
FDA U.S. FOOD & DRUG ADMINISTRATION

## Careers in Pharmacology Symposium:

# The FDA

**Markham C. Luke, MD PhD – JHU Med '94**

**Labs – D. Coffey, T. August, S. Snyder, P. Pitha-Rowe**

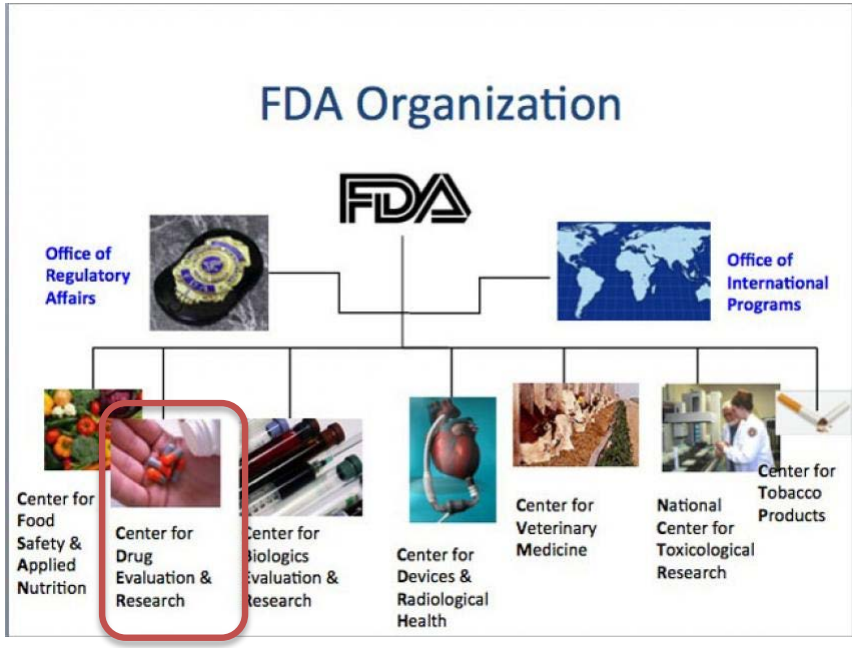
**Director, Division of Therapeutic Performance**

**OGD, ORS, CDER, Food and Drug Administration**

**Friday, June 1, 2018, Johns Hopkins University**

FDA Campus


FDA
U.S. Department of Health and Human Services
Food and Drug Administration


FDA Organization
FDA
Office of Regulatory Affairs
Office of International Programs
Center for Food Safety & Applied Nutrition
Center for Drug Evaluation & Research
Center for Biologics Evaluation & Research
Center for Devices & Radiological Health
Center for Veterinary Medicine
National Center for Toxicological Research
Center for Tobacco Products

# Office of Generic Drugs (OGD)

- Located in the Center for Drug Evaluation and Research
- Four Sub-Offices: Bioequivalence, Regulatory Operations, Generic Drug Policy, Research and Standards
- Office of Research and Standards (ORS) – leads the implementation of regulatory science commitments and translates research results into standards for safe, effective, and equivalent generic drugs.

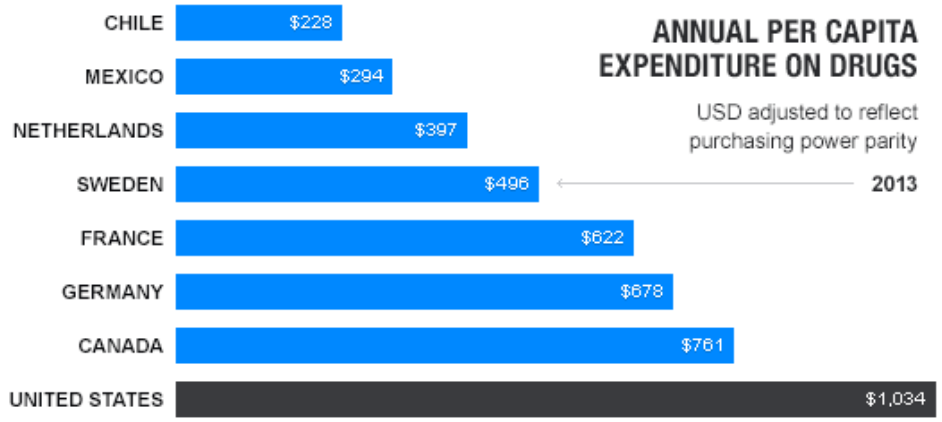
## Generic Drugs:

- Are duplicates of brand-name drugs
- Are the same as those brand name drugs in active ingredients, dosage form, strength, route of administration, quality, performance characteristics, safety, efficacy, and intended use.

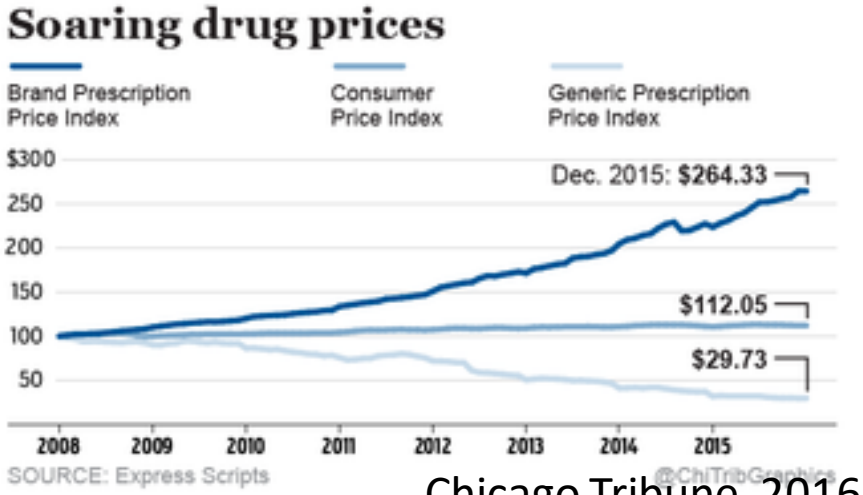
From FDA website – Understanding Generic Drugs
https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/default.htm

# Introduction to Generic Drugs

- Each ANDA (Abbreviated New Drug Application) relies on a reference listed drug (RLD)
- Generic drugs cost less to develop because applicants do not repeat the safety and efficacy studies conducted for RLD approval
- An ANDA generally demonstrates
  - It is the same as the RLD with respect to the active ingredient(s), conditions of use, route of administration, dosage form, strength, and labeling (with certain permissible differences)
  - It is bioequivalent to the RLD

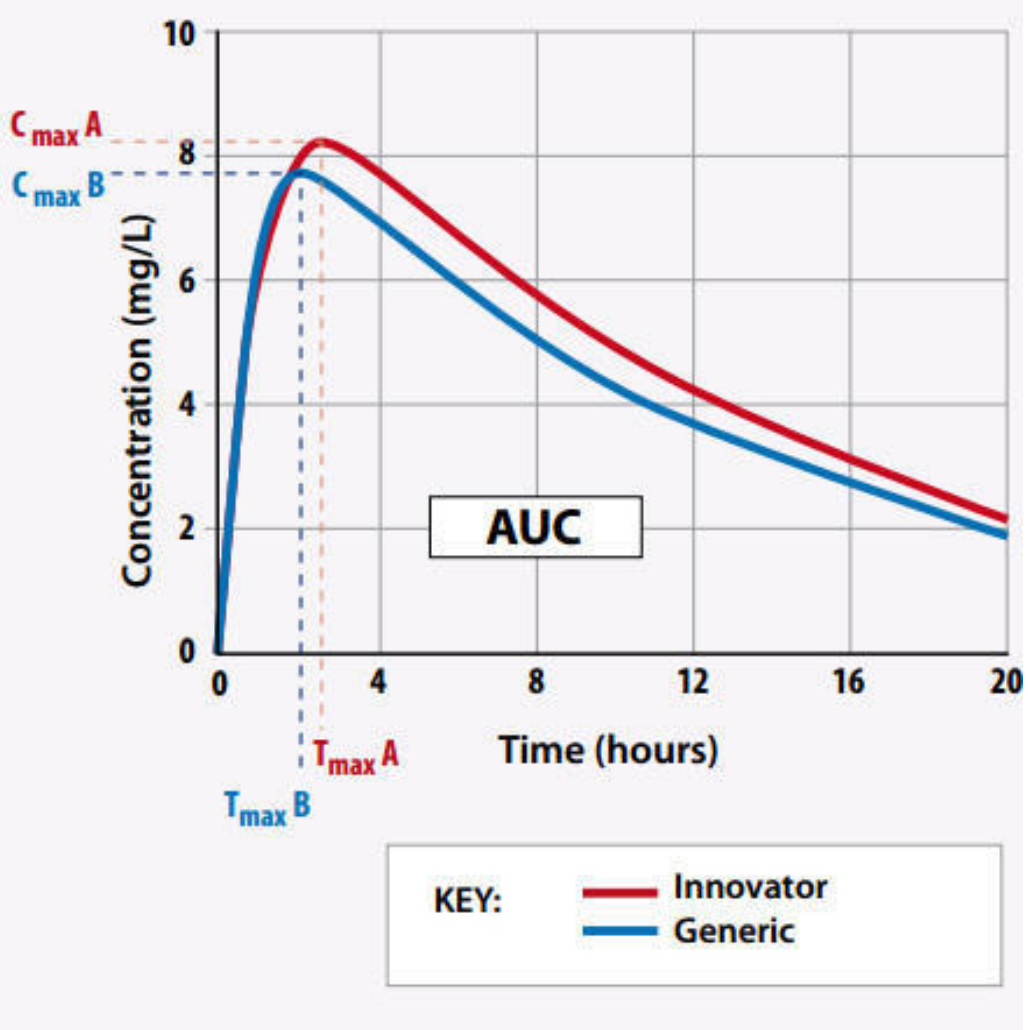



Fortune, 2015




Chicago Tribune, 2016

# Bioequivalence (BE) Determinations




- For products with systemic site of action, BE via systemic PK endpoints (e.g. $C_{max}$ and AUC) helps infer comparable safety and efficacy
- For products that are locally acting, it is more difficult to assess local exposure
- The site of action may not be directly correlated with systemic PK

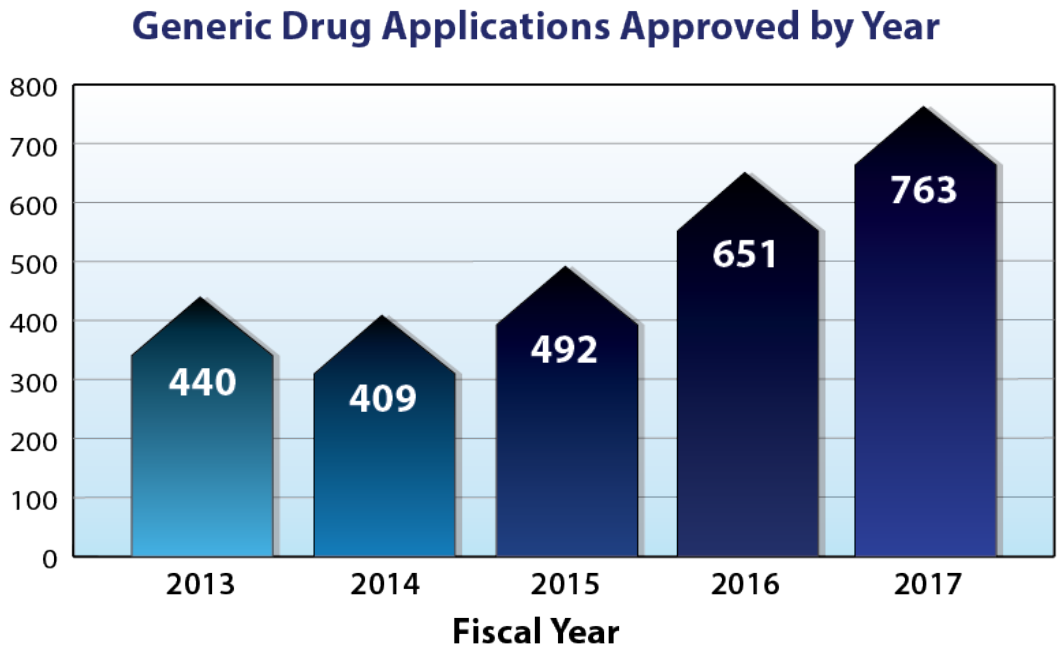
# Complex Generic Products in GDUFA II

- Complex active ingredients
  - Complex mixtures of APIs, polymeric compounds, peptides
- Complex formulations
  - Liposomes, suspensions, emulsions, gels
- Complex routes of delivery
  - Locally acting such as dermatological and inhalational drugs
- Complex dosage forms
  - Long acting injectables and implantables, transdermals, metered-dose inhalers
- Complex drug-device combination products
- Other products where complexity or uncertainty concerning the approval pathway or other alternative approach would benefit from early scientific engagement

https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf

# GDUFA Regulatory Science

- FDA has a role in advancing drug science and pharmacologic knowledge helps increase drug access by providing science-based methods and standards for determining equivalence.
- ~$25 million per year on stakeholder-driven generic drug regulatory science
  - Goal: Access to generics in all product categories
  - 90+ on-going projects
  - Recent focus on complex products




**Generic Drug Science & Research Website:**
https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm

# ISO – A few good scientist/pharmacologists/modelers

- Post-doctoral fellowship opportunities are available in CDER/OGD/ORS – multiple positions available – fellowship program is administered by Oak Ridge Institute for Science and Education (ORISE) and established via inter-agency agreement
- See handout for details
- Specific areas
  - Oral Inhalation/Nasal Drug Products
  - Solid Oral dosage forms
  - Modeling and simulation

OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION

# Full-time employment

- Looking for a full-time career in regulatory pharmacology?
- If you are an experienced pharmacologist, scientist, or physician with interest in drug development send CV/resume for consideration

  Markham.Luke@FDA.HHS.GOV

# Extramural Collaborative Funding Opportunities

- Contracts (Broad Agency Agreements)
- Collaborative Grants

https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/ucm585566.htm

# Regulatory Pharmacology in Action

Kara Scheibner, PhD

Office of Translational Sciences, CDER, FDA

# Who am I???

- Kara A. Scheibner, Ph.D.
  - 1998 - 2003 – Ph.D. under Phil Cole
  - 2003 - 2007 – post-doctoral fellow with Maureen Horton, Johns Hopkins
  - 2007 - 2009 – post-doctoral fellow with Curt Civin, Johns Hopkins
  - 2009 - 2014 – Assistant Professor, University of Maryland School of Medicine
    - Primary research focus – microRNAs, hematopoiesis, leukemia
    - Lecturer and course director
    - Molecular Medicine department admissions committee
    - Nathan Schnaper Cancer Research Internship admissions committee and mentor
- My Current Position (July 2014 – present):
  - Interdisciplinary Scientist/Pharmacologist/Reviewer in CDER/Office of Translational Sciences (OTS)/OSIS

# Office of Study Integrity and Surveillance (OSIS)

- Coordinate inspections, review, and make recommendations on data acceptance for the clinical portions of bioequivalence/ biosimilar studies
- Do on-site review and audits of bioanalytical data (PK data, immunogenicity data) for bioequivalence/biosimilar studies
  - Travel is a large portion of our jobs (Yay!)
- Make recommendations on bioanalytical data acceptance


- kara.scheibner@fda.hhs.gov

- No reviewer FTEs currently; opening in our project manager and Collaboration, Risk assessment and Surveillance Team (CREST)

# Pharmacologist/Toxicologist Drug Reviewer

Ijeoma Uzoma, Ph.D.

**Graduate Training – Heng Zhu (2007-2014),**
**Post Doctoral Training- USAMRIID (2014-2017)**

**US FDA**

**Center for Drug Evaluation and Research**

**Office of New Drugs**

**DPARP**

# Division of Pulmonary Allergy Rheumatology Products

- Common Indications: Asthma, COPD, Cystic Fibrosis, Anaphylaxis, Rheumatoid arthritis, Gout, Osteoarthritis, Systemic lupus erythematosus, Cough/Cold/Allergic Rhinitis

- Routes of administration: oral, subcutaneous, inhalation, intraarticular injection, intravenous, intranasal routes

- Biologics and small molecules

- All prescription products

# New Drug Review Process

- Investigational New Drug (IND) Application
  - Required to support clinical study of a new drug, a new indication, new route of administration or dose, new patient population
  - FDA Review division determines whether drug is reasonably safe to test in human population
  - Nonclinical studies, Chemistry Manufacturing Control (CMC), Clinical Protocol
  - 30 day clock

- New Drug Application (NDA)/Biologic License Applications (BLA)
  - following clinical studies, application must be submitted to support marketing
  - 8-12 month clock

# Interdisciplinary Review Team

| | |
|---|---|
| Medical Officer | • Clinical expert on the team. Reviews and evaluates scientific data to assess new drugs and biologics, biosimilar biologics, and generic drugs |
| Pharmacologist/Toxicologist | • Review and evaluate pharmacological and toxicological data in IND and NDA applications |
| Chemist | • Evaluate adequacy of methods, facilities, and controls used to manufacture drugs |
| Clinical Pharmacologist | • Evaluate drug metabolism in clinical studies, understand inter-patient variabilities, optimize dose and dose regiment |
| Statistician | • Review and evaluate scientific data and mathematical and statistical methods involved with New Drug Applications e.g. experimental design and clinical research methods |
| Microbiologist | • Evaluate chemical, microbiological, and manufacturing data submitted in New Drug Applications |
| Regulatory Project Manager | • Plan and organize the work flow for the review team to accomplish activities and meet due dates related to regulatory guidelines for INDs and NDAs. Liaison for communication with Sponsors. |

# Pharm/Tox

- Pharmacologist and Toxicologist Roles are equivalent in OND. The discipline is called PharmTox

- Pharmacology: The science of drugs, including their composition, uses, and effects. The properties of a drug which confer efficacy.

- Toxicology: The study of the adverse effects of chemical substances on living organisms

# FDA Pharmacologist/Toxicologist Duties

- Reviews and evaluates the results of preclinical pharmacological studies submitted in support of INDs, NDAs, and reports to new drug applications to assess the safety of the drug based on experiments conducted by the applicant.
- Meets with industry or drug sponsor representatives to exchange information and to provide guidance regarding those aspects of the applications
- Prepares a comprehensive summary of the data reviewed and submits substantive recommendations and conclusions for approval by the Supervisor.
- Studies and maintains familiarity with the pharmacological, biochemical, and toxicological scientific literature
- Attends meetings, conferences of relevant organizations

# Qualifications for Pharm/Tox Reviewer Role

- Pharmacologist: A degree in an appropriate biological, medical, veterinary, or physical science, or in pharmacy that included at least **30 semester hours in chemistry and physiology and 12 semester hours in pharmacology.**

- Toxicologist: A degree in toxicology or an appropriate discipline of the biological, medical, or veterinary sciences that included at least **30 semester hours in chemistry, biochemistry, or physiology, and 12 semester hours in toxicology.**
  - A doctorate degree in a relevant scientific discipline with **at least two years post-doctorate experience is required.**

- Relevant experience:
  - Drug discovery, animal efficacy models, pharmacology or toxicology research, GLP studies, industry roles, DVM degree

# Contact Information

We encourage you to reach out if interested!

- Ijeoma Uzoma, PhD (PharmTox Reviewer DPARP)

Ijeoma.Uzoma@FDA.HHS.gov

- Andrew Goodwin, PhD (PharmTox Supervisor DPARP)

Andrew.Goodwin@FDA.HHS.gov

# Clinical pharmacologists in FDA

Jianmeng Chen, M.D, Ph.D

**Labs – R. Ambinder (2001-2007, predoctoral),**
**C. Flexner, C. Hendrix (2007-2011, postdoc)**

Division of Clinical Pharmacology II

US FDA/CDER/OTS/OCP

# What do we review?
# -General clinical pharmacology studies

**Clinical Pharmacology**

- First-in-Human
- SAD and MAD PK Studies
- Healthy vs. Patient population
- ADME (Mass Balance)
- Specific Populations/dose adjustment
  - Renal Impairment
  - Hepatic Impairment
  - Age, gender, etc.
  - Pediatrics
- Drug Interactions (CYPs, transporter)
- Population PK (Modeling, R, NONMEM)
- Biomarkers (optional)
- Pharmacogenomics (optional)
- Special Safety (e.g., TQTc study)

**Exposure-response (PK/PD, dose selection)**

- Efficacy
- Safety

**Biopharmaceutics**

- Bioavailability/Bioequivalence (BA/BE)
- Food Effect

***In Vitro* Studies**

- Protein Binding
- Blood to Plasma Partitioning
- In vitro drug metabolism, transport and drug interactions

**Bioanalytical Methods (LC/MS, ELISA, etc)**

- Assay Validation & Performance Reports

# Some of the Things we do……

- Opioid
- Biosimilar
- Epipen
- Cold and cough over the counter medications
- NMEs (Rare disease, diabetes, RA, etc)
- Many other interesting and exciting things


23

# Mimi's list

- How did your pharmacology training help in your professional path?
- Were there shortcomings in your training that you had to compensate for on the job?
- What are the most important things you have learned about succeeding in your job?
- What have been the most challenging times in your career? How did you manage these events?
- What advice would you give to new graduates trying to enter your profession?
- What is the most enjoyable part of your job? What is the least enjoyable part of your job?
- What strategies do you use to achieve work-life balance? Have you found your employer to be supportive of employee work-life balance?


24

# Positions

- ORISE fellow- No H1

- FTE (depend on the agency/position)
  - H1 visa: Visiting associate
  - Green card: staff fellow
  - Citizen: GS positions (USAJOBS)

# Questions?

- Current Openings:
  - Clin pharm reviewer
  - ORISE fellow: https://orise.orau.gov/fda/applicants/

- Contact:

Jianmeng.Chen@fda.hhs.gov

Chandrahas.Sahajwalla@fda.hhs.gov


FDA
U.S. FOOD & DRUG
ADMINISTRATION


Home to
Hopkins
Celebrating 125 Years of the Johns Hopkins University School of Medicine
School of Medicine
Reunion & Alumni Weekend
June 1-2, 2018