BBCIC
Biologics & Biosimilars
Collective Intelligence Consortium
AMCP BBCIC, LLC

# Biosimilars in the United States: Current status, barriers to utilization, and a growing evidence base to support treatment and coverage decisions

Cate Lockhart, MS, PharmD, PhD
Executive Director, BBCIC
October 10, 2019

# Outline

- It All Started with Generics
- Then Came Biosimilars
- Barriers to Biosimilars
- Data Sources for Decision Makers
- BBCIC: Research Progress

# It All Started With Generics

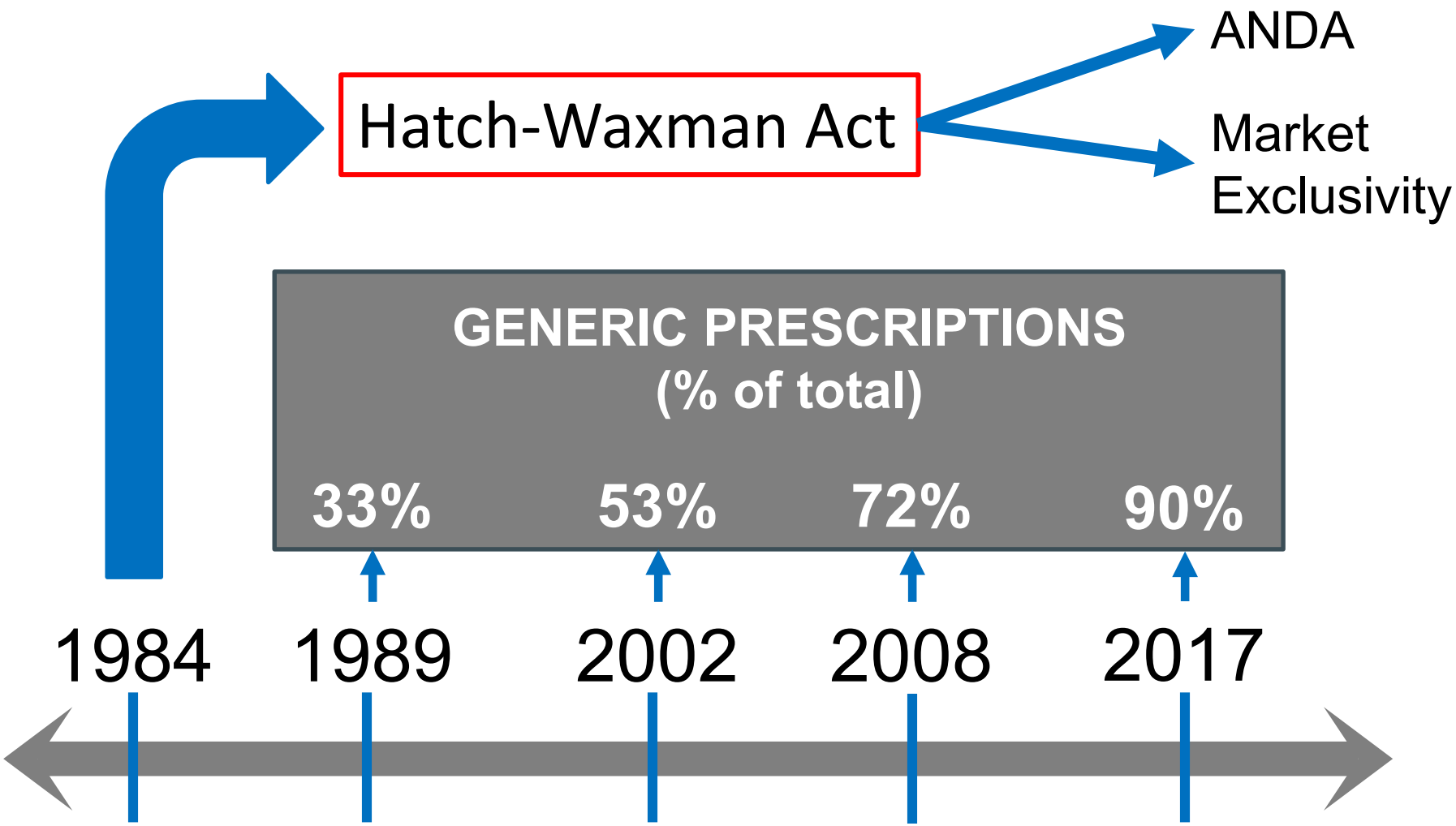
# History of Generic Drugs in the U.S.

1984



Lewis, et al. *J Contemporary Health Law & Policy*. 1992;8(1):361-378.
Boehm, et al. *Acta Pharmaceutica Sinica B*. 2013;3(5):297-311.

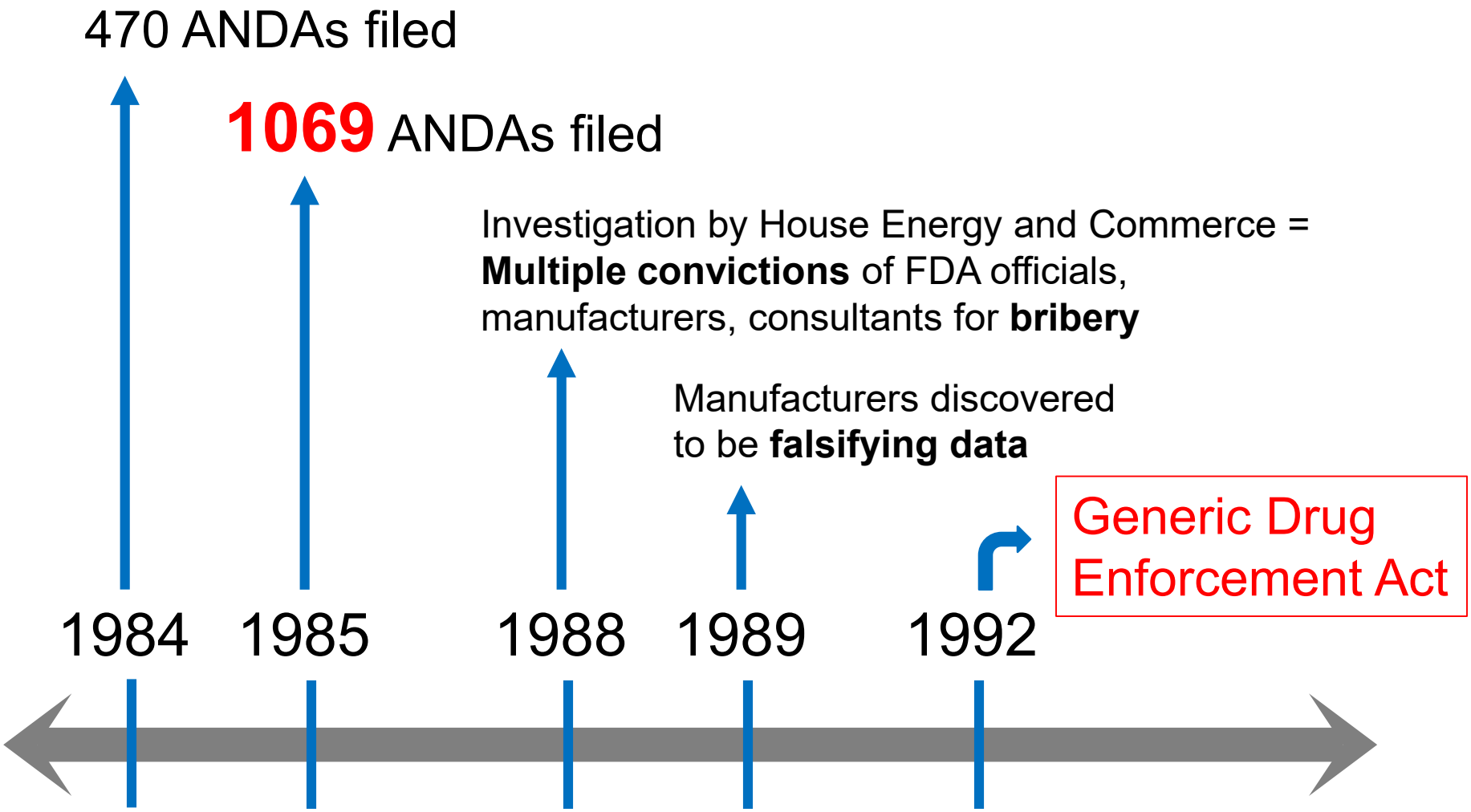
# History of Generic Drugs in the U.S.






Lewis, et al. *J Contemporary Health Law & Policy*. 1992;8(1):361-378.
Boehm, et al. *Acta Pharmaceutica Sinica B*. 2013;3(5):297-311.
Thayer. *Chemical & Engineering News*. 2014;92(39):8-16.

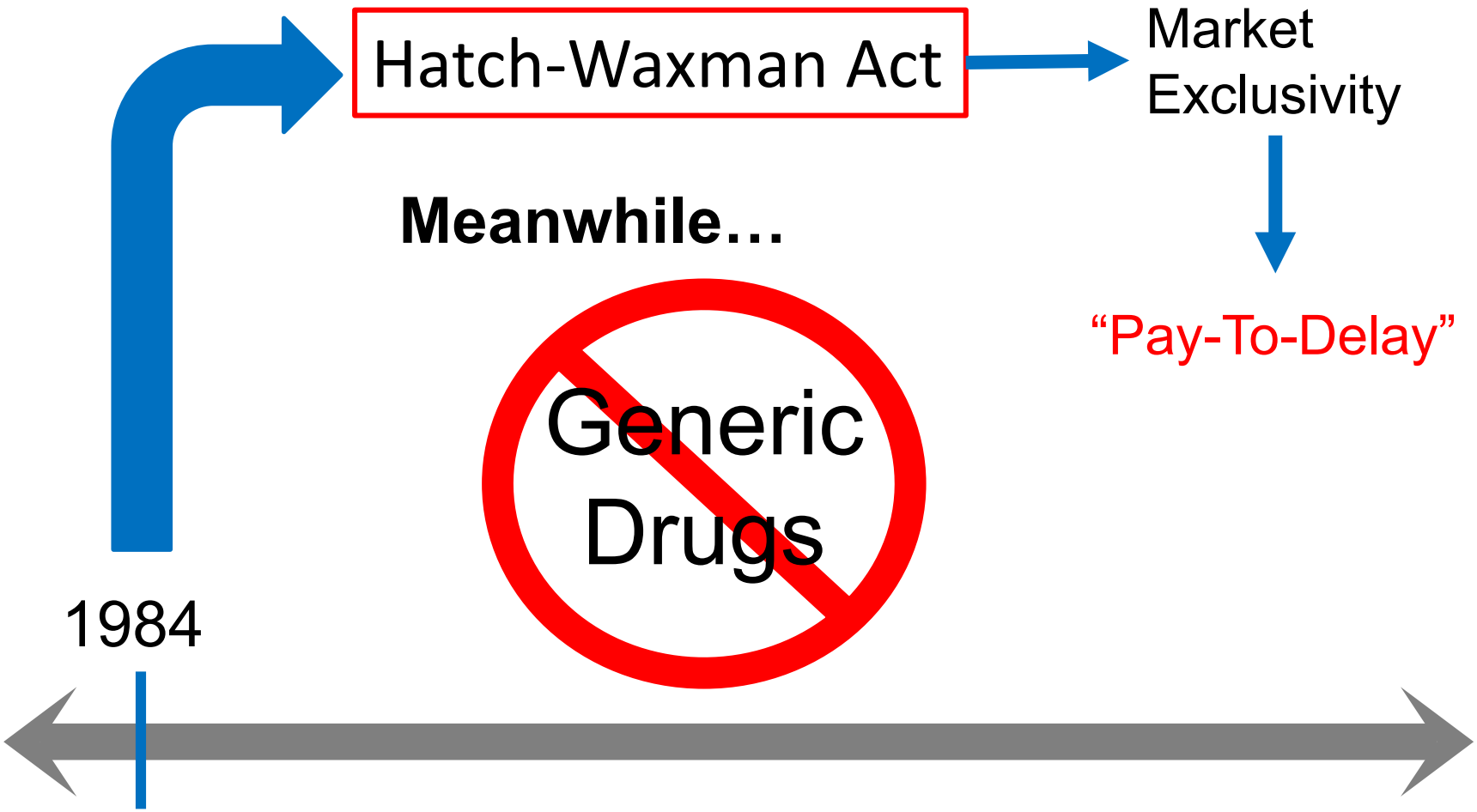
# Adverse Events






Lewis, et al. *J Contemporary Health Law & Policy*. 1992;8(1):361-378.
Kesselheim AS. CMAJ 2011;183(12):1350-1351.
Eban K. *Self* 2009. www.self.com /health/2009/06/dangers-of-generic-drugs?currentPage=1.
Huckman M. CNBC. 2007 Oct. 29. Available: www.cnbc.com/id/21528009.

# Adverse Events






Lewis, et al. *J Contemporary Health Law & Policy*. 1992;8(1):361-378.
Kesselheim AS. CMAJ 2011;183(12):1350-1351.
Eban K. *Self* 2009. www.self.com /health/2009/06/dangers-of-generic-drugs?currentPage=1.
Huckman M. CNBC. 2007 Oct. 29. Available: www.cnbc.com/id/21528009.

# Economic Impact of Generics in the U.S.

**90%** Prescriptions **filled** with **generics** in 2017

**23%** Prescription drug **spending** attributed to **generics**

**$1.6 trillion** Savings to U.S. healthcare system in the past **decade**

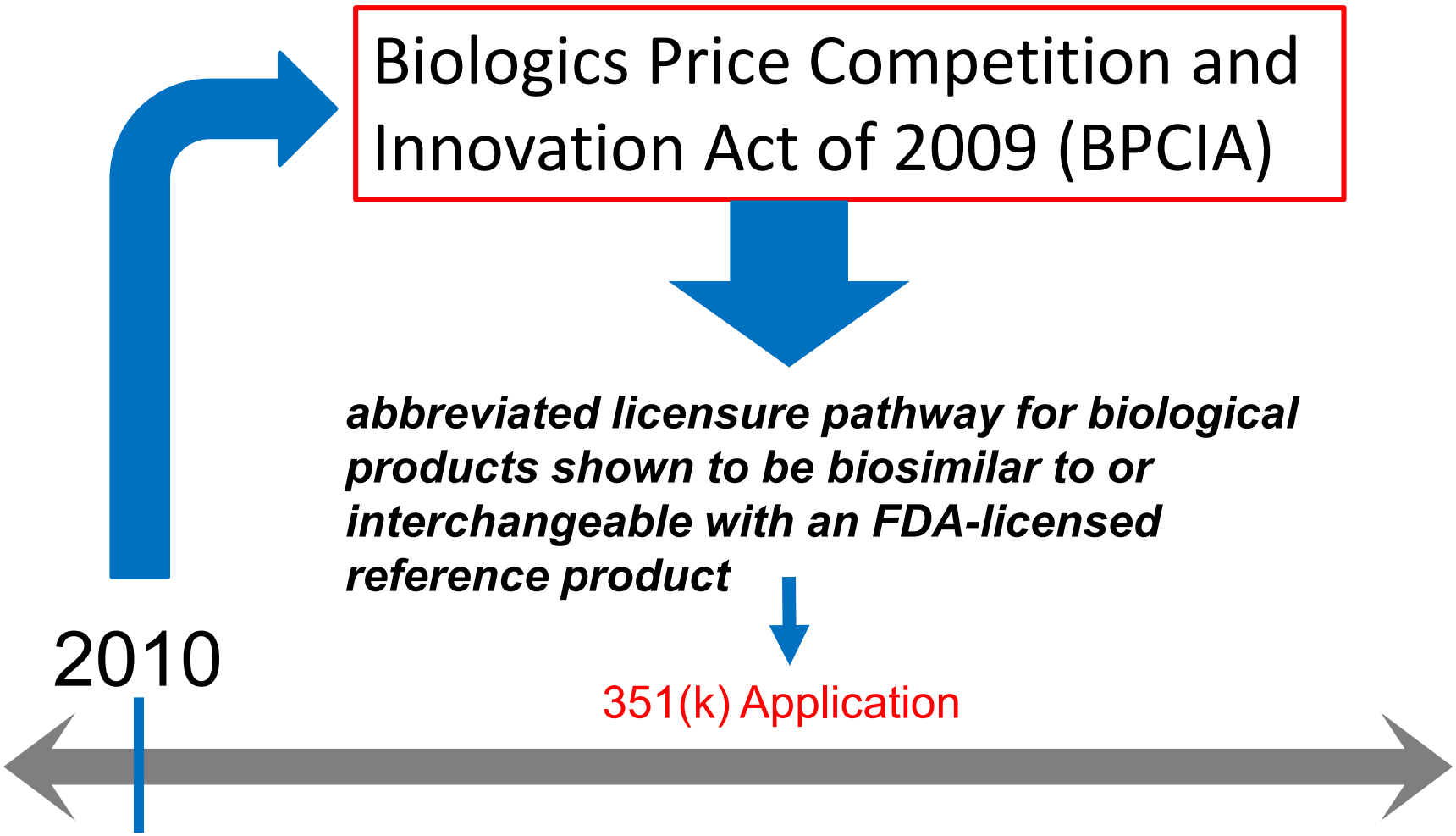
**$265 billion** Savings to the U.S. healthcare system in **2017 alone**



https://accessiblemeds.org/resources/blog/2018-generic-drug-access-and-savings-report
https://accessiblemeds.org/resources/blog/2017-generic-drug-access-and-savings-us-report
https://accessiblemeds.org/resources/blog/2018-generic-drug-access-and-savings-report

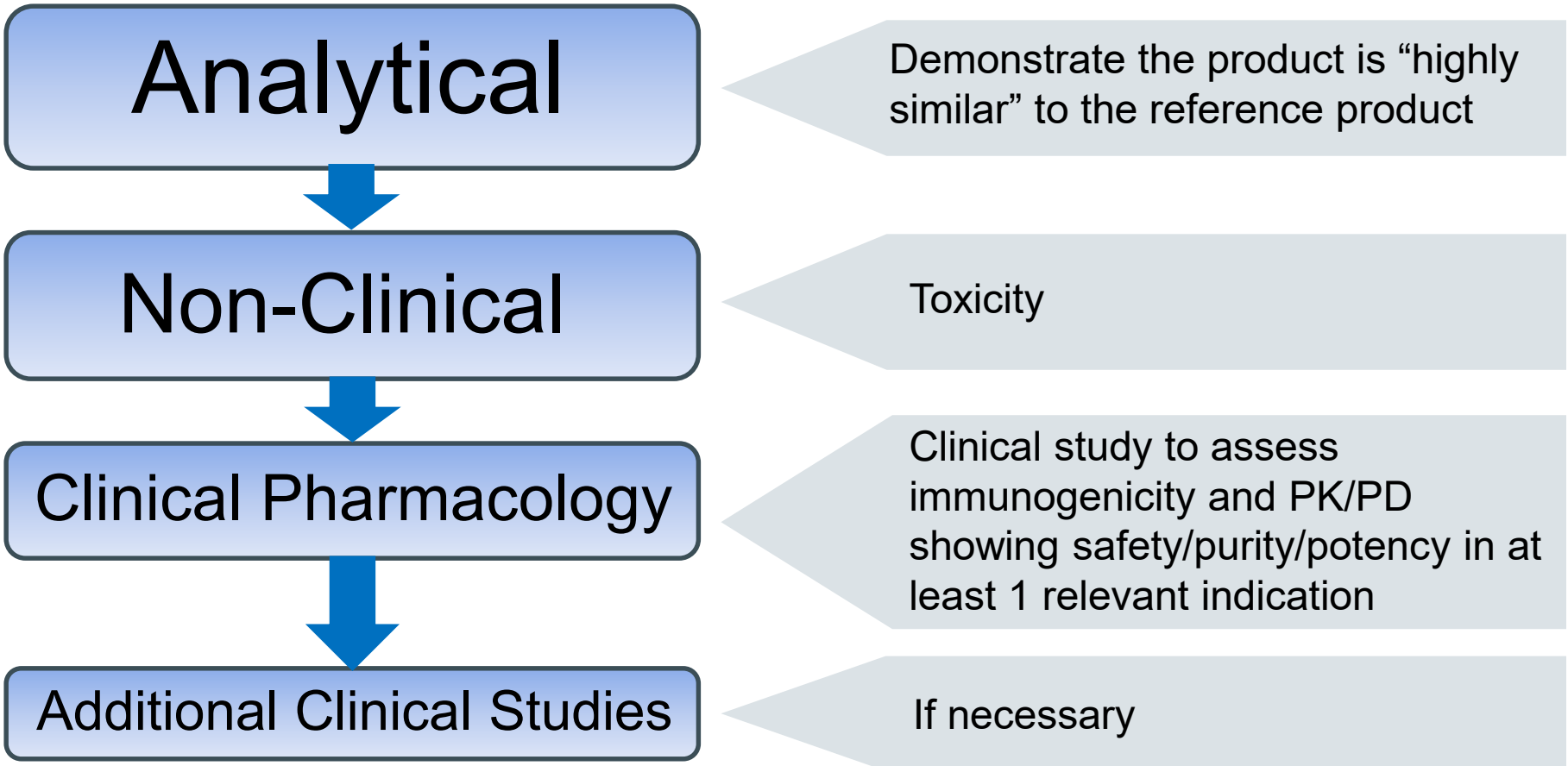
# Then Came Biosimilars…

# Biosimilars in the U.S.

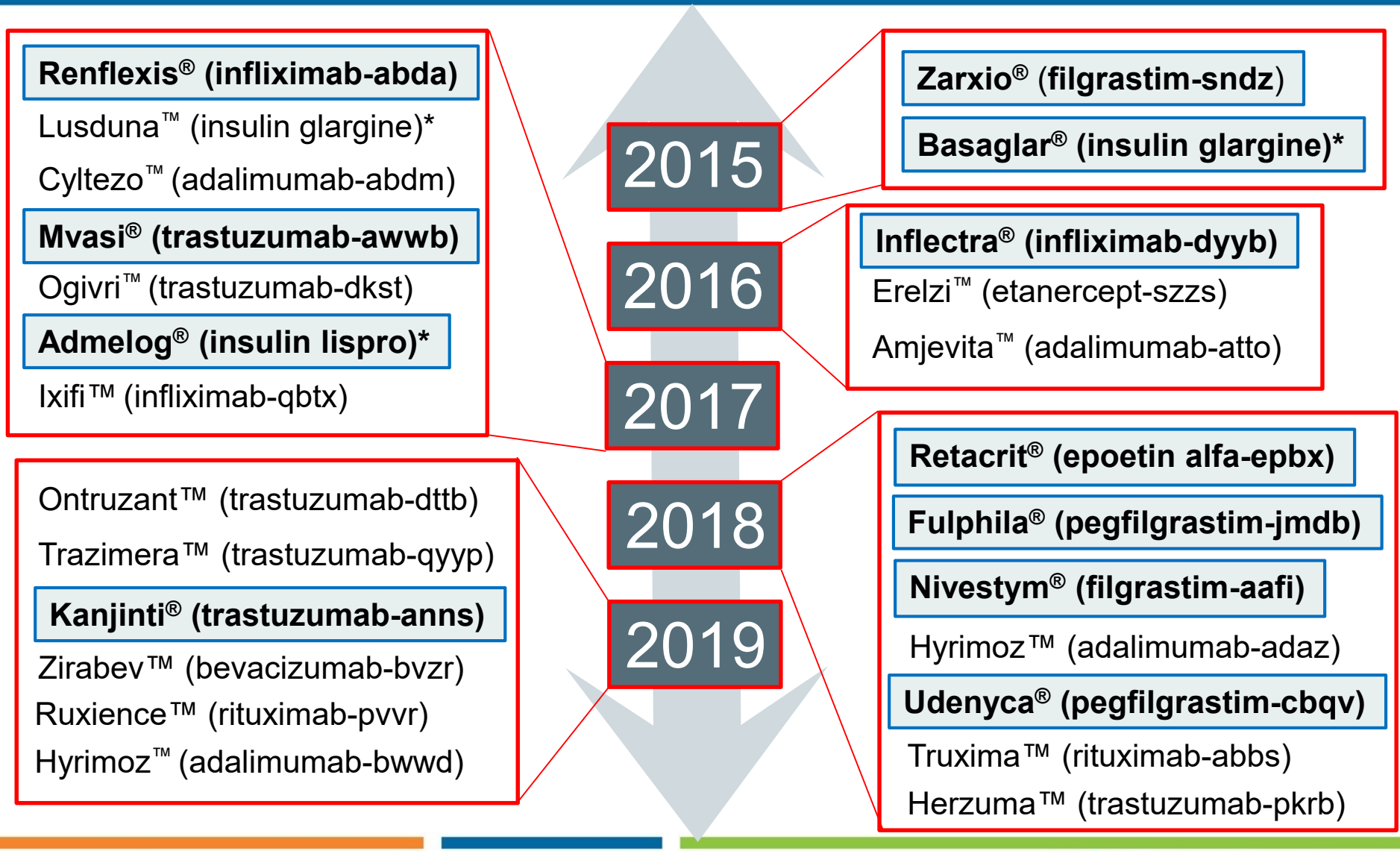


# Requirements for FDA Registration

**Demonstrating Biosimilarity → TOTALITY of EVIDENCE**



# Biosimilars Approved in US – as of Sept. 2019




www.bbcic.org

*FDA approval as a follow-on biologic

Biosimilars Review & Report. https://biosimilarsrr.com/us-biosimilar-filings/ (accessed September 5, 2018)
US Food and Drug Administration CDER List of Licensed Biological Products http://www.fda.gov (accessed September 5, 2018)

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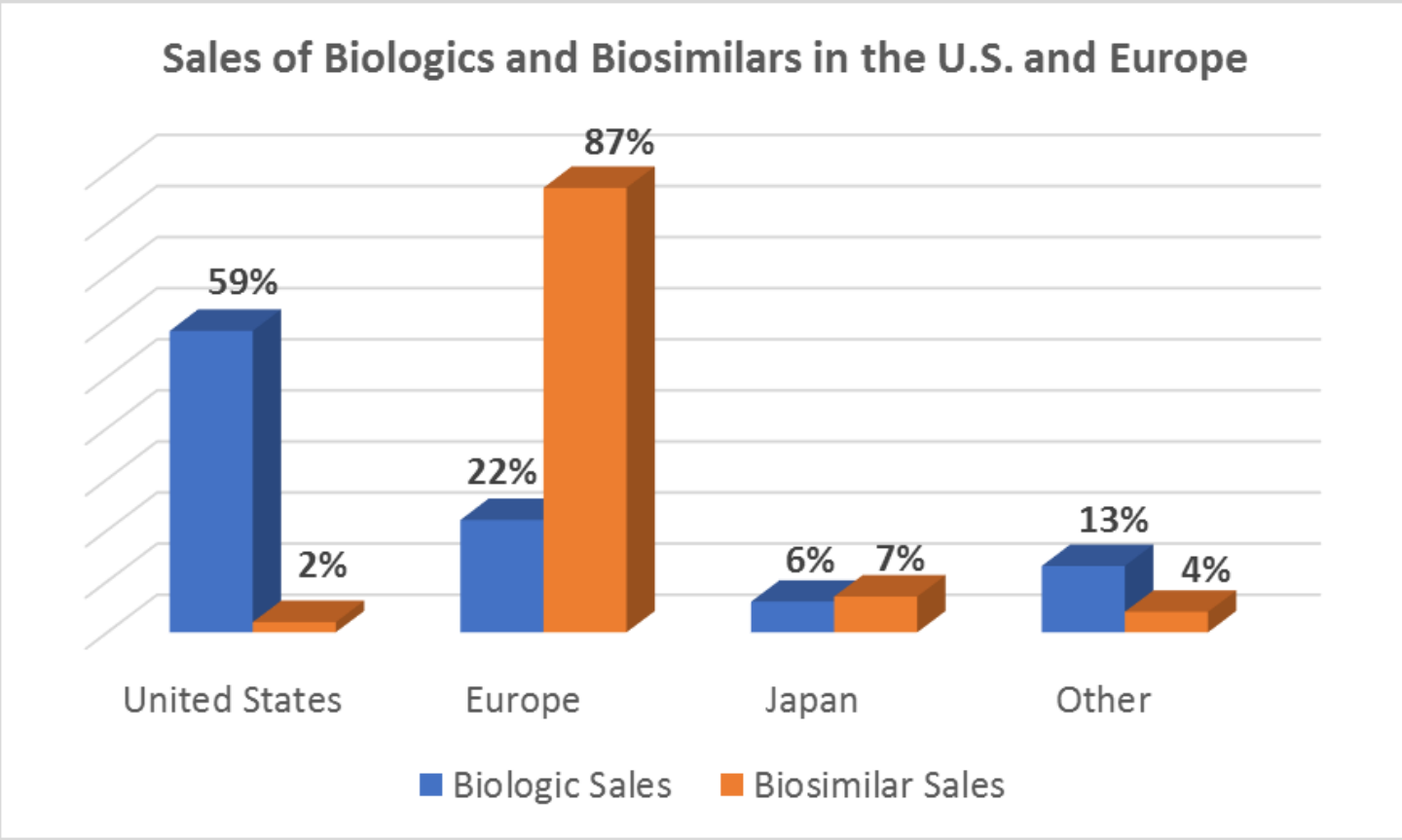
# Biosimilar Sales

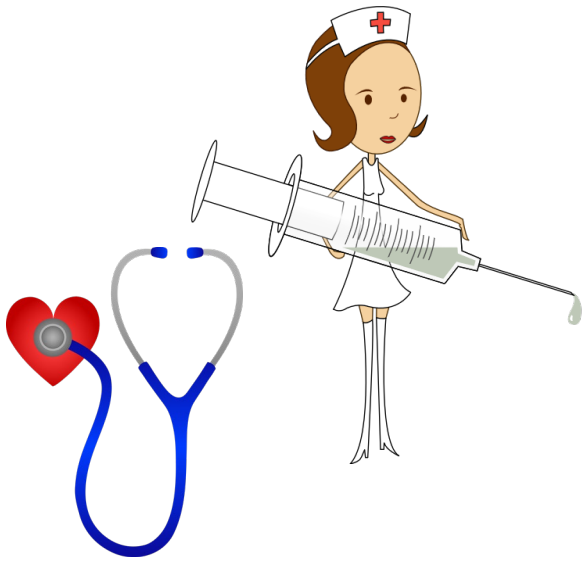


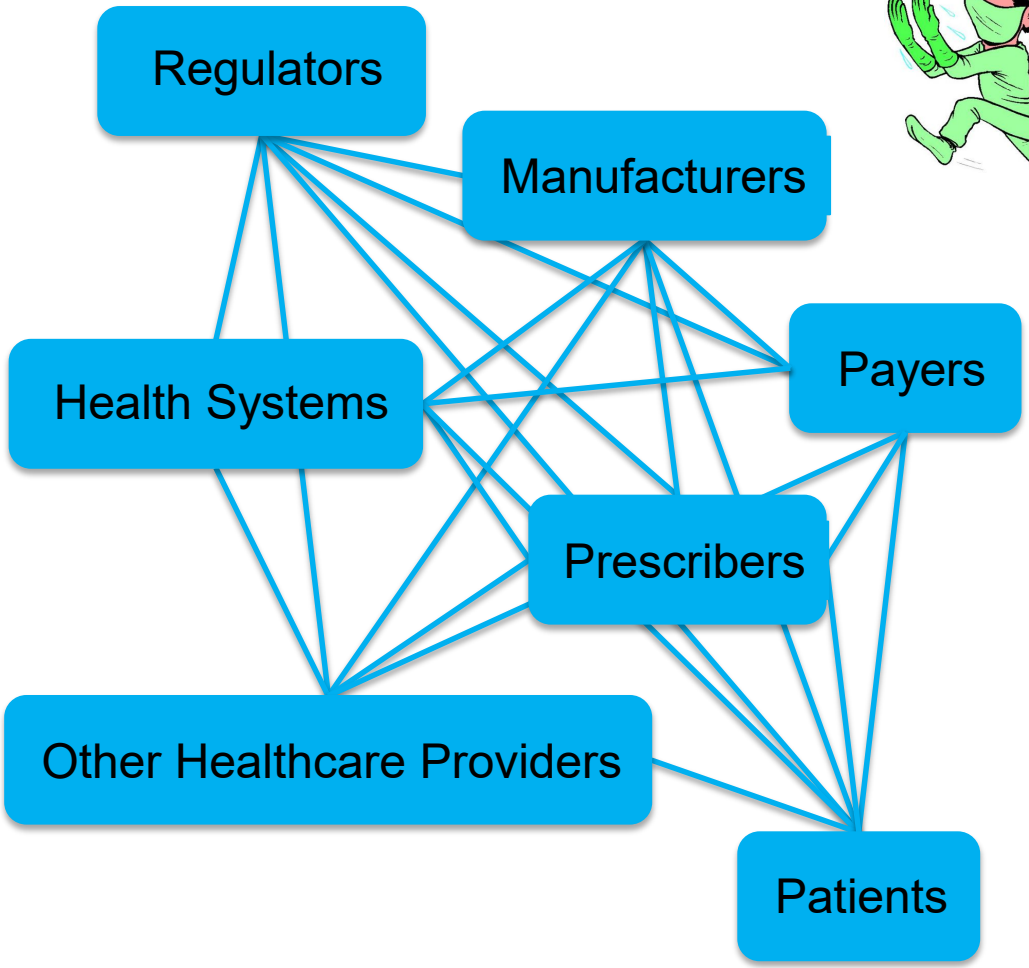



Adapted from: International Generic and Biosimilar medicines Association (IGBA). 2018. "Building on the Experience and Success of Biosimilar Medicines." February 1. www.igbamedicines.org/doc/Module6.pdf

# Barriers to Biosimilar Utilization

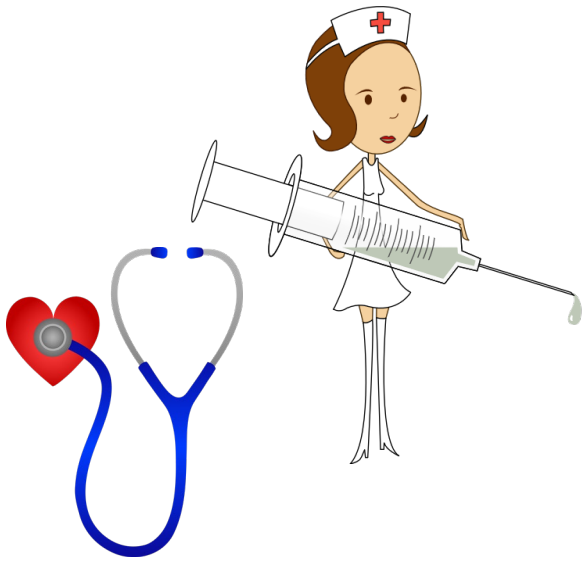
# Biosimilars – The Players

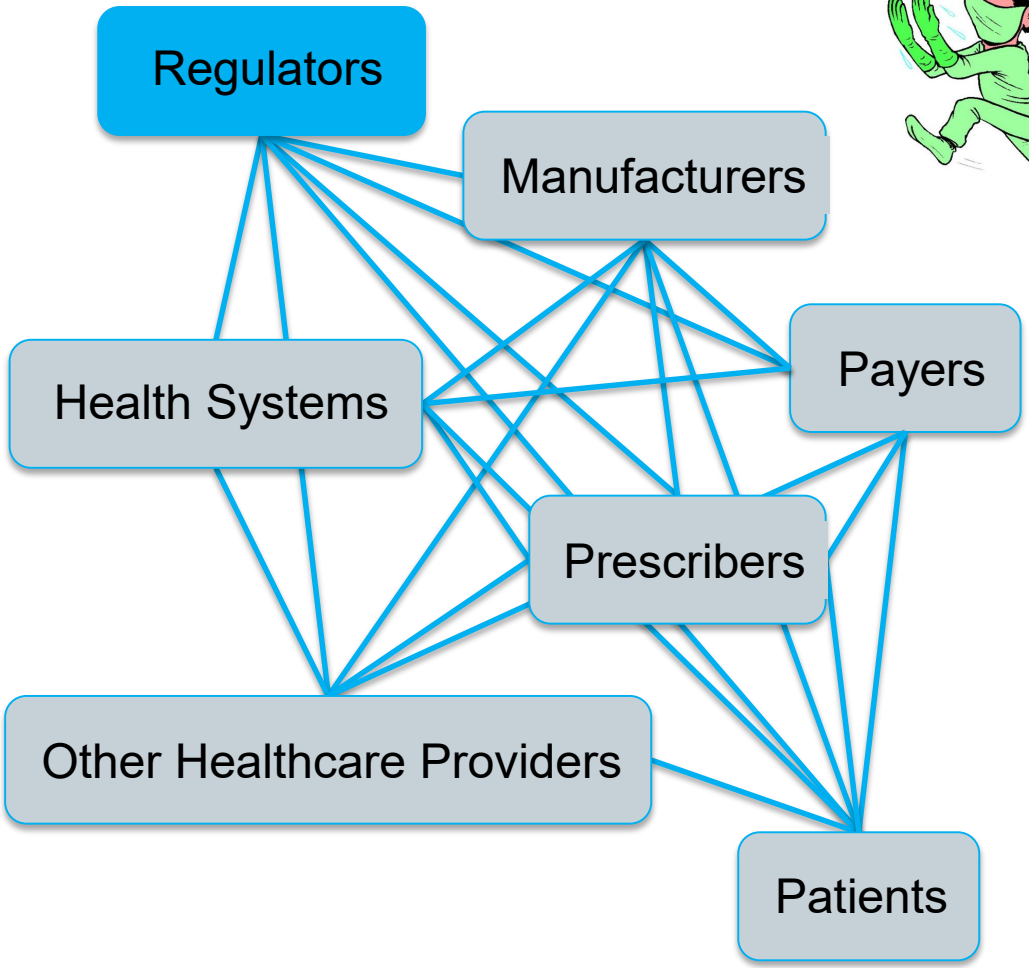





- Who are the stakeholders for biosimilars in the United States?

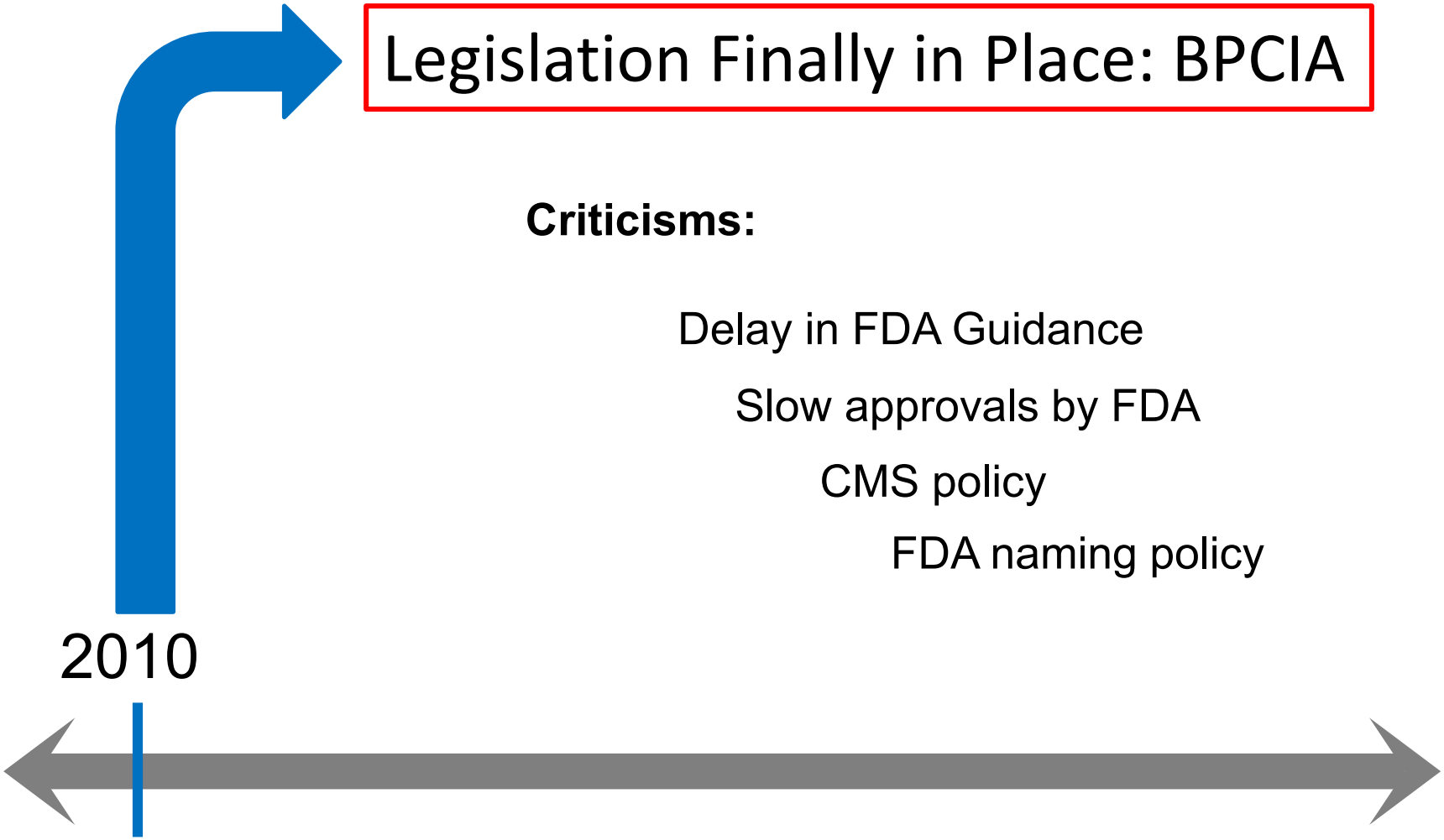
# Biosimilars – The Players






- Who are the stakeholders for biosimilars in the United States?

# Factors Influencing U.S. Biosimilar Utilization






www.fda.gov

Brill A, Robinson C. Steps to reducing barriers to biosimilars in the U.S. 2018. www.getmga.com.

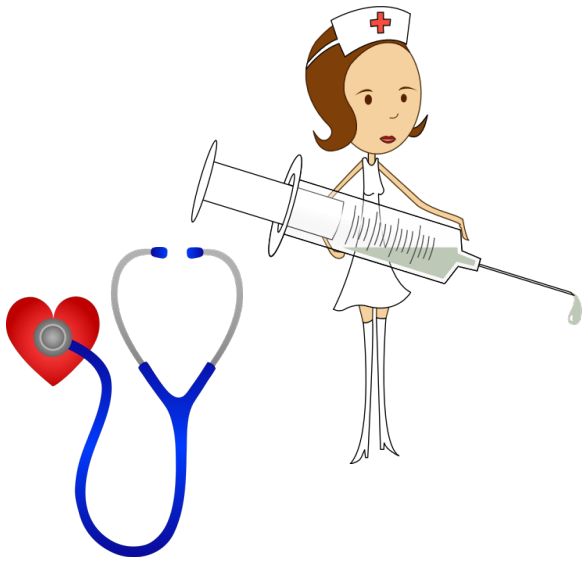
# FDA Biosimilars Action Plan (BAP) - 2018

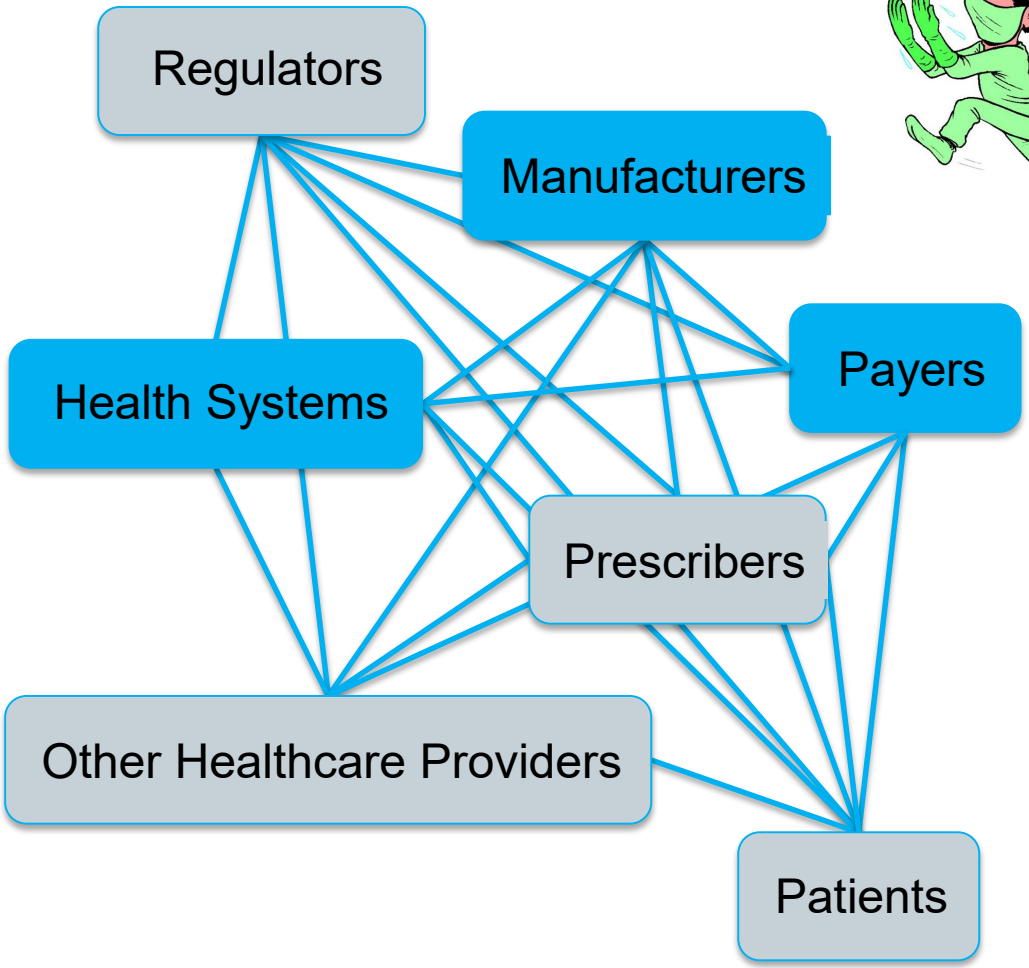
1. Improving the efficiency of the biosimilar and interchangeable product development and approval process;
2. Maximizing scientific and regulatory clarity for the biosimilar product development community;
3. Developing effective communications to improve understanding of biosimilars among patients, clinicians, and payors; and
4. Supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition.



https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM613761.pdf

# Biosimilars – The Players



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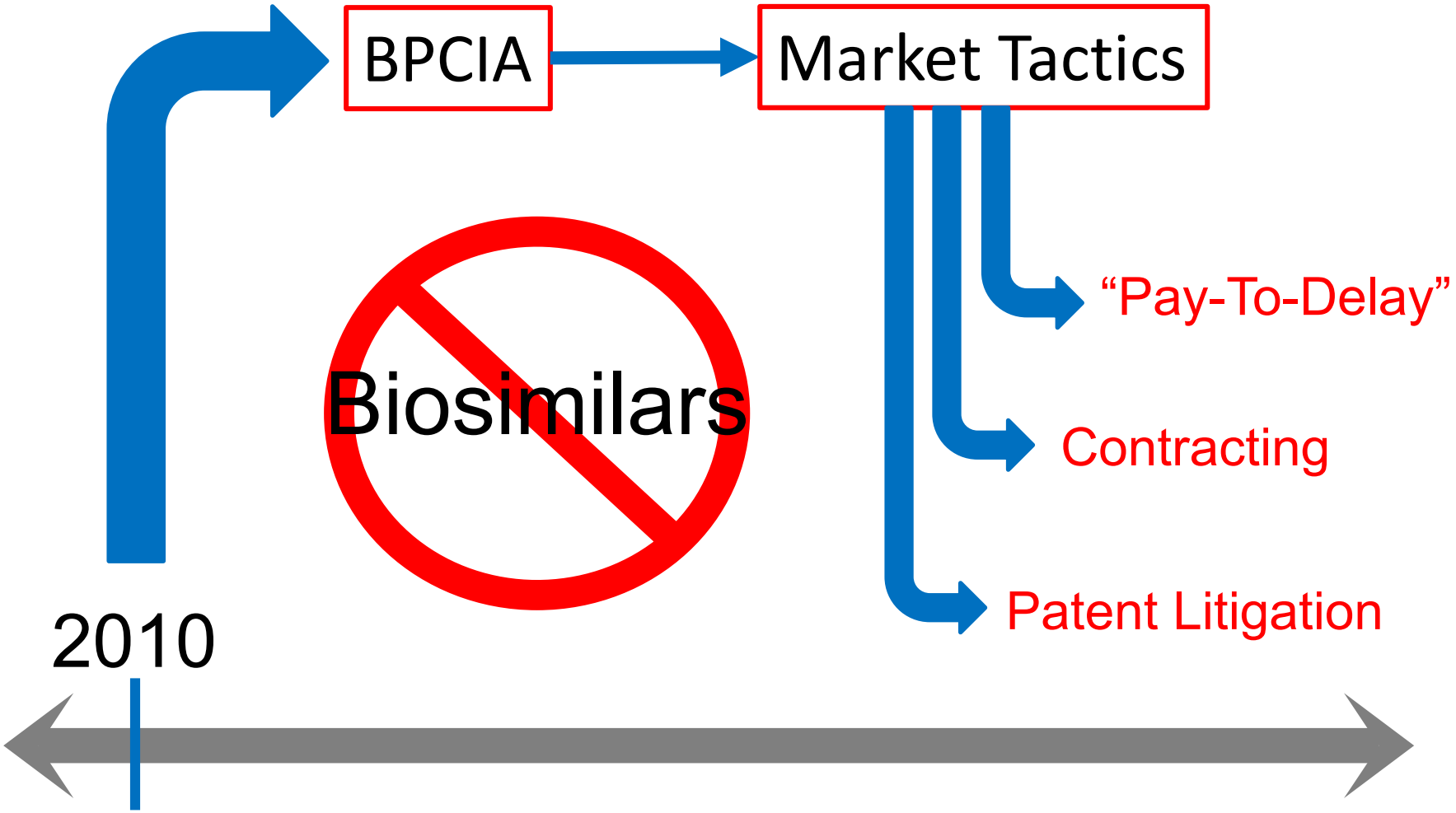




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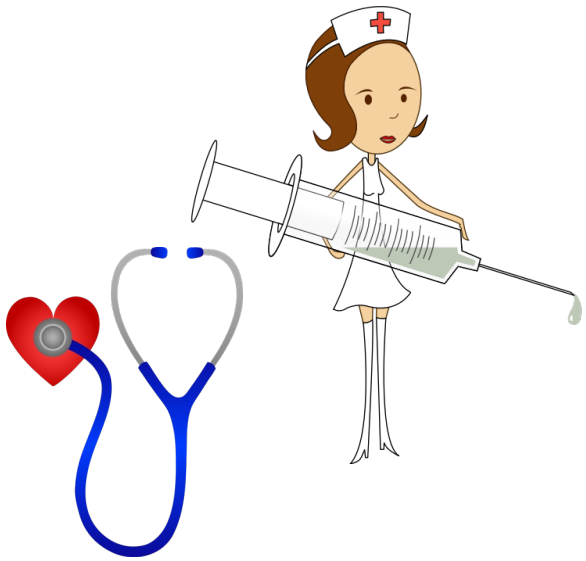
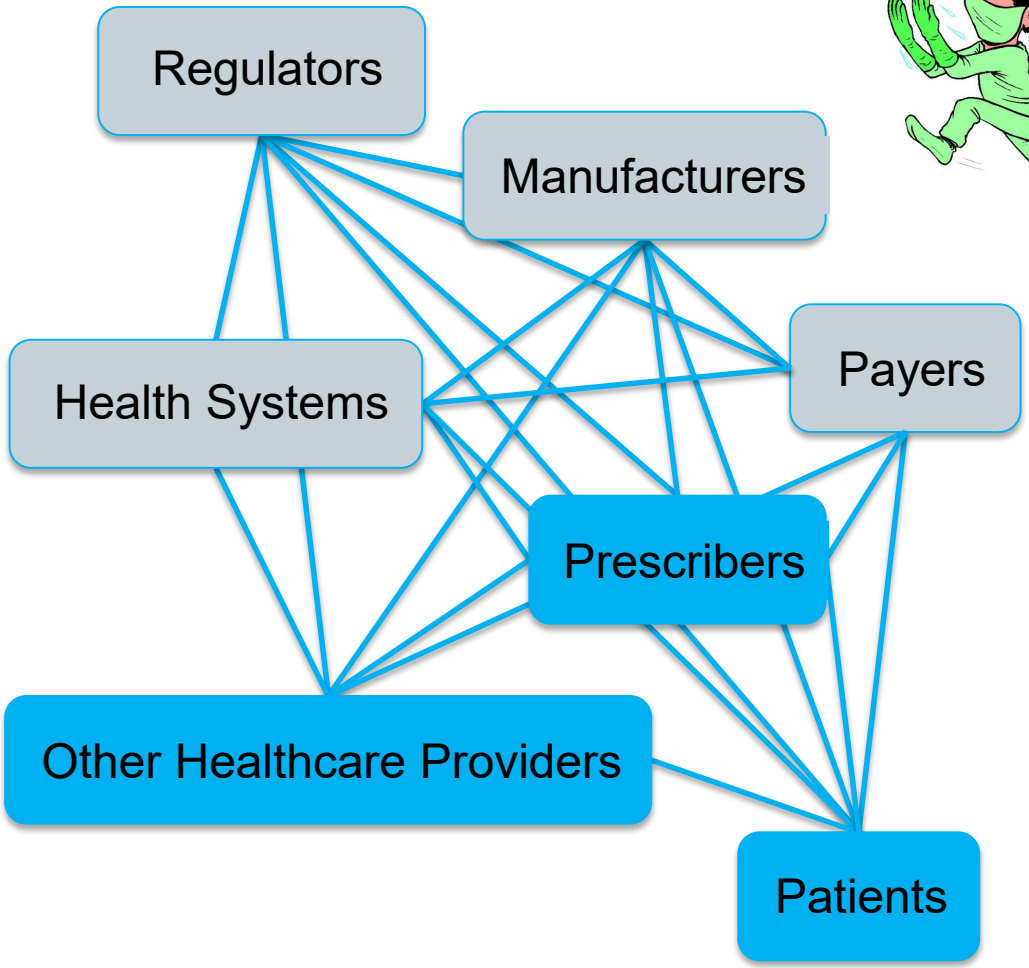





- Who are the stakeholders for biosimilars in the United States?

# Factors Influencing US Biosimilar Utilization

## Uncertainty - Prescribers

- **297 US physicians** in specialties that are high biologics prescribers
  - Rheumatologists
  - Dermatologists
  - Gastroenterologists
- **Survey** of experience and attitudes around non-medical switching to a biosimilar

| | |
|---|---|
| **63%** | Not enough long-term data to be comfortable prescribing |
| **44%** | Trust biosimilars are safe |
| **42%** | Taking a biosimilar is more risky than an originator |
| **33%** | Trust biosimilars are effective for individuals, not just groups |
| **31%** | Comfortable with a different FDA process for biosimilars |
| **30%** | Comfortable with approval by extrapolation |



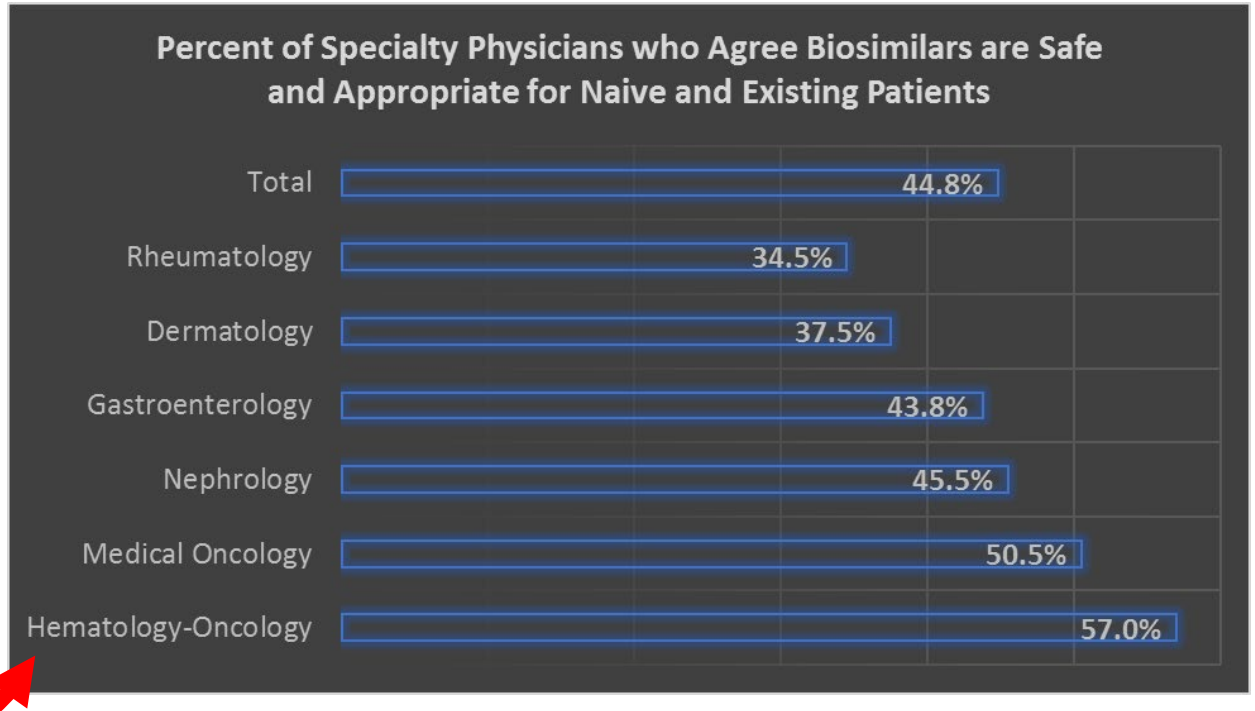
Teeple et al. *Curr Med Res Opin* 2019;35(4):611-617.

# Factors Influencing U.S. Biosimilar Utilization

## Uncertainty - Prescribers

Adapted from: Cohen et al. **Awareness, Knowledge, and Perceptions of Biosimilars Among Specialty Physicians**. *Adv Ther* 2017;12(2):2160-2172.

- **1,201 US physicians** in specialties that are high biologics prescribers
- **75%** trust the FDA approval decisions, but…
- When asked if they believe biosimilars are safe and appropriate for naïve and existing patients….



# Factors Influencing US Biosimilar Utilization

Uncertainty
- Prescribers

Leonard et al. **Factors affecting health care provider knowledge and acceptance of biosimilar medicines: a systematic review**. *J Manag Care Spec Pharm 2019;25(1):102-112.*

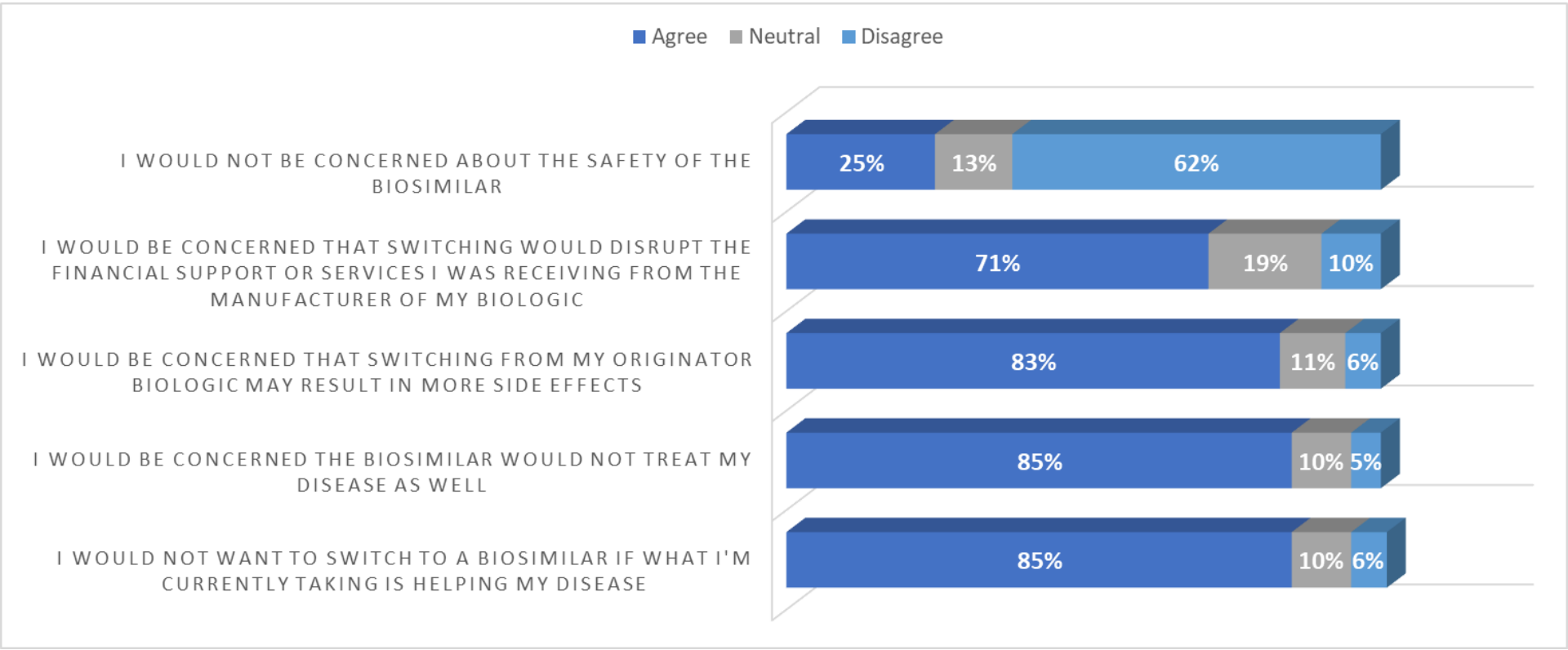
## Global themes:

- More comfortable with initiating biosimilars in naïve patients than switching stable patients
- Generally NOT comfortable with indication extrapolation
- Level of biosimilar knowledge varied, but the majority were unsure

# Factors Influencing US Biosimilar Utilization

## Uncertainty - Patients

- **1,696 US patients** with rheumatoid arthritis, Chrohn's, ulcerative colitis, psoriasis, psoriatic arthritis currently taking a biologic






Adapted from: Teeple et al. *Curr Med Res Opin* 2019;35(4):603-609.

# Factors Influencing US Biosimilar Utilization

## Uncertainty

….and other studies

Post-approval studies evaluating comparative safety and effectiveness are critical to generating real-world evidence to inform clinical practice and policy decisions

OPPORTUNITY FOR EDUCATION

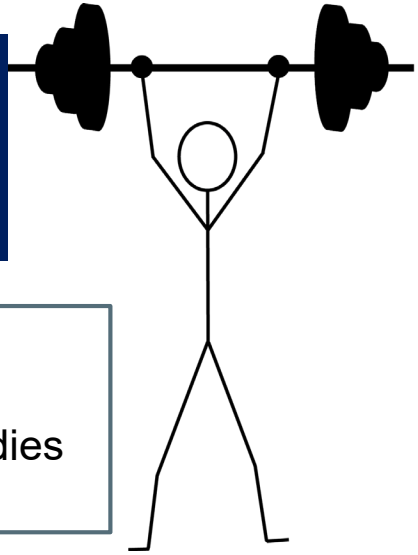
# Biosimilars:
# Data Sources for Decision-Makers

# Data Sources – Real World Evidence


**RWE and Regulatory Use**— 21st Century Cures requires FDA to establish a program to evaluate potential use of RWE for approval of new indications or to satisfy post-approval study requirements, label expansion or revision, and benefit/risk profiles

"The FDA uses RWE for regulatory decisions, albeit primarily related to safety. Nevertheless, for some drugs, the demonstration of efficacy has been based on RWE from case series or registries." – Jarrow et al.

"Multiple converging sub-studies from the same populations, or independent studies combining multiple data sources, could bring real-world data closer to 'causality' and could be perceived as acceptable alternatives to randomized trials." - Greenfield



"…on average, there is little evidence for significant effect estimate differences between observational studies and RCTs, regardless of specific observational study design, heterogeneity, or inclusion of studies of pharmacological interventions." – Anglemyer et al.



https://healthpolicy.duke.edu/sites/default/files/atoms/files/rwe_white_paper_2017.09.06.pdf
Greenfield. *Value in Health* 2017;20:1023-4
Jarow et al. *JAMA* 2017;318(8):703.
Anglemyer et al. Cochrane Database Syst Rev 2014 Apr 29;(4):MR000034

# Origins in the Gap in Evidence

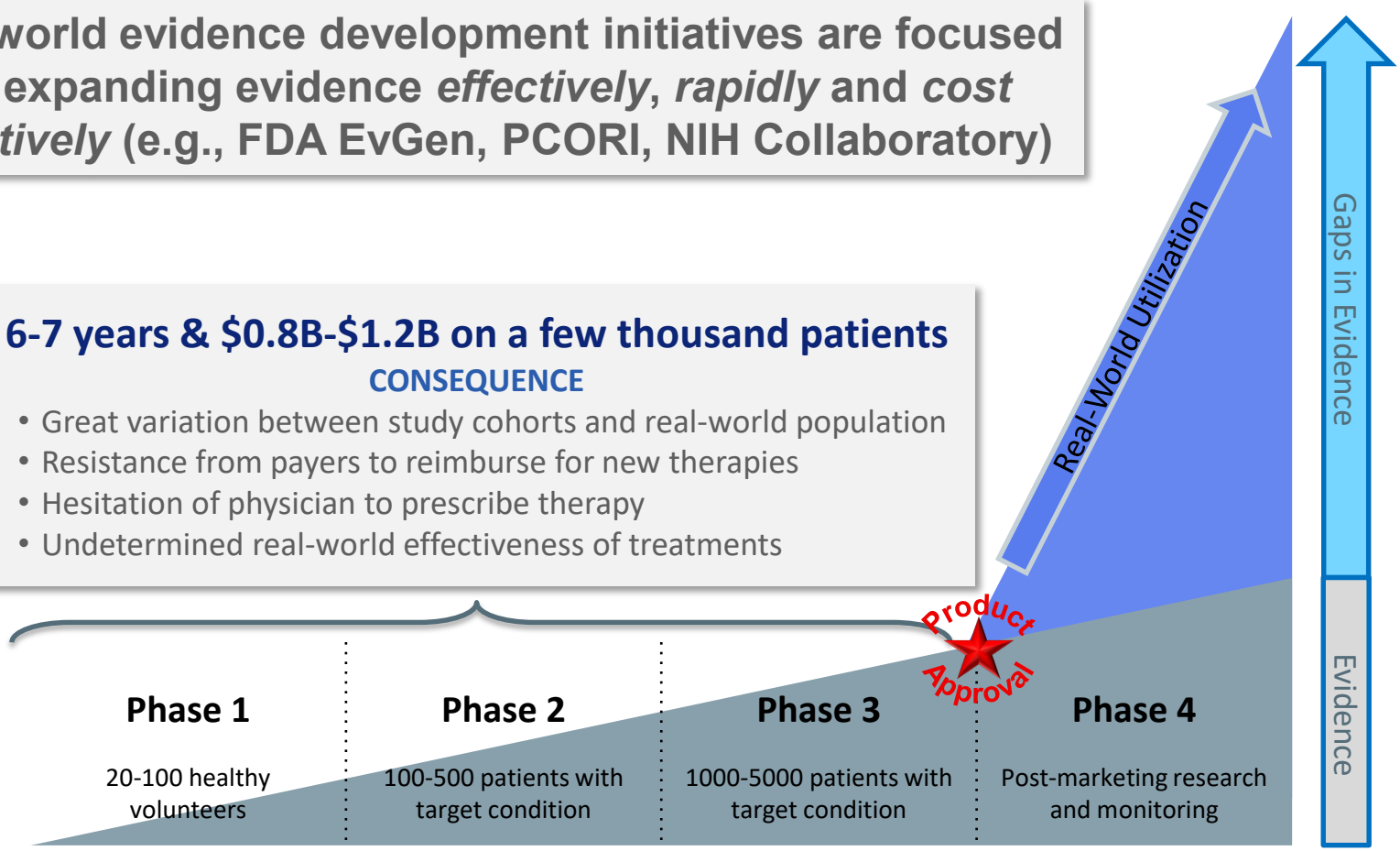
Real-world utilization quickly outpaces available clinical evidence

**Real world evidence development initiatives are focused on expanding evidence *effectively*, *rapidly* and *cost effectively* (e.g., FDA EvGen, PCORI, NIH Collaboratory)**

**6-7 years & $0.8B-$1.2B on a few thousand patients**

**CONSEQUENCE**

- Great variation between study cohorts and real-world population
- Resistance from payers to reimburse for new therapies
- Hesitation of physician to prescribe therapy
- Undetermined real-world effectiveness of treatments



# Real-World Data Sources

- Study Types
  - Pragmatic Clinical Trials
  - Prospective Observational Studies
  - Registry Studies
  - Retrospective Database Studies
  - Case Reports
- Data Sources
  - Pragmatic or Prospective Trials
  - Administrative Claims
  - Electronic Health Records
  - Patient-Reported/Self-Generated
  - Registries

# Strength of Secondary Data

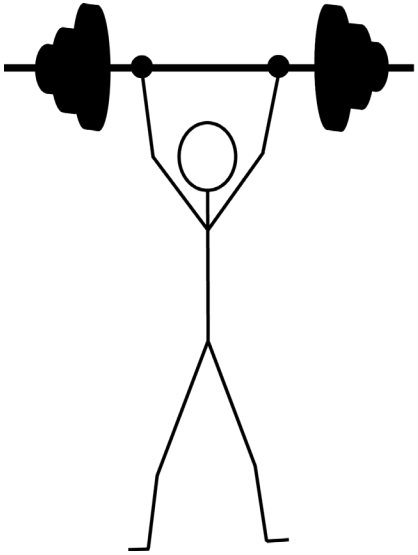
Commonly Used Data Sources

- Administrative Claims
- Electronic Medical Records

Patient interaction with the U.S. healthcare system generates data

## Why is data collected?

- Payment/billing
- Document clinical care
- Physician decision support
- Recordkeeping
- Registries
- Rich source of information for patient safety evaluations



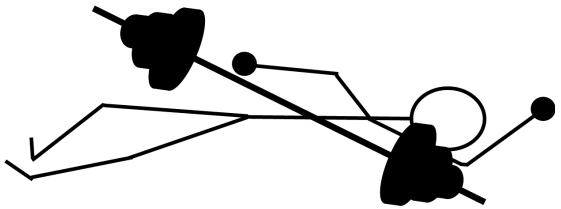


*Platt R, et al. The U.S. Food and Drug Administration's Mini-Sentinel program: status and direction. Pharmacoepidemiol Drug Saf. 2012 Jan;21 Suppl 1:1-8.*

# Real World Evidence

## Limitations:

- Data is usually collected for reasons **OTHER THAN** research, **NOT RANDOMIZED**
- Longitudinal: Requires consistent care in one healthcare delivery system and/or insurance plan
- Clinical outcomes: may not be readily identified
- Market uptake: influences research capability
- Coding: Non-specific codes or errors





Hannan EL. *J Am Cardiol Intv*. 2008;1(3):211-217.

# Patient-Generated Data

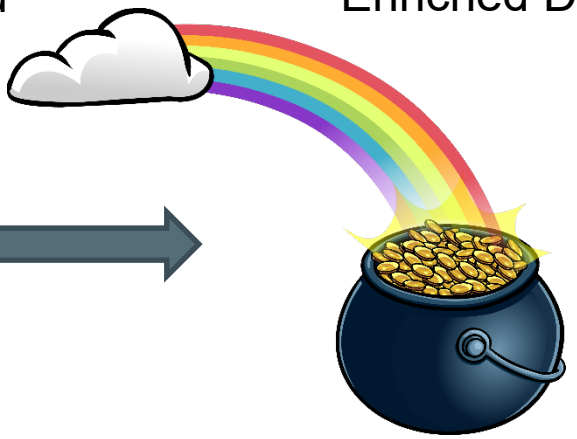
- Not just a PRO Instrument anymore…
  - Wearable devices
  - Mobile phone applications
  - Social Media

- Mobile app
  Social Media

- Electronic Health Record
- Administrative Claims

- Enriched Data

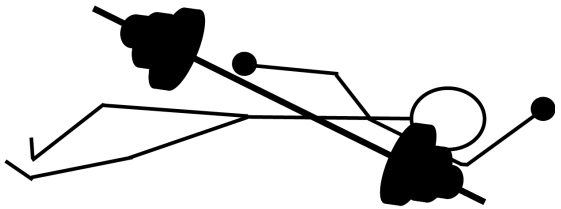
LINK

# Patient-Generated Data

## Limitations:

- Requires careful privacy protections
- Subject to recall bias and other reporting errors
- Requires active and willing participation
- Must be able to LINK DATA to a longitudinal source (administrative claims) or electronic medical record to be useful





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# BBCIC:
# One Approach to
# Real-World Evidence Generation

# BBCIC - Background


A non-profit, multi-stakeholder, collaborative, scientific public service initiative conducting rigorous post-marketing observational research to monitor biosimilar products and novel biologics for effectiveness and safety in a real-world setting

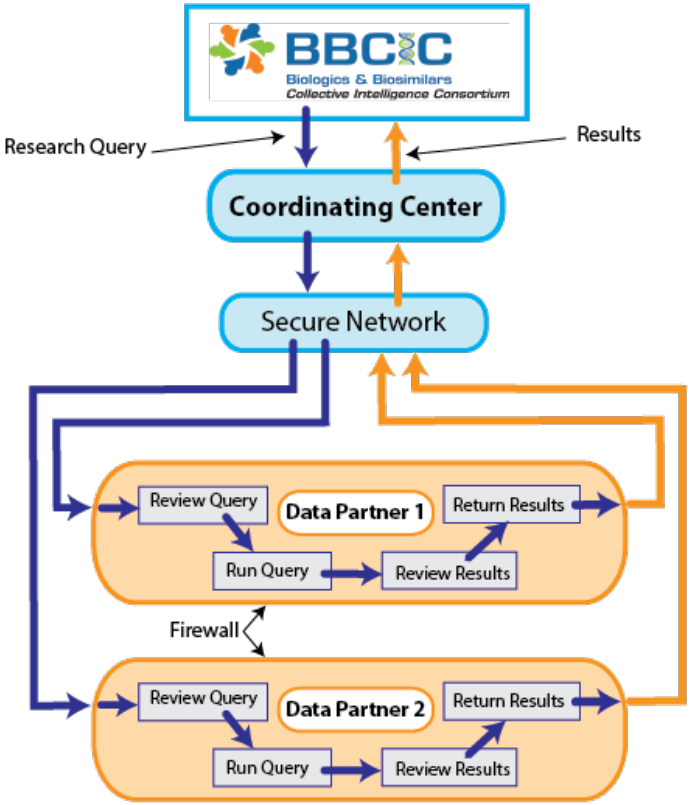
# BBCIC Surveillance – Leveraging Sentinel Capabilities

**The AMCP BBCIC strategy provides a unique opportunity for Managed Care to support public knowledge of biologic and biosimilar drugs with robust science.**

**BBCIC leverages the Sentinel Initiative** → Improves the efficiency and cost-effectiveness of post-marketed observational studies.

**BBCIC actively monitors biosimilars and innovators** → Anonymous data from ~95 million patients

**BBCIC is a multi-stakeholder collaboration** → Diverse expertise allows for a larger voice with more credibility

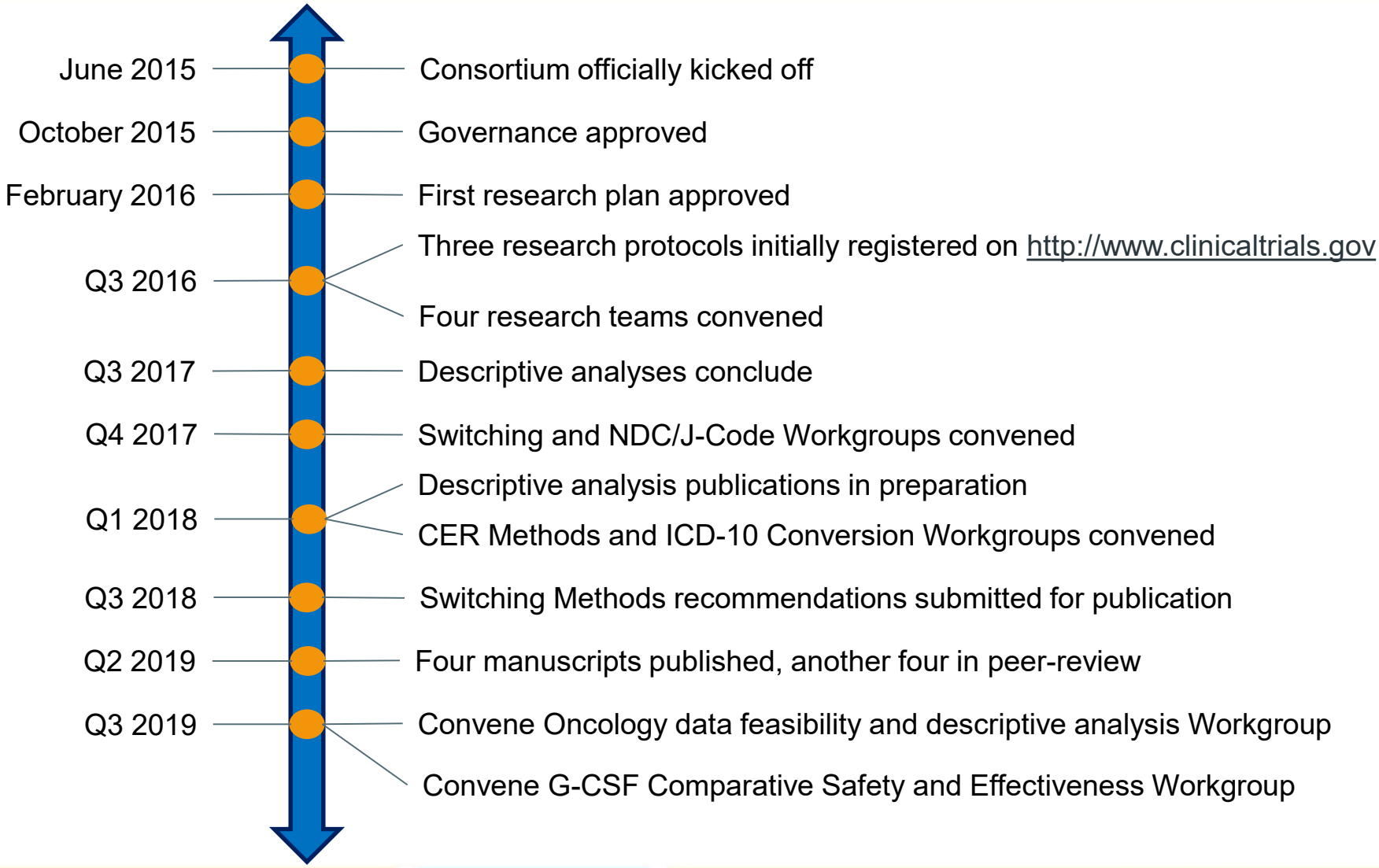



*A forum for collaboration between managed care organizations, integrated delivery networks, PBMs, pharma companies and research institutions*

# BBCIC Governance Overview

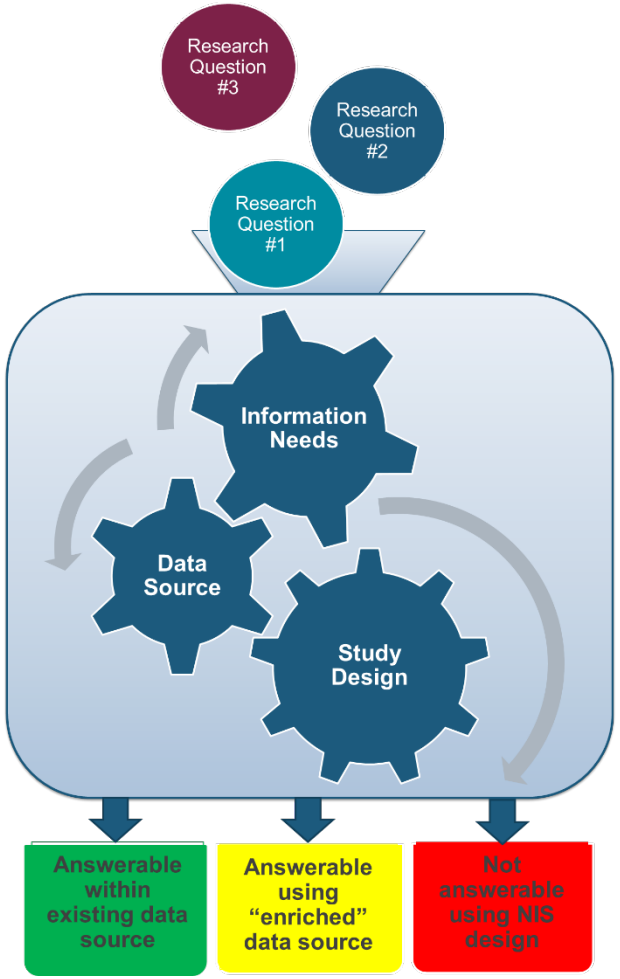
- The BBCIC Charter outlines transparent organized process for conducting research. There are no surprises.
- CER protocols, designed by KOLs and following ISPOR-ISPE guidelines, must explicitly pre-specify the epidemiologic, statistical and clinical thresholds required to identify a safety-related finding.
- 18 founding participants including Managed Care Organizations, Integrated Delivery Networks, PBMs & Harvard-Pilgrim Health Care Institute
- Public representatives on Planning Board: ASCO, American College of Rheumatology, National Health Council

# BBCIC Progress to Date



# BBCIC 2017-2019: Lines of inquiry

- Data fitness / infrastructure
  - Data availability and characterization
    - Capture of NDC information on medical claims
  - Impact of transition from ICD-9 to ICD-10, claims-based algorithms
- Descriptive studies
- Study design and methods
  - Switching study design and analytic approaches
  - Comparative safety/effectiveness study design and analytic approaches
- Protocol-Driven Comparative Safety/Effectiveness Studies



# BBCIC - Progress

- What we have **DONE**
- What we are **DOING**
- What we **PLAN to DO**

# BBCIC - Progress

- What we have **DONE**
- What we are **DOING**
- What we **PLAN to DO**

# Completed Projects - Descriptive Analysis

| Project | Objective | Of Note |
|---|---|---|
| **Insulins** | Describe treatment patterns and outcomes of adults with diabetes treated with long- or intermediate-acting insulin | • Rates consistent with other studies<br>• Algorithms and robust methods required to more reliably identify cohorts |

## Harnessing the Biologics and Biosimilars Collective Intelligence Consortium to Evaluate Patterns of Care

Cheryl N. McMahill-Walraven, MSW, PhD; Daniel J. Kent, BSPharm, PharmD, CDE; Catherine A. Panozzo, PhD, MPH; Pamala A. Pawloski, PharmD, BCOP, FCCP; Kevin Haynes, PharmD, MSCE; James Marshall, MPH; Jeffrey Brown, PhD, MA; Bernadette Eichelberger, PharmD; and Catherine M. Lockhart, MS, PharmD, PhD

*J Manag Care Spec Pharm.* Published online August 2019. https://www.jmcp.org/doi/abs/10.18553/jmcp.2019.19041

## Descriptive Analysis of Long- and Intermediate-Acting Insulin and Key Safety Outcomes in Adults with Type 2 Diabetes Mellitus

Daniel J. Kent, BSPharm, PharmD, CDE; Cheryl N. McMahill-Walraven, MSW, PhD; Catherine A. Panozzo, PhD, MPH; Pamala A. Pawloski, PharmD, BCOP, FCCP; Kevin Haynes, PharmD, MSCE; James Marshall, MPH; Jeffrey Brown, PhD, MA; Bernadette Eichelberger, PharmD; and Catherine M. Lockhart, MS, PharmD, PhD

*J Manag Care Spec Pharm.* Published online August 2019. https://www.jmcp.org/doi/abs/10.18553/jmcp.2019.19042

# Completed Projects - Descriptive Analysis

| Project | Objective | Of Note |
|---|---|---|
| **Erythropoietin Stimulating Agents (ESAs)** | Feasibility assessment of comparability between BBCIC data and the U.S. Renal Data System (USRDS) in evaluating outcomes in hemodialysis patients | • BBCIC hemodialysis population is similar to the USRDS in age and sex distributions, but is **not** sufficiently similar in duration of dialysis. |
| **Granulocyte Colony Stimulating Factors (G-CSFs)** | Describe utilization, characteristics, and outcomes in patients receiving GCSF treatment as neutropenia prophylaxis due to high-risk chemotherapy regimens | • Initial evidence that cohorts and outcomes of interest can be identified in the BBCIC data network<br>• Foundation for comparative studies |
| **Anti-Inflammatories** | Describe treatment patterns and outcomes among patients with auto-immune diseases treated with biologic therapy | • Measuring effectiveness is challenging beyond surrogates such as dosage or therapy change<br>• Exploring enriching data linkages |

**Manuscripts in Preparation or Undergoing Peer-Review**

# Completed Projects – Methods/Infrastructure

| Project | Objective |
| --- | --- |
| **Switching Methods** | Best practices and recommendations for treatment of medication switching or sequencing as a covariate or confounder in future BBCIC studies |

## Methodologic considerations for noninterventional studies of switching from reference biologic to biosimilars

Rishi J. Desai[1] | Seoyoung C. Kim[1] | Jeffrey R. Curtis[2] | Jaclyn L.F. Bosco[3] | Bernadette Eichelberger[4] | Charles E. Barr[4] | Catherine M. Lockhart[4] | Brian D. Bradbury[5] | Jerry Clewell[6] | Hillel P. Cohen[7] | Joshua J. Gagne[1] |
on behalf of the Biologics and Biosimilars Collective Intelligence Consortium (BBCIC) Switching Workgroup

*Pharmacoepidemiol Drug Saf.* 2019:1-13. Epub ahead of print.
https://onlinelibrary.wiley.com/doi/full/10.1002/pds.4809

# Completed Projects – Methods/Infrastructure

| Project | Objective |
|---|---|
| **CER Methods** | Best practices and recommendations for conducting robust, large-scale, observational comparative safety and effectiveness research in the BBCIC |
| **ICD-10 Mapping** | Recommended methods and complete conversion of ICD-9-CM codes to ICD-10-CM codes for all diseases of current interest to the BBCIC |
| **NDC/J-Code Use** | Investigate the extent to which NDC codes, and product-specific J-Codes, are reported in physician-office medical claims for drugs administered in the clinic |

**Manuscripts in Preparation or Undergoing Peer-Review**

# Completed Projects - OVERALL

- Outcome rates were **consistent with other clinical and observational studies**.
- With the BBCIC DRN we are able to **reliably identify and characterize** exposures, outcomes, and potential confounders for the disease cohorts of interest.
- Improved **methods and data infrastructure** will enrich BBCIC research capabilities

## Barriers and facilitators to conduct high-quality, large-scale safety and comparative effectiveness research: The Biologics and Biosimilars Collective Intelligence Consortium experience

Catherine M. Lockhart[1] | Cara L. McDermott[1] | Thomas Felix[2] | Nancy D. Lin[3] | Mark J. Cziraky[4] | Aaron B. Mendelsohn[5] | Jeffrey S. Brown[5]

*Pharmacoepidemiol Drug Saf.* 2019:1-3. Epub ahead of print.
https://onlinelibrary.wiley.com/doi/full/10.1002/pds.4885

# 2018 Presentations

**5** Podium Presentations

- ICPE
- ISPOR
- DIA
- AMCP Nexus
- NW AMCP

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**7** Poster Presentations

- HCSRN
- ICPE
- AMCP Nexus

# 2019 Presentations

**6** Podium Presentations

- CBI
- BioTech
- ISPOR
- ICPE
- DIA Biosimilars
- AMCP Nexus

**6** Poster Presentations

- HCSRN
- AMCP Annual
- ISPOR
- ICPE
- AMCP Nexus

# BBCIC - Progress

- What we have **DONE**
- What we are **DOING**
- What we **PLAN to DO**

# Current Projects

## COMPARATIVE EFFECTIVENESS RESEARCH – G-CSFs

**Co-Investigators:**
- Pamala A. Pawloski, PharmD, BCOP, FCCP - Senior Research Investigator, HealthPartners Institute
- Cara McDermott, MS, PharmD, PhD - Research Consultant, BBCIC

**The BBCIC has started our FIRST formal Comparative Safety and Effectiveness study of granulocyte-colony stimulating factors (filgrastim, pegfilgrastim) between the originator biologics and their available biosimilars.**

**Background and Rationale**

For over two decades, recombinant human granulocyte colony-stimulating factors (G-CSFs) have been used to treat and prevent chemotherapy-induced neutropenia. Currently two biosimilar products to reference filgrastim (filgrastim-sndz, filgrastim-aafi), and two biosimilars to reference pegfilgrastim (pegfilgrastim-jmdb, pegfilgrastim-cbqv) have been approved in the US. Building upon a previous BBCIC descriptive analysis, we are starting our first Comparative Effectiveness Research (CER) project focused on G-CSFs.

# Current Projects

## ONCOLOGY FEASIBILITY AND DATA FITNESS

**Principal Investigator:**

- Nancy Lin, ScD - Senior Scientist, Optum Epidemiology

**The BBCIC has begun a new infrastructure project to identify, evaluate, and test potential new data sources to enrich the BBCIC distributed research network (DRN) capabilities in conducting robust, cancer-specific safety and effectiveness research.**

**Background and Rationale**

A marked increase in the approval of biosimilar products, particularly in cancer therapy, is anticipated as a result of patent expirations for a number of originator biologics. As such, there is a need to generate robust real-world evidence for biosimilar cancer therapeutics. Given the number of biosimilars in oncology expected to be considered for approval in the near future, BBCIC is establishing the necessary resources to do product- or disease-specific comparative effectiveness research.

# BBCIC - Progress

- What we have **DONE**
- What we are **DOING**
- What we **PLAN to DO**

# Potential BBCIC Research

- **Insulins Comparative Safety and Effectiveness**
- **Trastuzumab Descriptive Analysis**
- **Bevacizumab Descriptive Analysis**
- **Evaluation of Switching and Treatment Patterns in Rheumatoid Arthritis**
- **Feasibility Analysis of an Electronic Medical Records Research Network**
- **BBCIC Committees are actively identifying new research topics**

**NOTE: The annual research agenda is not finalized until voted on and approved by the BBCIC Science Committee and Planning Board. All BBCIC Participants have a seat on both committees to guide BBCIC research. These projects represent a selection of current interests of the BBCIC, but is not an exhaustive list and may not yet be prioritized on the research agenda.**

# Practical Application of BBCIC Research

## WHAT WE PROVIDE:

### REAL-WORLD EVIDENCE

Fill **evidence gap** with large-scale, multi-stakeholder, post-marketing assessment of novel biologics and biosimilars

Support the scientific community with methods development for research best practices in real-world evidence generation

### EDUCATION

Source of **education** for stakeholders

## WHAT WE NEED:

**ENGAGEMENT and SUPPORT!**

- Manufacturers
- Pharmacy Benefit Managers
- Prescribers / Practitioners
- Patients
- Health Plans

# QUESTIONS?

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