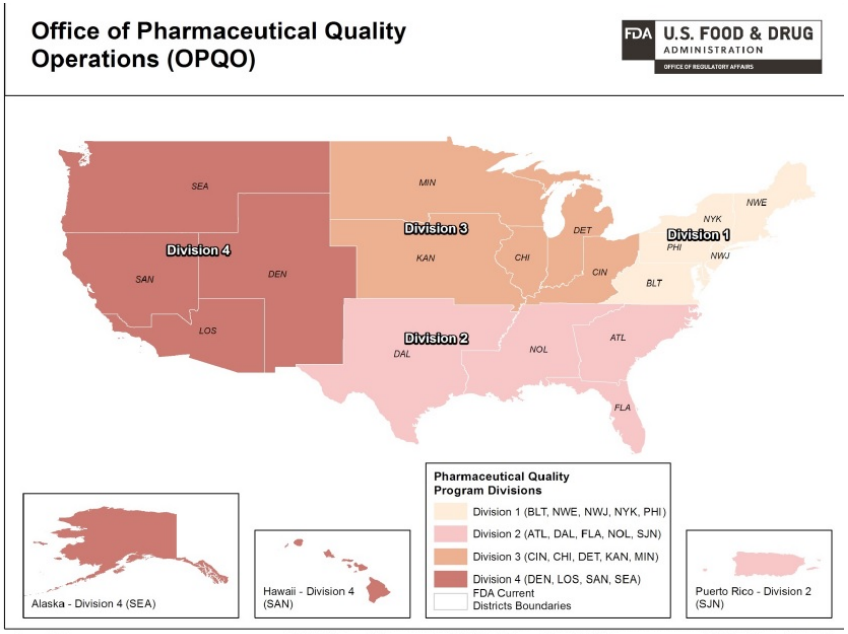
- Common mission and goals that U.S. patients have access to a secure and consistent supply of critical pharmaceuticals
- Our nation needs a diverse and resilient pharmaceutical supply chain
- Industry has the primary responsibility to reliably produce safe, effective, and quality products

An Overview of ORA

- Protects consumers and enhances public health
- Lead office for FDA inspections, oversight inclusive of all FDA regulated industries, including generic drugs
- Unique cross-commodity, cross-Agency perspective
- Reviews imported products offered for entry into the United States

Office of Pharmaceutical Quality Operations (OPQO)

- 200 total Investigators in OPQO
  - 78 Investigators funded by GDUFA user fees
  - 11 Investigators Foreign Drug Cadre
- Foreign office workforce
  - China – 25 FTEs
  - India – 18 FTEs



Pandemic

- Onset of the COVID-19 pandemic and travel restrictions
- On March 10 and 18, respectively, FDA postponed conducting routine foreign and domestic inspections
- ORA continued to do mission-critical on-site work
  - for-cause inspections,
  - import review,
  - laboratory analysis of samples

Pandemic, cont.

- On July 10, FDA announced a plan to resume prioritized domestic inspections
- ORA stands ready to resume any postponed inspections as soon as feasible, applying a strategic benefit versus risk calculus to our inspectional work

Lessons from Crisis: A Changed World

- Ability to conduct on-site facility inspections is important to carrying out our mission
- Implemented alternative ways to conduct inspectional work that do not jeopardize public safety and that protect firms as well as FDA staff

Innovation and Alternative Approaches

- Using our authority to request records and other information in ‘advance of’ or ‘in lieu of’ inspections
- Relying on global partnerships in requesting establishment inspection reports from capable foreign regulatory authorities under the MRA
- Looking critically at ways to innovate and optimize use of these tools to better serve the American public in the future

Facilitating New Approaches

- To create efficiencies and regulatory predictability we will need to engage on new approaches and new tools
- Leveraging technologies, such as secure data platforms to share, assess, and exchange records
- Further enhancing relationships with capable regulatory partners to reduce redundant and duplicative work and disperse critical resources more effectively

Facilitating New Approaches, cont.

- Benchmarking operations against other inspectorates to identify new and improved strategies
- An open and honest dialogue about a true partnership to advance medical product quality and accessibility
- Expanded cooperation with industry, working collaboratively to evaluate facility processes and ways to achieve inspectional operations in innovative and creative ways

Opportunities

- Understand how the pandemic changed generic industry
- Identify how we work together toward achieving outcomes in the best interest of American people
- Engaging on ideas for strengthening partnerships particularly in the area of inspection operations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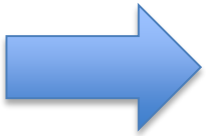
The Future of Pharmaceutical Quality

Ashley B. Boam, MSBE
Director, Office of Policy for Pharmaceutical Quality
CDER/OPQ

The Past

- Minimalist approach to quality
  - Minimal compliance with CGMP
  - Reactive approach to address problems
  - Few post-approval changes to improve processes
  - Single entity supply chains



- Leading to:
  - Outdated equipment
  - Old analytical technology
  - Supply disruptions
  - Drug shortages

The Future

- Continual improvement
- Proactive approach to post-approval change management
- Risk management plans
- Innovation

Continual Improvement

- ICH Q10 Pharmaceutical Quality System augments CGMP with the concept of an effective pharmaceutical quality system (PQS)
  - Applies to the entire lifecycle of a product
  - Activities to manage and continually improve the PQS
- Consistent implementation of ICH Q10 is a hallmark of a *mature quality management system*
  - Focus on performance and continual improvement, especially outcomes and metrics that impact the patient
  - Use data-driven approaches (e.g., predictive analytics, statistics, process capabilities) to reduce quality issues that lead to complaints, shortages, and adverse events

Achieving Quality Management Maturity

- Manufacturers and those with oversight and controls over manufacturing take ownership for quality:
  - Management sets the tone of commitment to quality
  - Investment in people
  - Organizational objectives drive quality
  - Quality systems shape culture
  - Focus on innovation and continual improvement
  - Move to performance-based quality management
  - Robust metrics program with a focus on analytics
  - Include risk management plans and forecasting to ensure reliability of supply

Post-Approval Change Management

- ICH Q12 – Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management
- Includes tools and enablers to facilitate continual improvement and innovation in a proactive manner
  - Established Conditions
  - Post-approval Change Management Protocols
    - Also known as “comparability protocols”
  - Product Lifecycle Management Document
  - Structured Approaches for Frequent CMC Post-Approval Changes (*for marketed products*)

Established Conditions (ECs)

- Offer an opportunity to gain clarity regarding:
  - Which elements of the control strategy must be reported if changed
  - Which elements can be managed under the PQS without reporting
  - How much flexibility exists to make changes to an identified EC
  - How to report changes to ECs
- Can provide additional regulatory flexibility in managing post-approval CMC changes globally

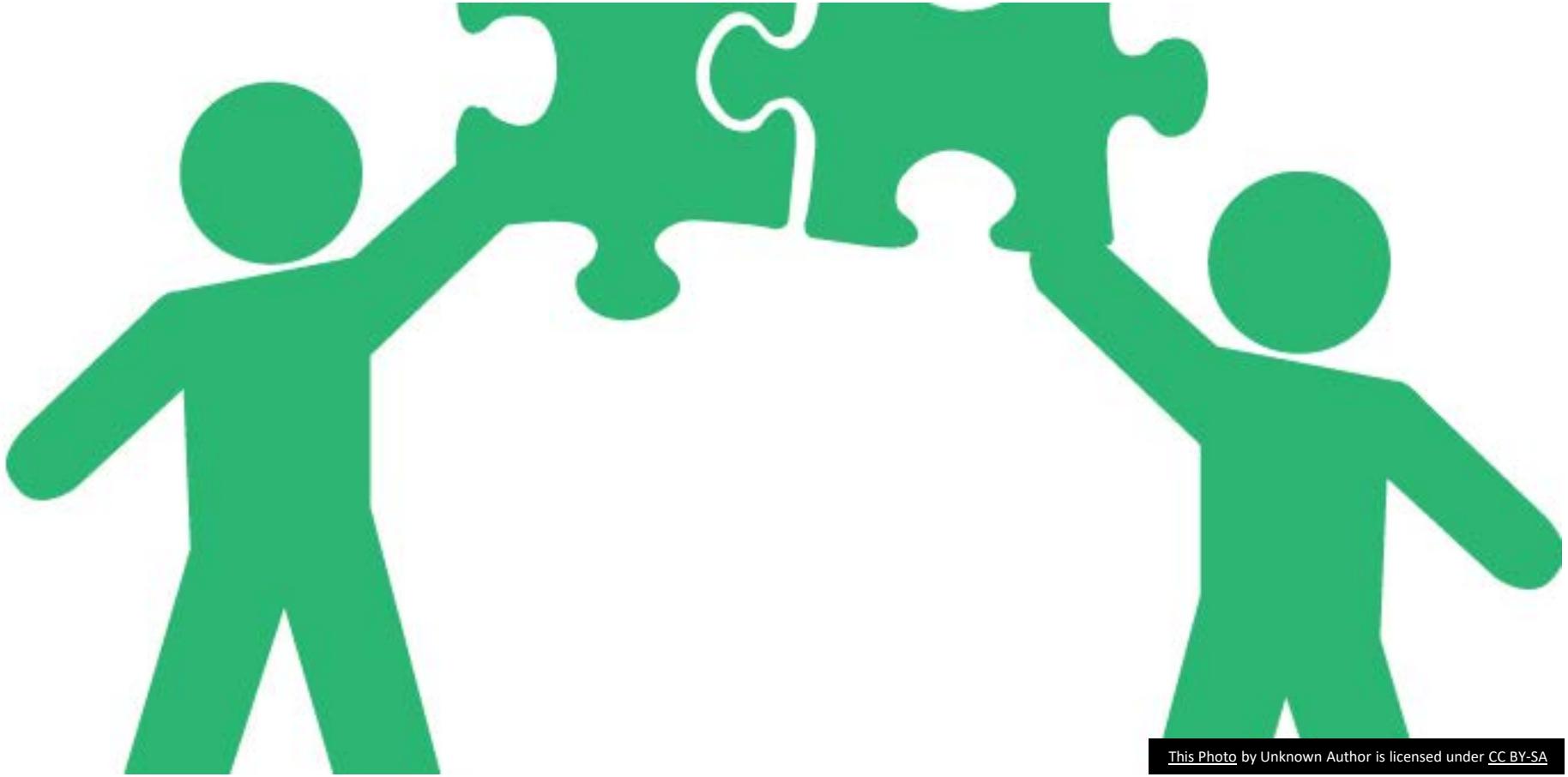
Use of Q12 tools

- Regulatory flexibility depends on robust product and process understanding and an effective PQS
  - Change management
- Implementation of ICH Q10 and QMM provide confidence in firm's quality system

Innovation

- Advanced Manufacturing
  - Includes, but not limited to, continuous manufacturing, container-closure systems, 3D printing
- Continuous Manufacturing
  - Not necessarily end-to-end continuous processing
  - Can be targeted to drug substance or only certain unit operations for drug product
  - May not be right for every product but can offer real advantages for many (e.g., higher volume, platform products)
    - Minimizes scale-up issues
    - Smaller footprint
    - Reduced environmental impact
    - More agile start-up and changeover
    - Lower costs over time
    - More robust process less likely to experience disruption

Opportunities for FDA and Industry



Global Harmonization

- Provides opportunities to reduce regulatory burden for postapproval changes and incentivize continual improvement and innovation
- ICH Q12 *Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management*
  - Reached Step 4 in November 2019; implementation ongoing
- ICH Q13 *Continuous Manufacturing*
- ICH Q2(R2)/Q14 *Analytical Procedure Development and Validation*
- ICH Q3E *Impurity: Assessment and Control of Extractables and Leachables for Pharmaceuticals and Biologics*

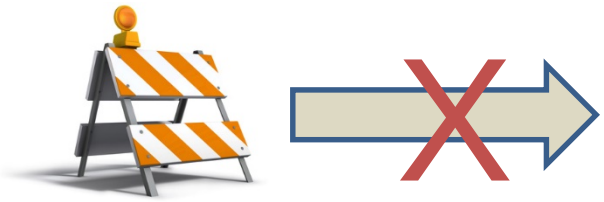
Global Harmonization – 2

- Renewed focus on quality risk management
  - PIC/S – Draft Recommendation "How to Evaluate/Demonstrate the Effectiveness of a Pharmaceutical Quality System in relation to Risk-based Change Management"
  - ICH revision of Q9 *Quality Risk Management*

Innovation in FDA Assessment

Current Challenges to Assessing Quality

Internal Challenges:



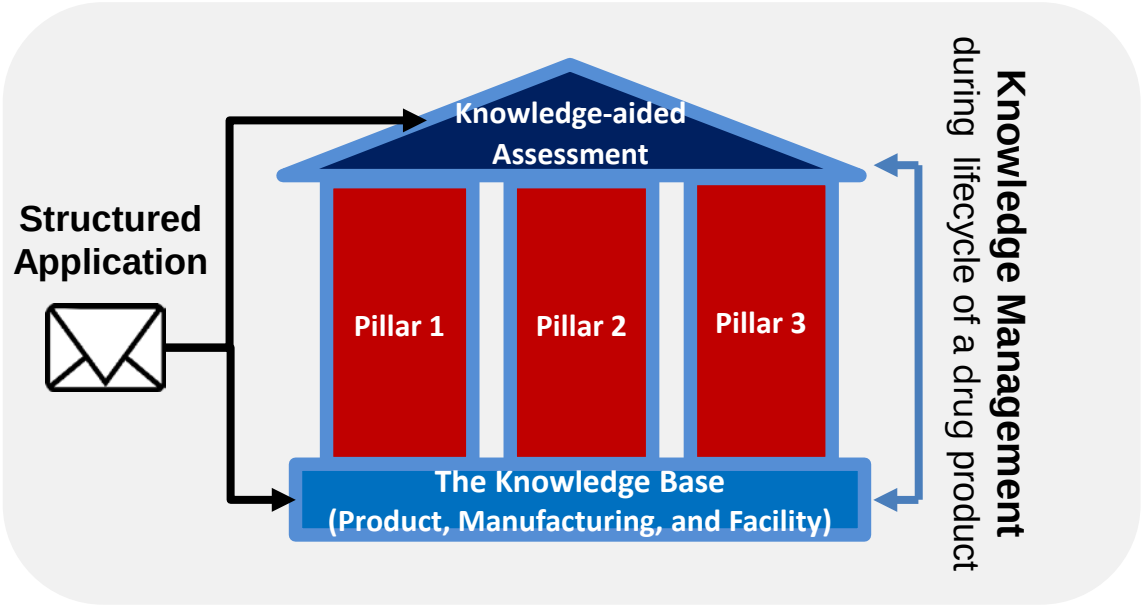
The quality assessment is a freestyle narrative:

- Unstructured text
- Summarization of application information
- "Copy and paste" data tables

Encumbers best practices for:

- Knowledge sharing
- Managing quality across the product lifecycle
- Overall modernization

The KASA System



The KASA System: A data-based platform for structured quality assessments and applications that supports knowledge management

KASA = **K**nowledge-aided **A**ssessment and **S**tructured **A**pplication

The KASA System

- The KASA system is being designed to:

  1. Capture and manage knowledge during the lifecycle of a drug product

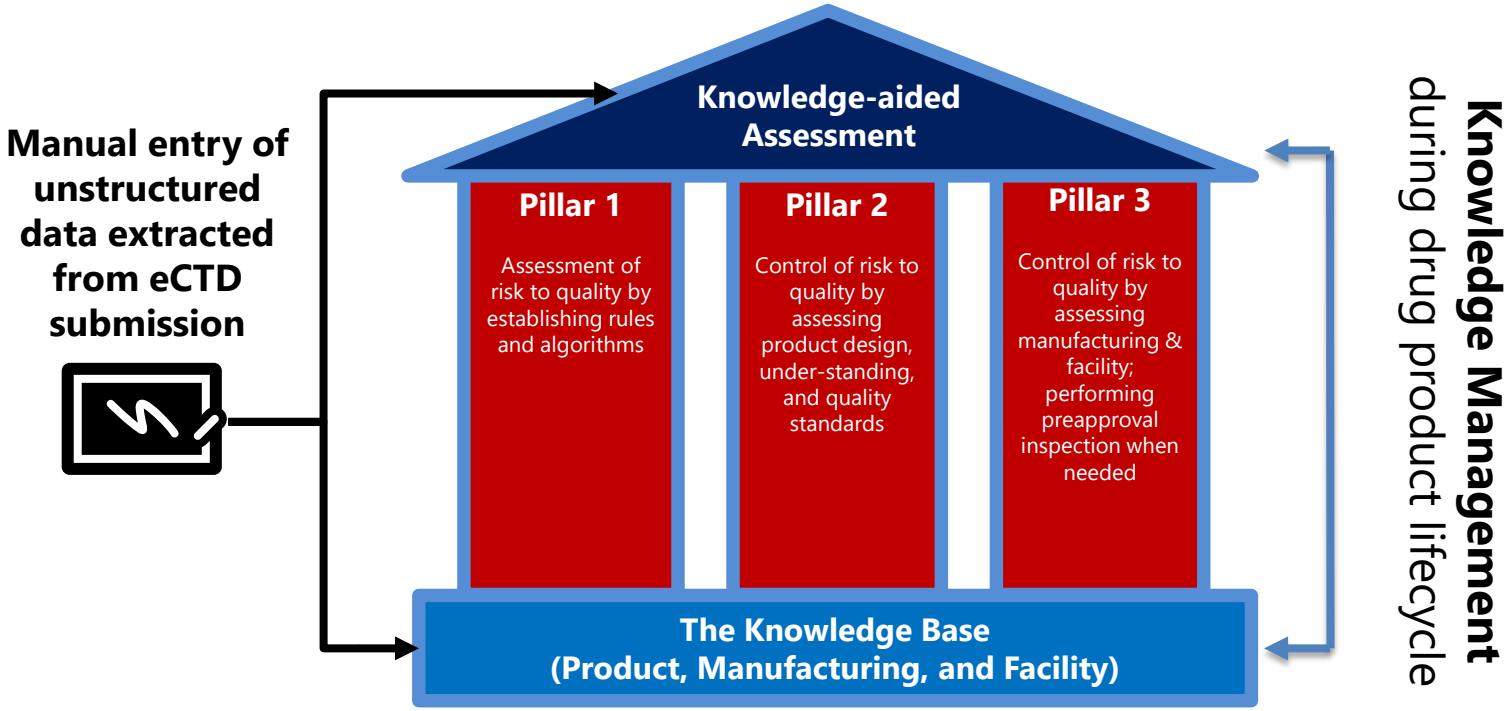
  2. Include established rules and algorithms to facilitate risk identification, mitigation, and communication for the drug product, manufacturing process, and facilities;

The KASA System

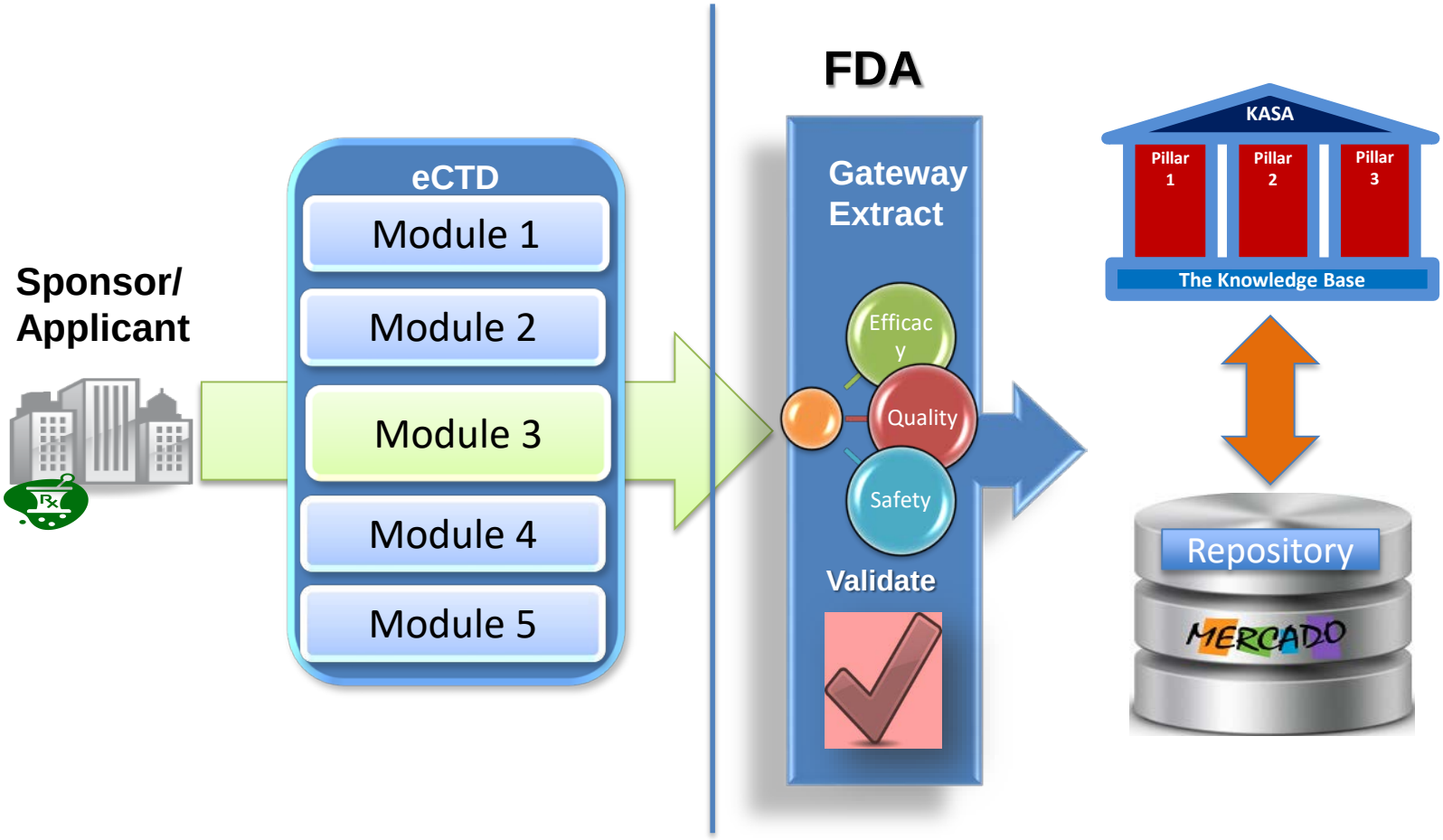
- The KASA system is being designed to:
  3. Perform computer-aided analyses of applications for a comparison of regulatory standards and quality risk across the repository of approved drug products and facilities

  4. Provide a structured assessment that radically eliminates text-based narratives and summarization of information from the applications

Current State



Future Vision with Structured Data



Conclusions

Industry and FDA working together and with global regulatory partners can achieve the future of pharmaceutical quality:

- More robust manufacturing processes
- A culture of continual improvement and innovation
- Fewer supply disruptions and drug shortages
- More consistent access to medicines for patients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Break until 11:00 a.m.

Overview of Pre-ANDA and Complex Generic Activity

Robert Lionberger

GDUFA III Public Meeting

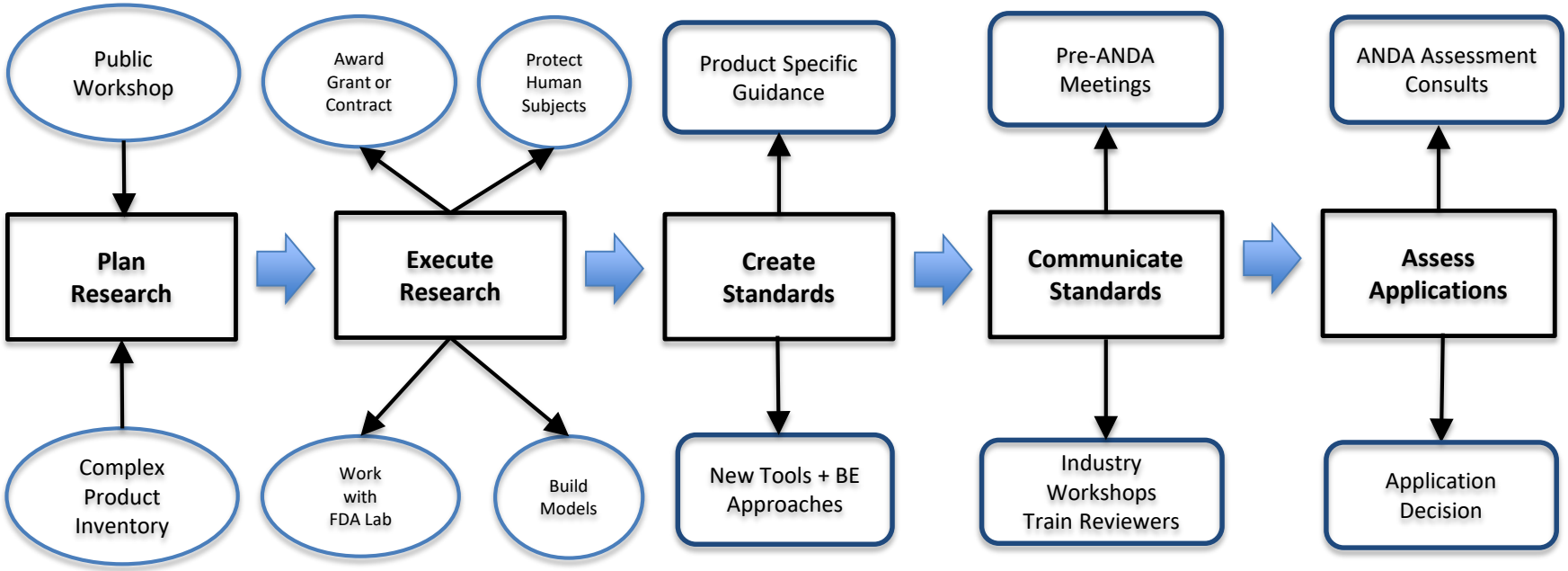
7/21/2020

Overview of GDUFA II Pre-ANDA System

- Research
- Product Specific Guidance (PSG)
- Controlled Correspondence (CC)
- Pre-ANDA Meetings

- GDUFA II defined the class of complex products

Integrated Pre-ANDA System



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Scale of Research

- Stable investment supports internal and external research activities
  - >100 active projects
  - ~20 new grants or contracts/per year to leverage external expertise
- Input from industry via public meeting and FDA-Industry meetings helps direct focus of the research program

- Publications

FY	Publication (peer reviewed / presentation)
2017	46/98
2018	65/152
2019	74/128

- Workshops
  - 12 GDUFA II Workshops
  - 3,000 in attendance at SBIA Workshop on Complex Generics each year
- Research supports PSG development for complex products

Research Examples

- Generic Access in All Product Categories

Efficient BE (non clinical endpoint) for complex and locally acting products
- In vitro BE methods for topical semi-solids
- In vitro BE methods for nasal suspensions
- In vitro BE methods for ophthalmic suspensions and emulsions
- Alternatives to FEV1 studies for inhaled corticosteroids

- Confidence in Generic Drug Substitution

Controlled studies that evaluate brand to generic switches in patient populations
- Lamotrigine, Tacrolimus and Bupropion completed

Development of surveillance tools for generics
- Sentinel tool for using NDC code to identify brand to generic switches

- Better Tools for Development and Review

Modeling, Simulation, and Data Science
- Jumpstart the application of PBPK models for locally acting drugs
- Machine learning for predicting ANDA submission probabilities

Advance analytical characterization methods
- Polymer characterization for sameness of long acting injectables

Scale of PSG

- ~1800 PSG are available
- Stable reliable quarterly postings because of GDUFA goals for non-complex NME
- FY 2019
  - 252 PSGs: 107 New, 145 Revised
    - 24 new PSGs and 117 revised PSGs for complex products
- Key Trends
  - GDUFA II steady increase in PSG activity for complex products
  - FY2019 saw ~30 new or revised PSG that provided a more efficient bioequivalence approach
  - Maintenance costs
  - No GDUFA goals related to complex PSG issuance

Scale of CC

- CC continue to increase
  - FY2019: 3206
  - FY2018: 2936
  - FY2017: 2668
  - FY2016: 1884
  - FY2015: 1677
- Analysis
  - ~40% of controls are about complex products
  - ~7% of controls are “complex controls” with 120 day goal date

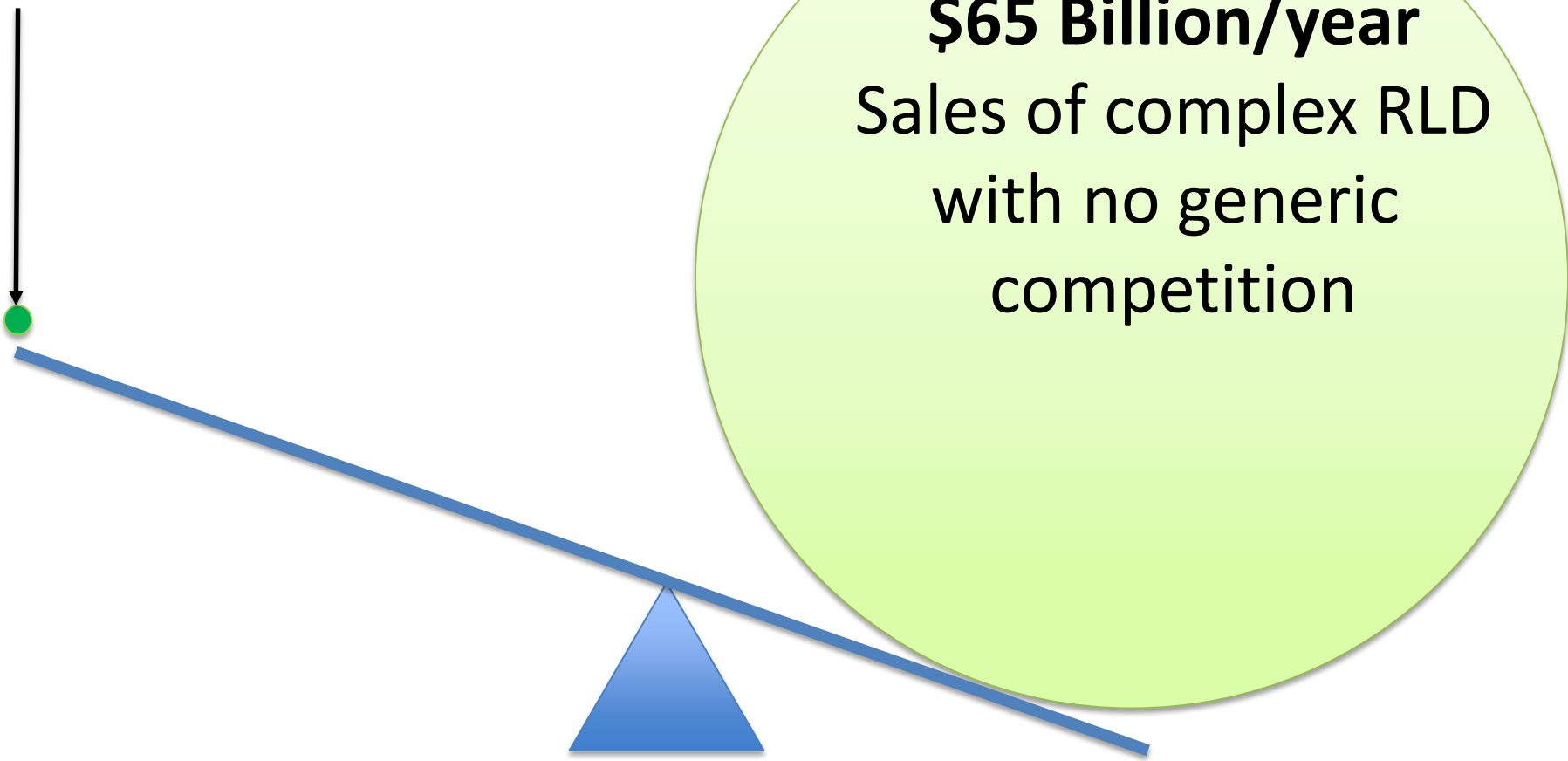
Scale of Pre-ANDA Meetings

- FY2019: 113 pre-ANDA meeting requests
- FY2018: 83 pre-ANDA meeting requests
- FY2017: 27 pre-ANDA meeting requests

- Use of the pre-ANDA meeting program continues to grow
- FDA has exceeded all GDUFA II goals related to pre-ANDA meetings
- Pre-ANDA meetings support innovation in BE approaches

Return on Pre-ANDA Investments

Pre-ANDA program
(~$25 Million for research)



Research Focus on Access to Complex Generics

Top 10 Product Areas

- Complex Active Ingredients
- Immunogenicity for Small Peptides
- Topical Dermatological Products
- Inhalation Products
- Ophthalmic Products
- Nasal Products
- Liposomes and Complex Injectables
- Long acting implants (Microspheres)
- Complex Drug-Device Combinations
- Abuse Deterrent Formulations

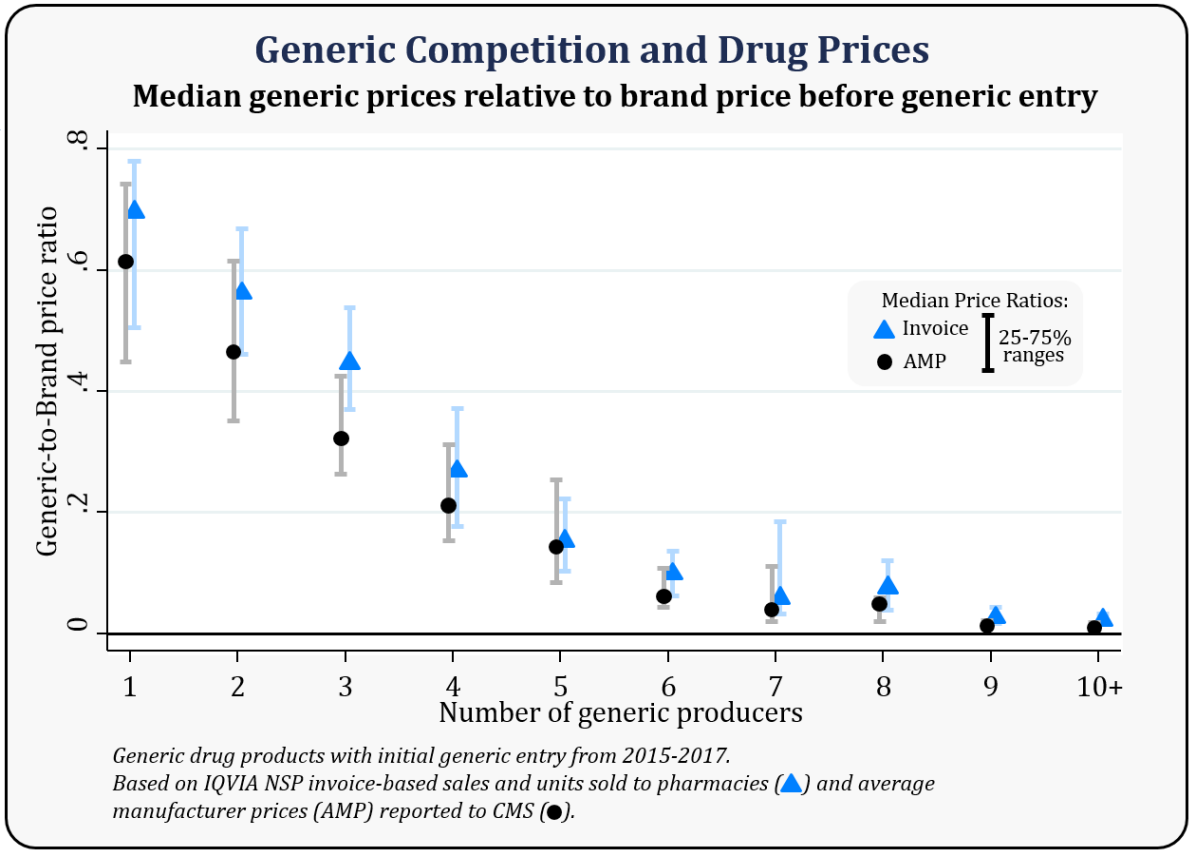
Each area has a >$billion/year market without generic competition

Coordinated internal and external research in each area drives progress

Communicated via PSG, CC, and pre-ANDA meetings

Return on Research Investment to the Public Depends on Successful ANDAs

Topical dermatological products with clinical endpoint BE ($20M study) often attract zero or one competitor



After 2012, in vitro BE guidance for Acyclovir Ointment

27 ANDA submissions

13 approved ANDA

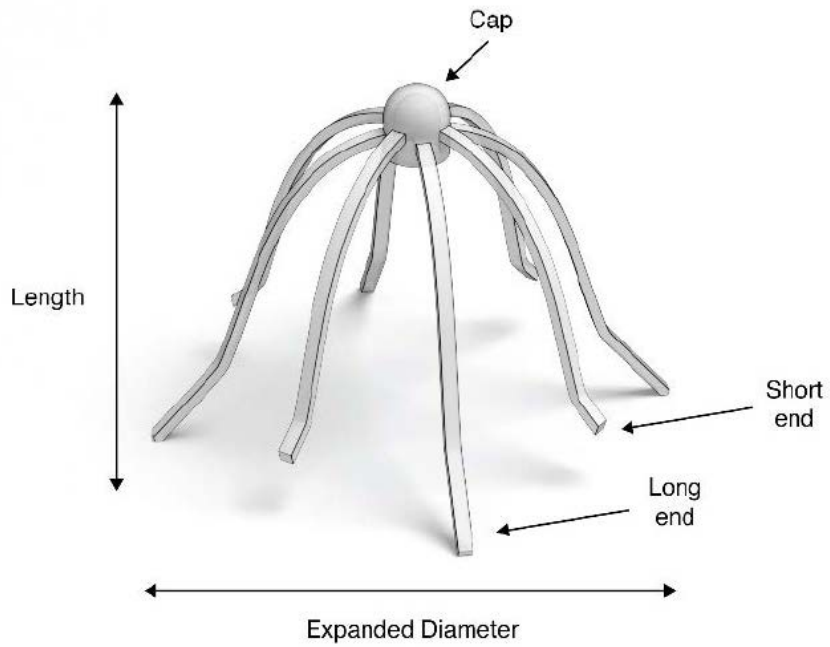
Savings to health care system 80% of pre-generic spend

Future Environment

- ~30% of potential RLD are for complex products
  - ~12% of approved ANDAs are for complex products
- Key is moving complex applications through the system

Future Environment

Research and PSG development should keep pace with new RLD product developments that add complexity



Summary

- The Pre-ANDA system provides clarity and improves development efficiency
- For complex products, research provides an essential input to the pre-ANDA system
- Pre-ANDA meetings support innovative approaches to BE that can accelerate access to complex generics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ADMINISTRATION

Jeffrey Kelman, MMSc, MD

Chief Medical Officer,
Center for Medicare and Medicaid Services

Value of Generic Drugs:
VA PBM Perspective

Peter A. Glassman MBBS, MSc, FACP

Chair, Medical Advisory Panel, Pharmacy Benefits Management Services, Department of Veterans Affairs

July 21, 2020

Information and Disclosures*

- Chair, Medical Advisory Panel, VA Pharmacy Benefit Management Services, Department of Veterans Affairs, Washington D.C.
- Co-Director, VA Center for Medication Safety, Hines IL.
  - Center works with and receives funds from FDA on various medication safety issues
- Physician, VA Greater Los Angeles Healthcare System, Los Angeles, CA
  - Primary Care, Palliative Care
- Professor of Clinical Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA
- VA Representative, Drug Safety Board, Food and Drug Administration, Center for Drug Evaluation and Research

* Does not necessarily represent the position of the Department of Veterans Affairs

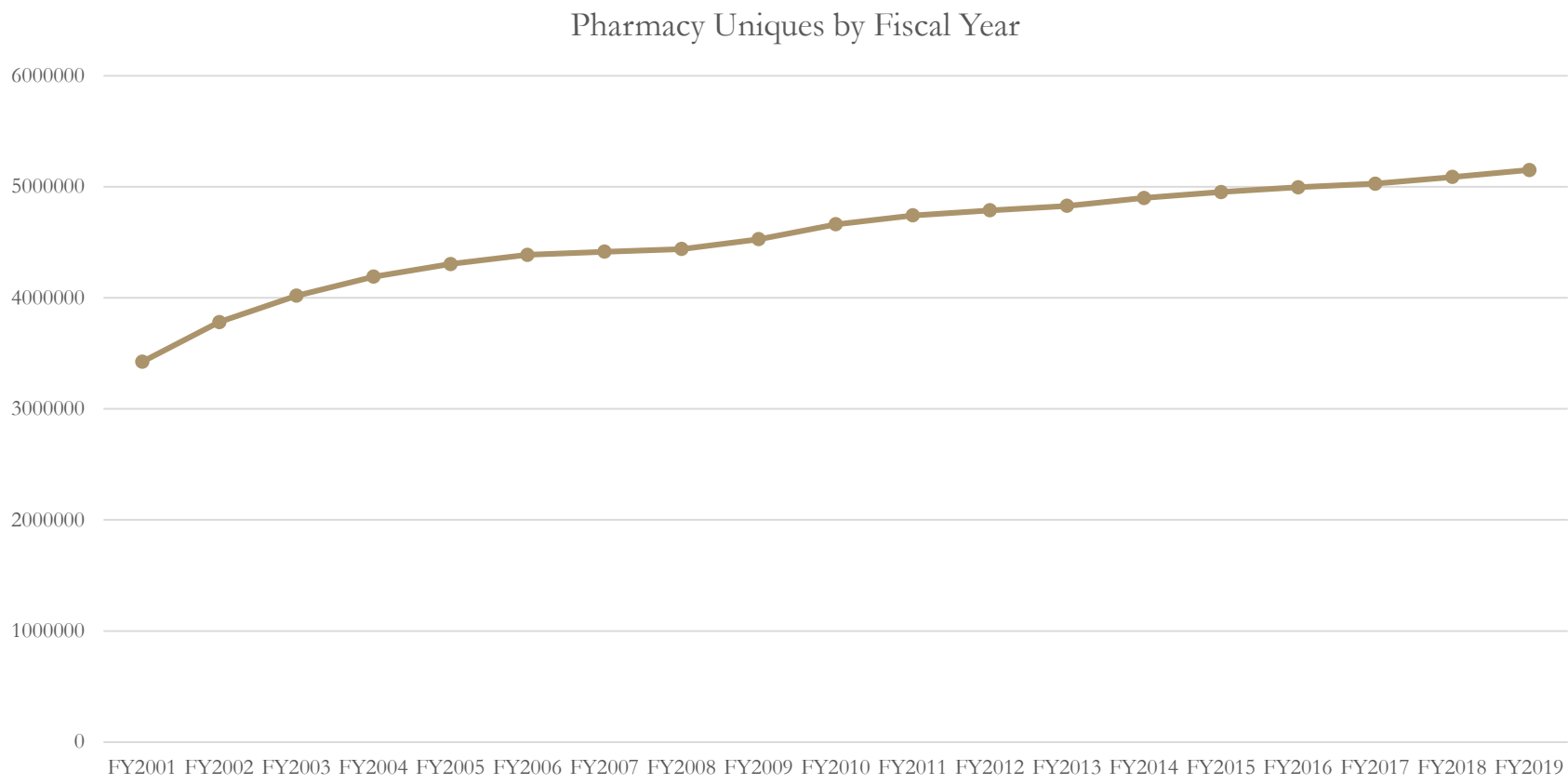
VA and its National Formulary

- Formulary Goals:
  - Evidenced-based, not preference-based
  - Promote appropriate drug therapy, discourage inappropriate therapy
  - Reduce geographic variability in utilization of pharmaceuticals across the VA system
  - Portable and uniform drug benefit

- Improve patient safety
- Outcomes assessment
- Improve distribution of pharmaceuticals
- Reduce inventory carrying costs, drug acquisition costs and the overall cost of care

VA Statistics (Fiscal Year 2019)

- 296 million outpatient prescription (30-day Equivalent)
  - 85% via mail order
  - 15% via local facility pharmacies
- $5.5 billion outpatient drug expenditures
  - Cost per 30-day Equivalent prescription nearly flat for 13 years
  - Cost is low for population cohort
    - elderly, male, multiple comorbidities


Pharmacy Uniques by Fiscal Year
6000000
5000000
4000000
3000000
2000000
1000000
0
FY2001 FY2002 FY2003 FY2004 FY2005 FY2006 FY2007 FY2008 FY2009 FY2010 FY2011 FY2012 FY2013 FY2014 FY2015 FY2016 FY2017 FY2018 FY2019

Value, Simply Stated

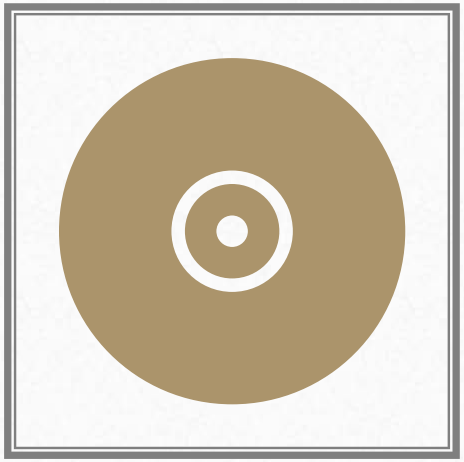
Value relates to: Intended Outcomes/Cost

Intended Outcomes IMPROVE relative to Cost = Better Value

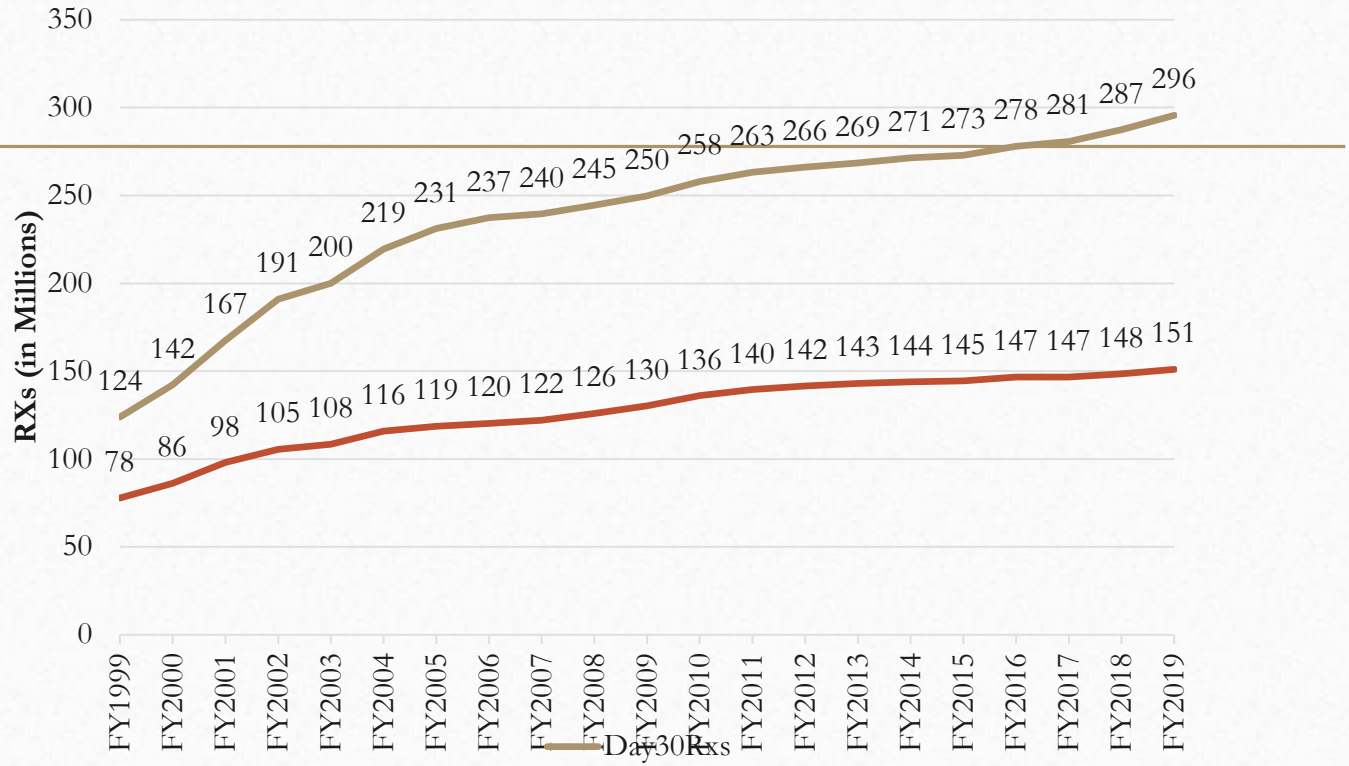
Intended Outcomes remain STABLE (or IMPROVE) with lower Cost = Better Value

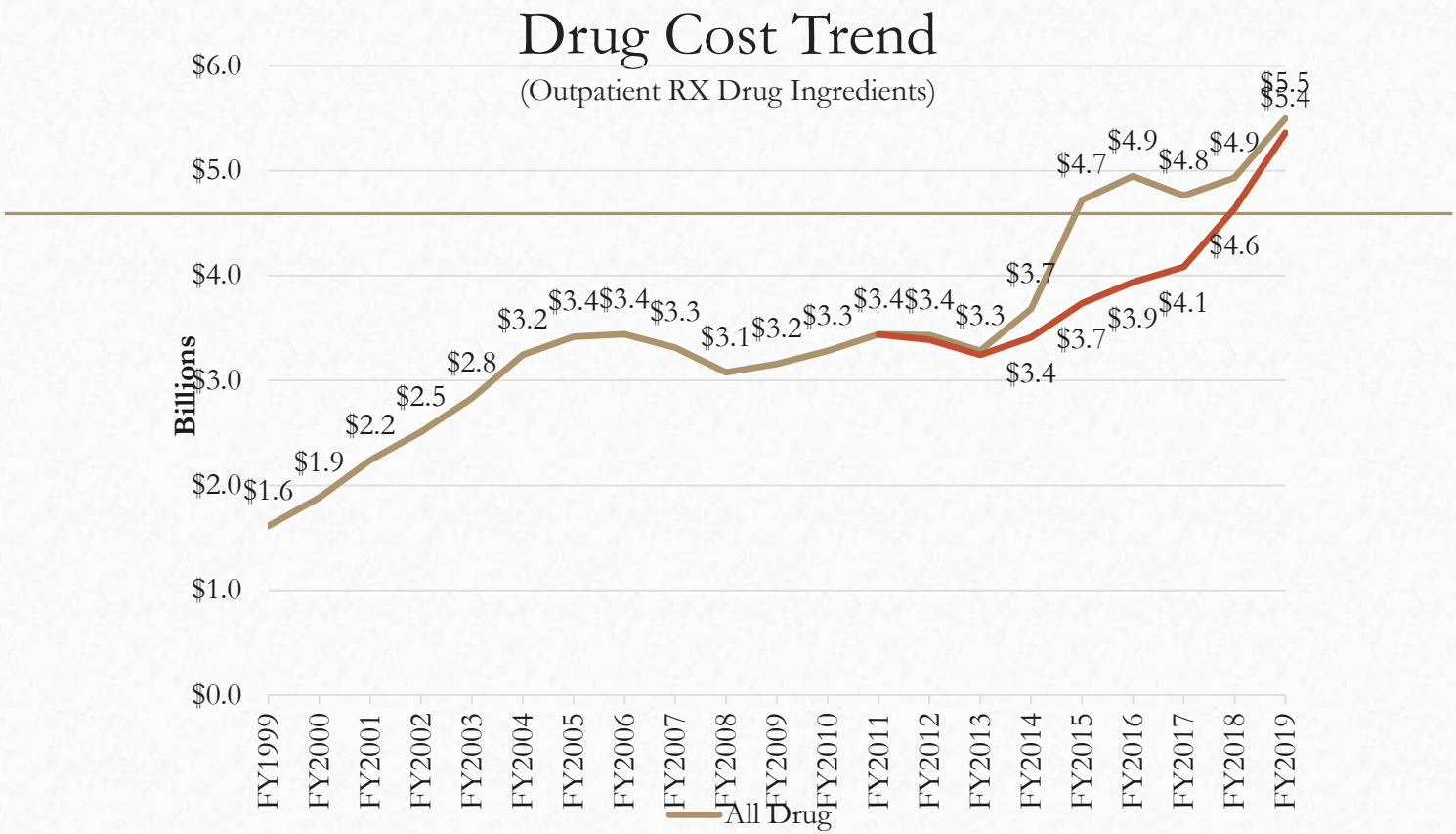
Generics and Their Inherent Value

- Generics, provided that they are safe and effective, provide similar outcomes to original products at a lower cost. Hence, better value
  - Value generally increases as generic competition rises and pushes prices downward



VA Prescription Dispensing Trends




Drug Cost Trend
(Outpatient RX Drug Ingredients)
Billions
$6.0
$5.0
$4.0
$3.0
$2.0
$1.0
$0.0
$1.6
$1.9
$2.2
$2.5
$2.8
$3.2
$3.4
$3.4
$3.3
$3.1
$3.2
$3.3
$3.4
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$4.8
$4.9
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$5.4
$3.7
$3.9
$4.1
$4.6
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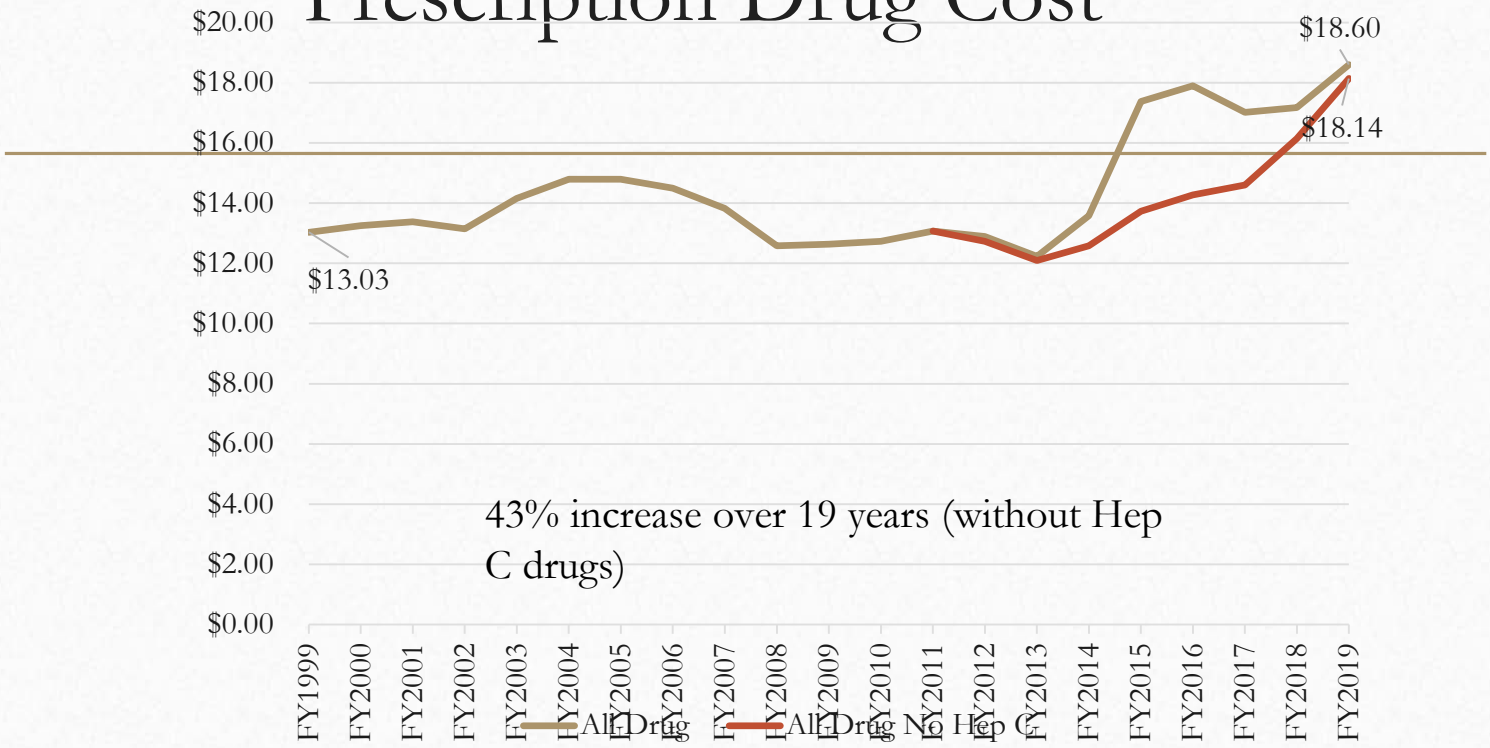
FY2014
FY2015
FY2016
FY2017
FY2018
FY2019
All Drug

VA Average 30-day Equivalent Prescription Drug Cost



What About VA vs Medicare?

- Annals of Internal Medicine, 2013 (Gellad et al):
- Brand-Name Prescription Drug Use Among Veterans Affairs and Medicare Part D Patients with Diabetes
- Budget Impact: 4 drug classes for diabetics
  - If VA were to be like Medicare: $108M more/year
  - If Medicare were to be like VA: $1.4B less/year

	% Brand Oral DM Meds	% Brand LA Insulin	% Brand Statin	% Brand ACEI/ARB
VA	7.4%	26.8%	12.3%	20%
Medicare	13.6%	60%	45.5%	37.8%

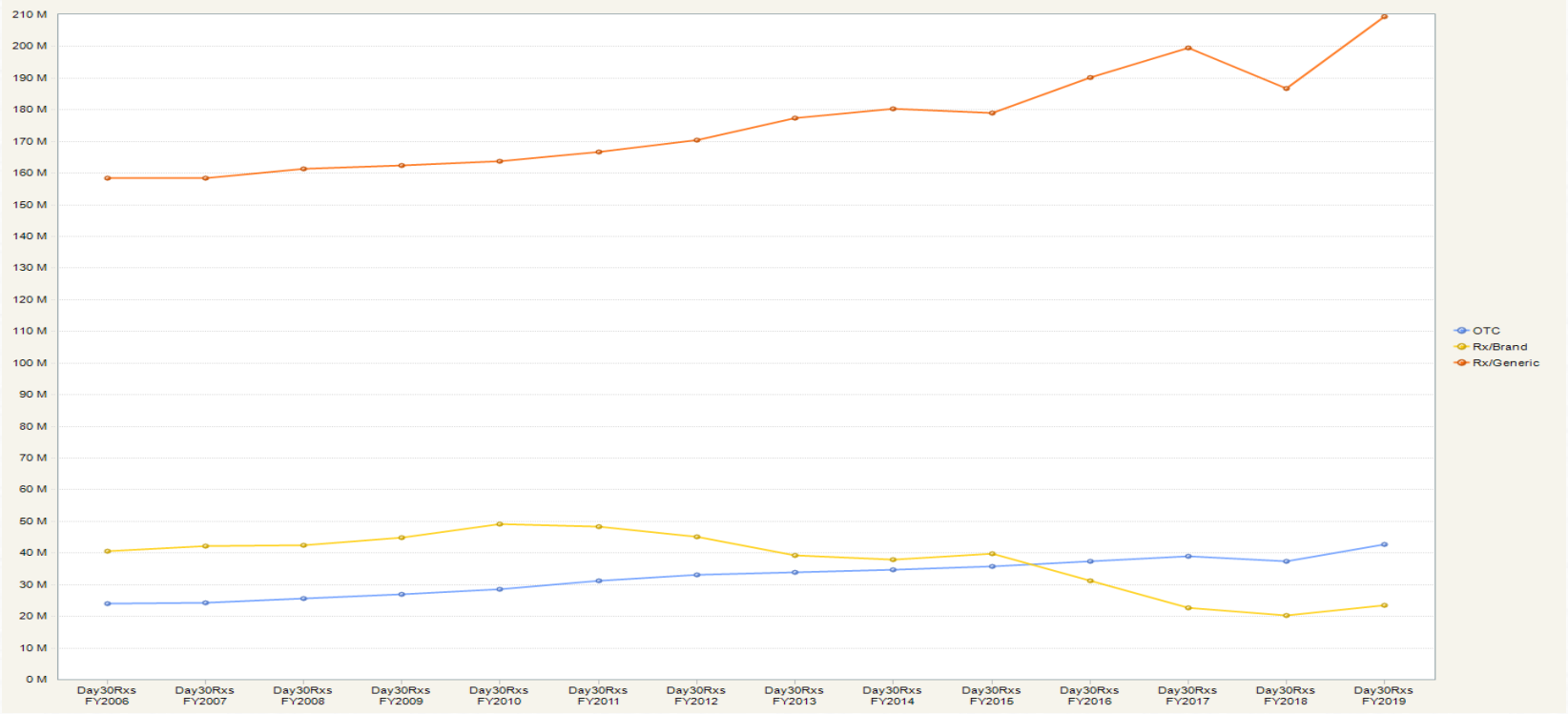
Generics Provide VA Savings
(Allowing fixed funds to be used elsewhere)

- Two components:
  - Initial price decline from Brand to generic (after exclusivity period)
  - When possible and available, contract for a sole generic product
    - Generally reduces cost further AND helps provide uniformity across VA
      - Important for certain drugs (e.g., warfarin, an anticoagulant blood thinner)

Patient Perspective

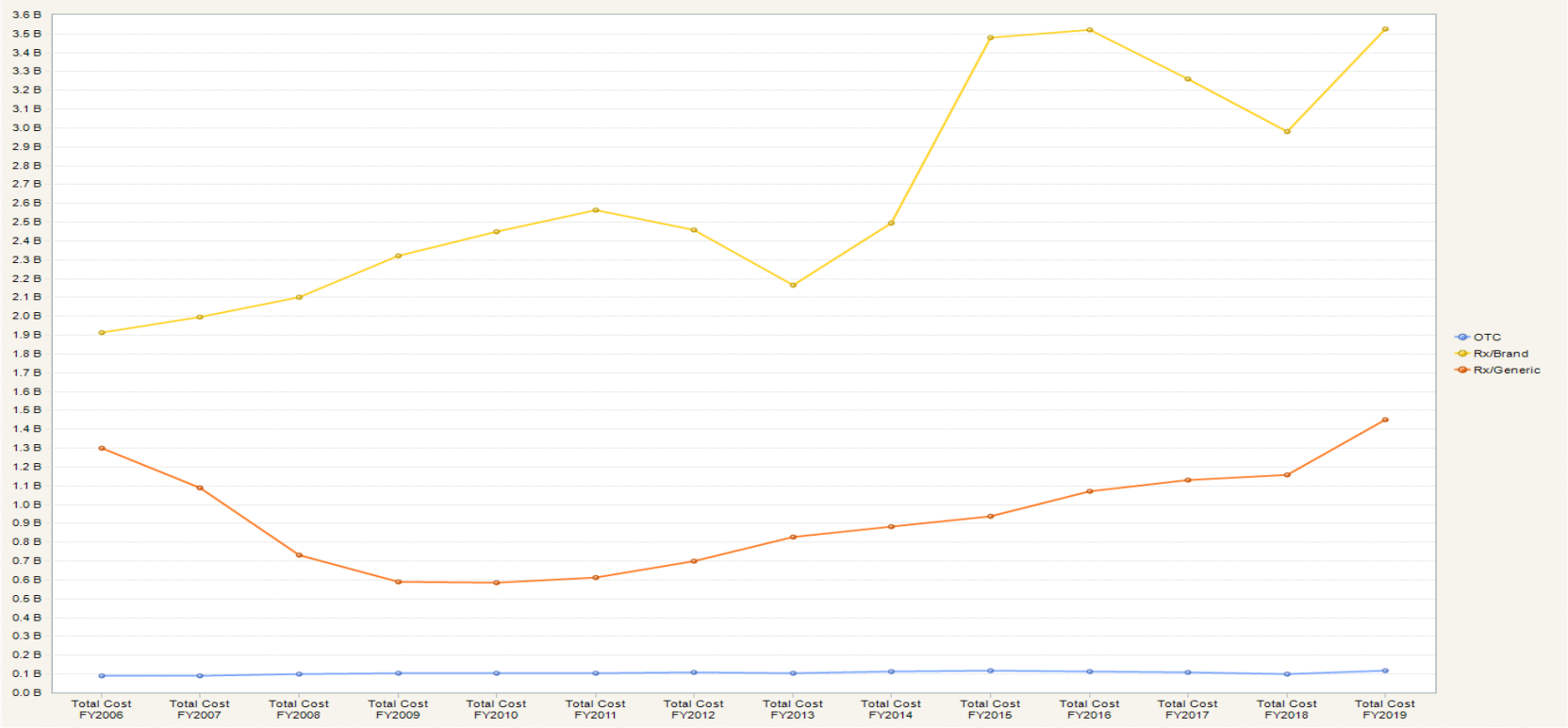
- Co-payment is tiered:
  - Tier 1 (preferred generics) $5 per 30-day supply
  - Tier 2 (non-preferred generics and some over the counter items) $8 per 30-day supply
  - Tier 3 (brand name) $11 per 30-day supply
- Affects only ~50% of Veterans based on eligibility
- Same co-payment for Formulary or Non-Formulary
  - Different than Private Sector (tiers)

Proportion of Generics in VA vs Brand*



*May not be exact due to database limitations

Costs of Generics vs Brand in VA*



*May not be exact due to database limitations

General Considerations That May Affect Generic Market

- Quality issues (off shore products such as precursor chemicals or active pharmaceutical ingredients)
- Price gouging (especially when there is lack of competition)
- Shortages (from various causes)

Other Considerations for VA

- Must be Trade Agreement Act (TAA) compliant unless a non-availability waiver is granted which determines that there is no TAA compliant source

- In order to be added to a VA contract, cGMP status based on FDA inspection must be confirmed
  - If cGMP status is deemed unacceptable for the manufacturing location of the product, then the drug will not be added to contract

Summary

- **Generics provide excellent value to the VA, to our patients and to US taxpayers, allowing access to numerous pharmaceuticals at reasonable cost.**

- Thank you for your consideration!
  - And thanks to the FDA, and to VA PBM colleagues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Public Meeting on Reauthorization of the Generic Drug User Fee Amendments (GDUFA): Indian Health Service

CAPT Christopher Lamer, PharmD, MHS, BCPS, CDE

Director of Pharmacovigilance, National Pharmacy and Therapeutics Committee

July 21, 2020

Indian Health Service

- Federal Agency under the Department of Health and Human Services comprised of:
  - Indian Health Service direct health care services
  - Tribally operated health care services
  - Urban Indian health care services and resource centers

- Mission: to raise the physical, mental, social, and spiritual health of American Indians and Alaska Natives to the highest level.

Reference: https://www.ihs.gov/newsroom/factsheets/ihsprofile/

Indian Health Service

- Provides care to 2.56 million American Indians and Alaska Natives from 573 federally recognized Tribes in 37 states(FY 2019).

Reference: https://www.ihs.gov/newsroom/factsheets/ihsprofile/

Increased Use of Medications

- Diseases of the heart, malignant neoplasm, unintentional injuries, and diabetes are leading causes of American Indian and Alaska Native deaths (2009-2011).
    - 12,752,394 outpatient visits (FY2018)
    - Often require management with chronic medication therapy.
        - Majority are generic medications

Reference: https://www.ihs.gov/newsroom/factsheets/disparities/
https://www.ihs.gov/newsroom/factsheets/ihsprofile/

Benefits of Generic Medications

- Increased options from suppliers
  - If one brand is recalled or out of stock, often other manufacturers can continue to provide.
- Competition
  - Competition among manufacturers of generic products results in lower costs compared to brand names, increasing the ability to improve access to pharmacologic therapy to AI/AN patients.
- Safety
  - Oversight from the FDA helps to assure the quality and safety of generic medications.

Areas of Improvement

- Recent widespread recalls of generic products:
  - Shortages or change in treatment (ranitidine, metformin ER)
  - Increased workload for health care providers to contact and inform patients of recalls and recall procedures.

- Although not considered to be “generics”, biosimilars remain an uncertain product for many prescribers.
  - Increased awareness of biosimilars and support of their safety and efficacy could improve access to these treatments for many patients.

Clarifying Questions

FDA GDUFA III Q&A Panel

Jacqueline Corrigan-Curay
Director, Office of Medical Policy
FDA/CDER

Alonza Cruse
Director, Office of Pharmaceutical Quality Operations
FDA/ORA

Ashley Boam
Director, Office of Policy for Pharmaceutical Quality
FDA/CDER/OPQ

Maryll Toufanian
Director, Office of Generic Drug Policy
FDA/CDER/OGD

Edward "Ted" Sherwood
Director, Office of Regulatory Operations
FDA/CDER/OGD

Robert Lionberger
Director, Office of Research and Standards
FDA/CDER/OGD

David Gaugh, R.Ph.

Senior Vice President for Science & Regulatory Affairs,
Association for Accessible Medicines (AAM)

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FDA/CDER/OGD

Robert Lionberger
Director, Office of Research and Standards
FDA/CDER/OGD

Lunch Break until 1:00 p.m.

Jillanne Schulte Wall

Senior Director, Health & Regulatory Policy,
American Society of Health-System Pharmacists

Anthony Barrueta

Senior Vice President, Government Relations,
Kaiser Permanente

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Scott D. Tomsky

Vice President, Regulatory Affairs, Generics, North America, TEVA

NATIONAL CENTER FOR HEALTH RESEARCH

The Voice For Prevention, Treatment And Policy

GDUFA: A Public Health Perspective
July 21, 2020

Diana Zuckerman, PhD, President
National Center for Health Research

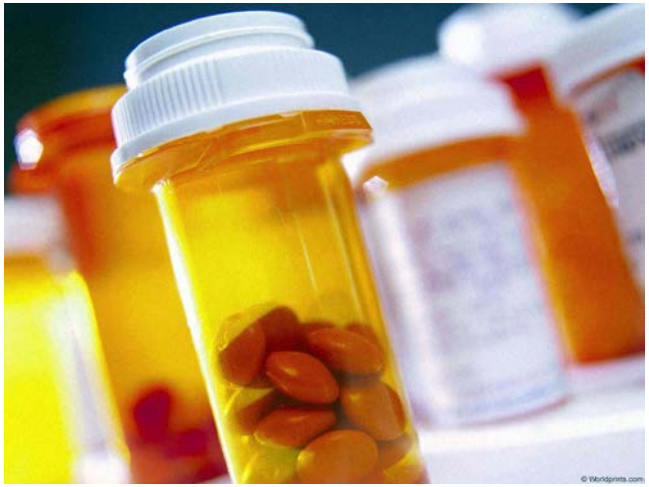
Disclosures

The National Center for Health Research is a nonprofit think tank that does not accept funding from companies that make medical products.

FDA Approval

Safe and Effective means the benefits outweigh the risks for most patients. The popularity of generic drugs is based on the assumption that the risks and benefits are essentially the same as those of brand name drugs.

FDA's Drug Approval Criteria



1. Safe
2. Effective
3. Inspected

Does it work as expected?

How sure can patients be that the generic works and is as safe as the label states?

How consistent is the label with the most recent data from postmarket surveillance?

How can GDUFA improve?

- Performance data currently based on speed
- Performance data should also be based on patient centered outcomes
- Generics cost less, but that's not the only issue of importance to patients.

How can GDUFA improve (cont'd)?

- **The most important priority for patients is having generic drugs that are safe and effective. How careful are FDA reviews? Is $$$ adequate?**

- **Patients want inspections to be thorough, especially foreign inspections. GDUFA should support inspections.**

How can GDUFA improve (cont'd)?

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How can GDUFA improve the info available to patients and providers?

- **GDUFA should support postmarket surveillance (as PDUFA does)**
- **GDUFA should provide support for FDA staff to create Patient Informed Consent Checklists when needed**
- **GDUFA should support FDA "Dear Doctor" letters and warnings to patients**

How can GDUFA improve the info available to patients and providers?

- GDUFA should support post-market surveillance (as PDUFA does)
- GDUFA should provide support for FDA staff to create Patient Informed Consent Checklists when needed
- GDUFA should support FDA “Dear Doctor” letters and warnings to patients

Post-market studies

- Clinical trials may sometimes be needed
- Sentinel, adverse event reports, and other real world data can provide useful info

Are generics as good as name brands?

?

NATIONAL CENTER FOR HEALTH RESEARCH

The Voice For Prevention, Treatment And Policy

Diana Zuckerman, PhD, President
National Center for Health Research
www.center4research.org


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IPEC-Americas Proposals for Consideration during GDUFA III Negotiations

FDA Public Meeting, July 21, 2020

Priscilla Zawislak
Immediate past chair, IPEC-Americas

Multiple stakeholders; **one objective.**

International Pharmaceutical Excipients Council

Collaborative solutions for excipient industry stakeholders

IPEC-Americas

IPEC-Americas represents ~50 excipient manufacturers, distributors and pharmaceutical/ biopharma companies to support the safe production and use of excipients. IPEC-Americas is dedicated to working closely with regulatory authorities, industry organizations and scientific bodies (globally) to advance public health on matters relating to the quality, safety, manufacture, distribution, use and functionality of excipients. IPEC is the sole association representing excipients.

Key excipient issues to address under GDUFA III

- Status of key excipient issues requested to be addressed under GDUFA II
- IID policy and integrity issues not addressed under GDUFA II
- Bridging justification policy, guidance, training
- Novel Excipient Pilot Review Program
- Improved communication channel related to excipient issues and formal inclusion of IPEC-Americas in GDUFA ongoing discussions

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Open Comment Period

U.S. FOOD & DRUG ADMINISTRATION

Jacqueline Corrigan-Curay

Office Director, Office of Medical Policy

FDA, CDER