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# [S5] The State of U.S. Biosimilar Utilization and Post-Marketing Surveillance Initiatives to Support Treatment and Coverage Decisions

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Biologics and Biosimilars Collective Intelligence Consortium
October 24, 2018

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# PRE-TEST

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# LQ1: Which of the following were barriers to generic drug adoption and utilization in the United States?

a. An unexpected side effect of the Hatch-Waxman Act that facilitated “pay-to-delay” arrangements
b. A 1988-1989 investigation resulted in convictions of FDA officials, manufacturers, and consultants for bribery
c. Patients and prescribers were uncomfortable with generic drugs
d. All of the above

# LQ2: Which of the following is a LIMITATION of clinical trial data?

a. Designed to reduce confounding and bias
b. Potentially excludes large segments of the population who may be treated with the drug in real-world practice
c. Provides evidence that assesses safety and efficacy of the drug to support regulatory requirements
d. All of the above

**LQ3: Data produced from research by organizations such as the Biologics and Biosimilars Collective Intelligence Consortium could be used to inform treatment and coverage decisions.**

a. True
b. False

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# LQ4: There are multiple organizations conducting post-marketing surveillance specifically on biosimilars and their reference biologics in the United States

a. True
b. False

# Outline

- It All Started With Generics
- Biosimilars: Definition and Regulatory Landscape
- Biosimilars: U.S. Market Access and Utilization
- Biosimilars: Data Sources for Decision-makers
- BBCIC: One Approach to Real-World Evidence Generation
- Sources of Post-Marketing Data
- Sources of Post-Marketing Data for BIOSIMILAR Research

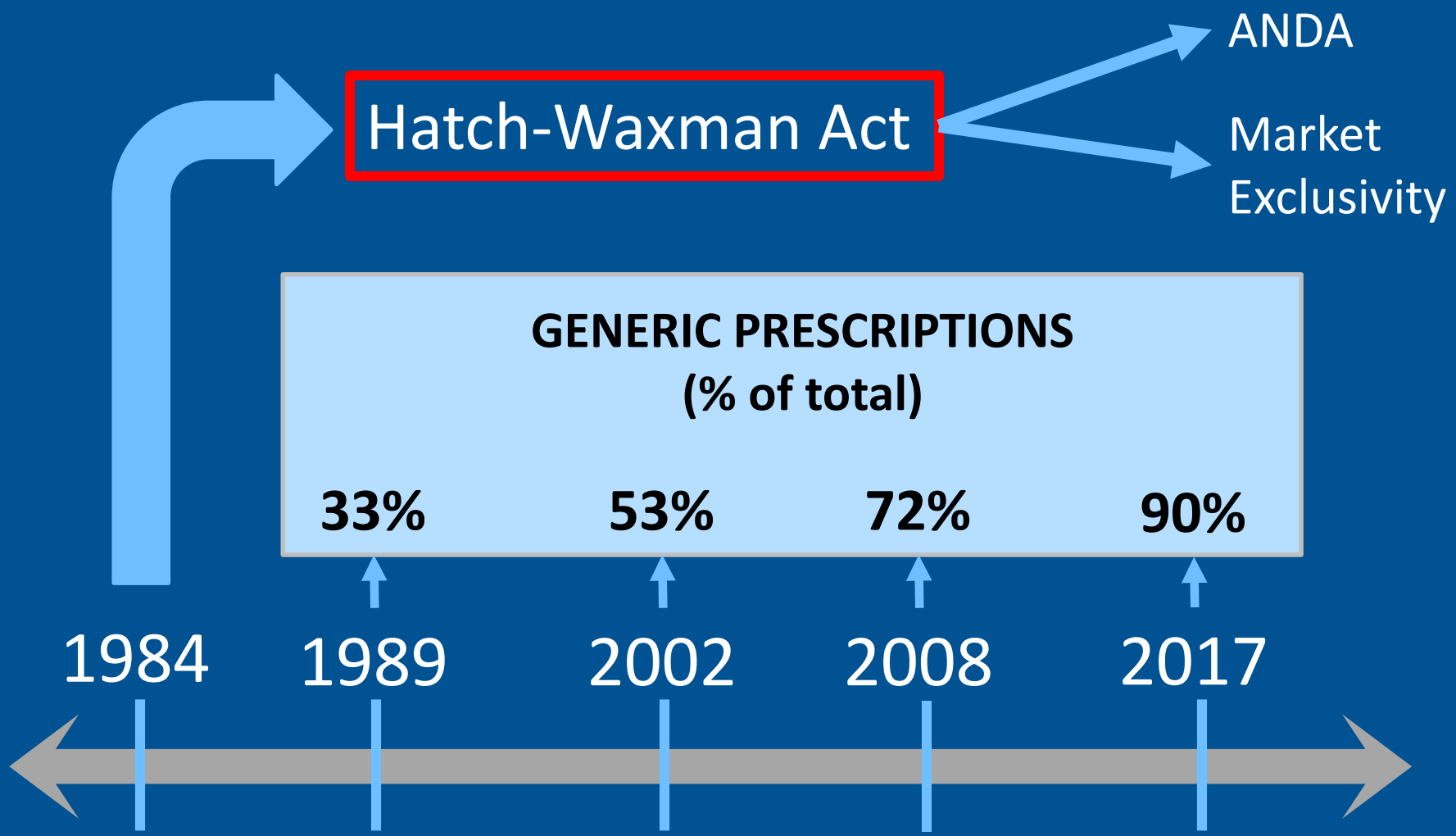
# It All Started With Generics

# History of Generic Drugs in the U.S.

1984

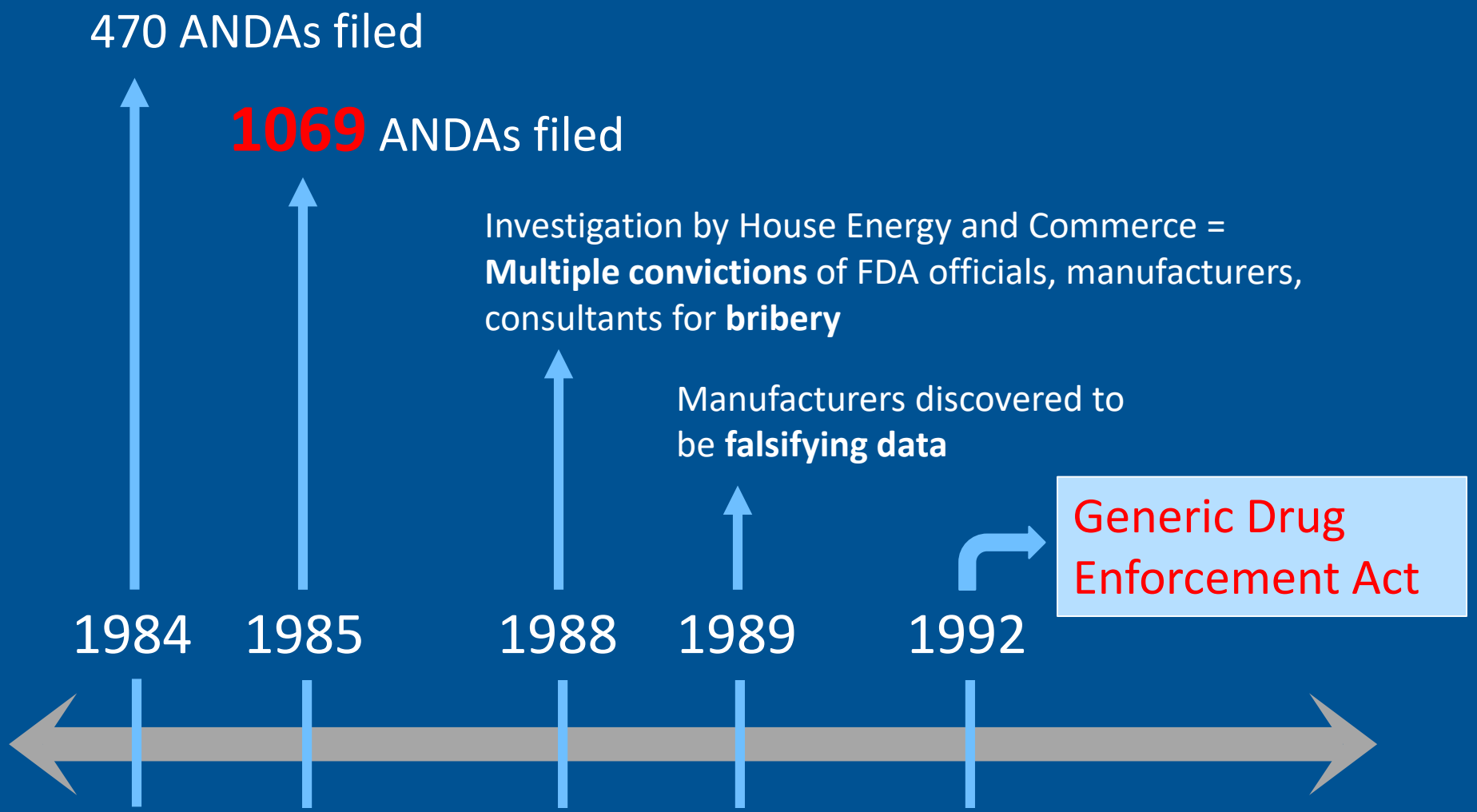
Lewis, et al. *J Contemporary Health Law & Policy*. 1992;8(1):361-378.
Boehm, et al. *Acta Pharmaceutica Sinica B*. 2013;3(5):297-311.

# 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.

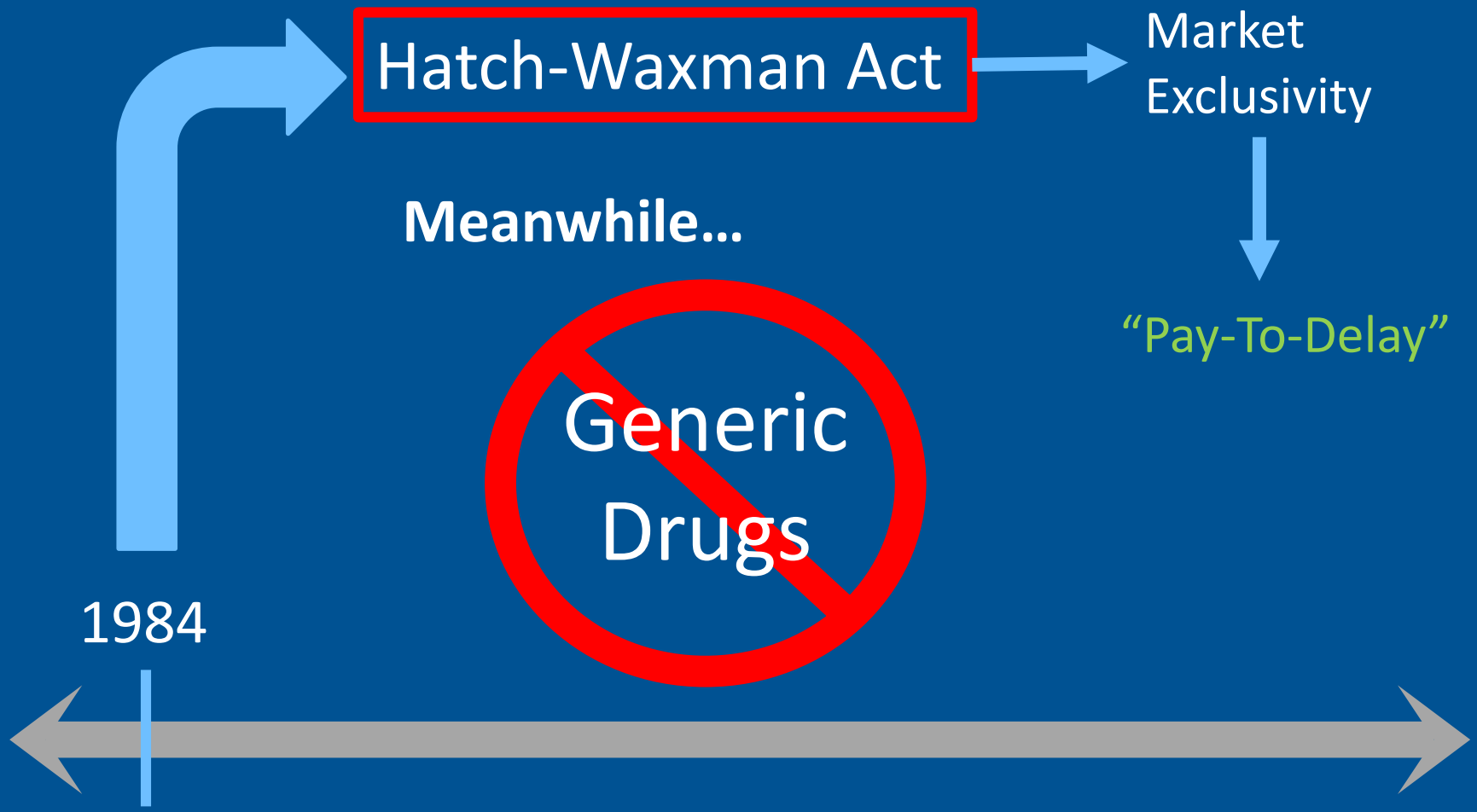
# Adverse Events





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

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# Biosimilars: Definition and Regulatory Landscape

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# Types of Drugs: Chemical vs Biologic

## Chemical Drugs

- Well-defined composition
- Simple structure
- Small size
- Minimal or no heterogeneity
- Typically have more than one pharmacological target

**Original** | **Generic**

## Biologic Drugs

- Composition defined to a certain extent
- Complex structure
- Big size
- Significant (micro) heterogeneity
- Often highly specific

**Original** | **Biosimilar**

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*Pharmacol Res. 2018 Jul;133:251-264.*

# Definitions

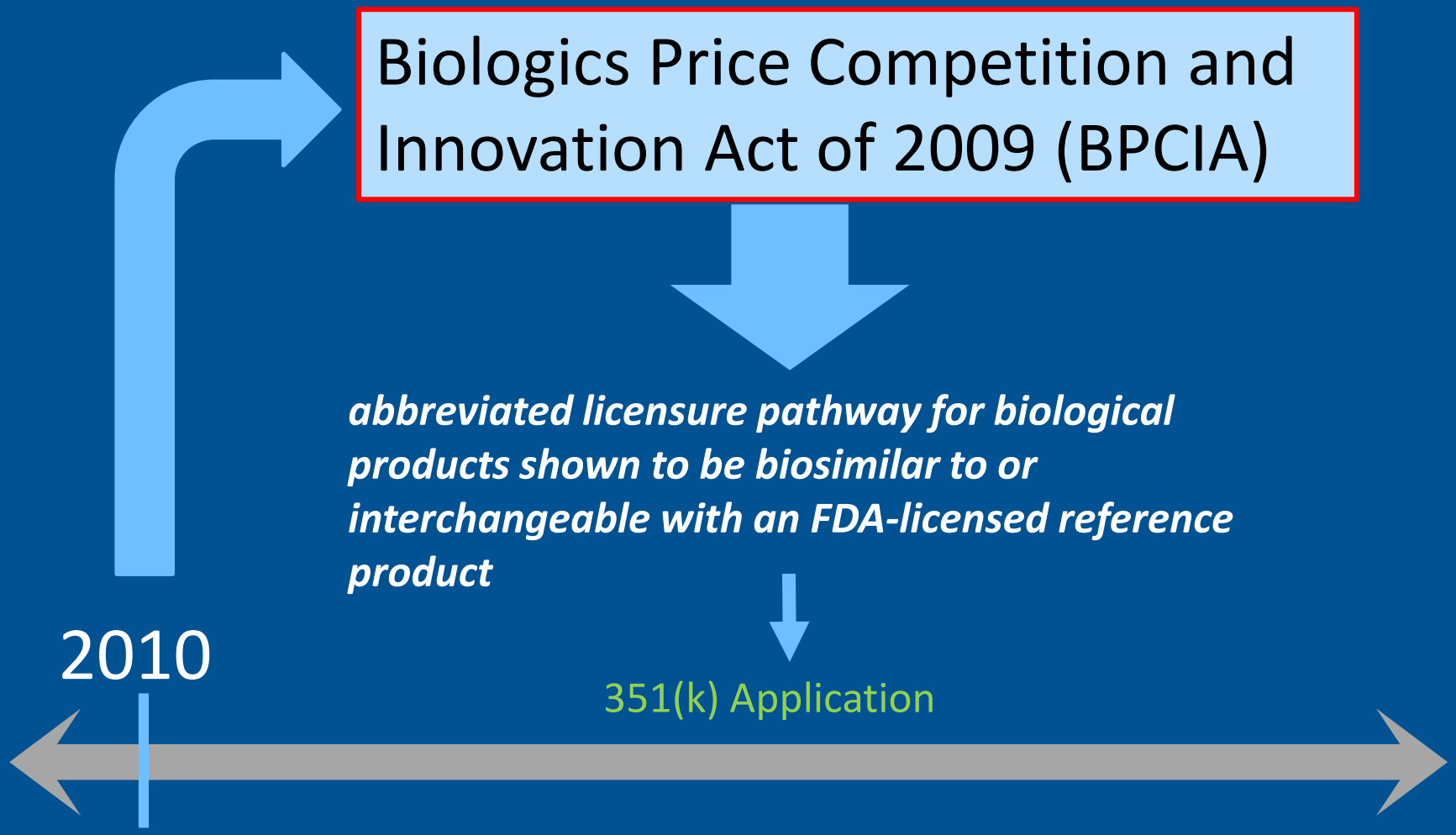
## Biosimilar or Biosimilarity

"the biological product is **highly similar** to the reference product notwithstanding minor differences in clinically inactive components" and "there are **no clinically meaningful differences** between the biological product and the reference product in terms of the safety, purity, and potency of the product" [PHS Act Section 351(i)(2)]

## Reference Product

"the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k)" [PHS Act Section 351(i)(4)]

# Biosimilars in the U.S.




www.fda.gov/biosimilars

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# Requirements for FDA Registration

**Compared to Reference Product:**

- ☑ Biosimilar*
- ☑ Mechanism of action
- ☑ Label Indications
- ☑ Dosage form/Route/Strength
- ☑ Manufacturing

https://www.fda.gov/biosimilars

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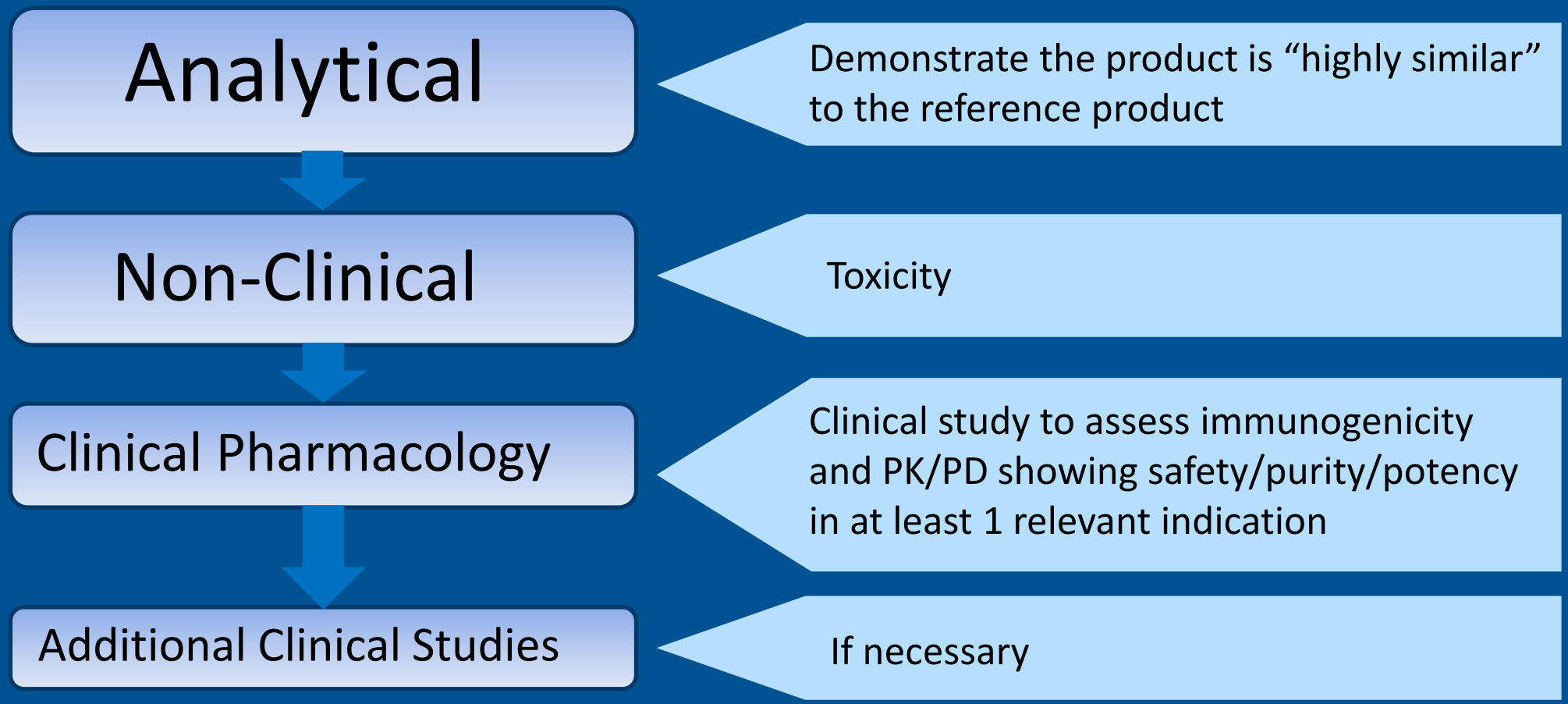
# Requirements for FDA Registration

**Demonstrating Biosimilarity → TOTALITY of EVIDENCE**




https://www.fda.gov/biosimilars

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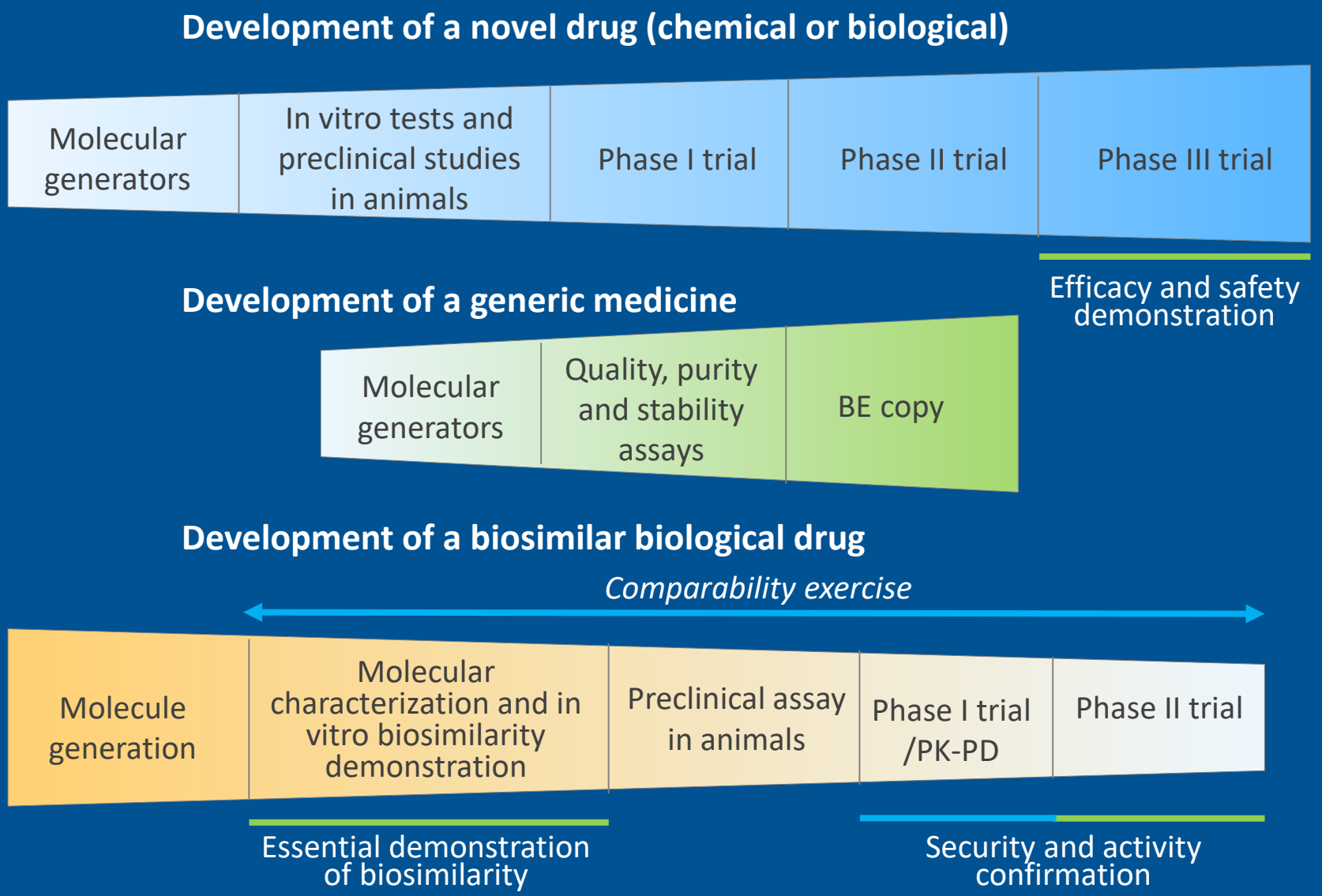
# Development of Original, Generic and Biosimilar Medicines




Gámez-Belmonte R et al, *Pharmacol Res. 2018 Jul;133:251-264.*

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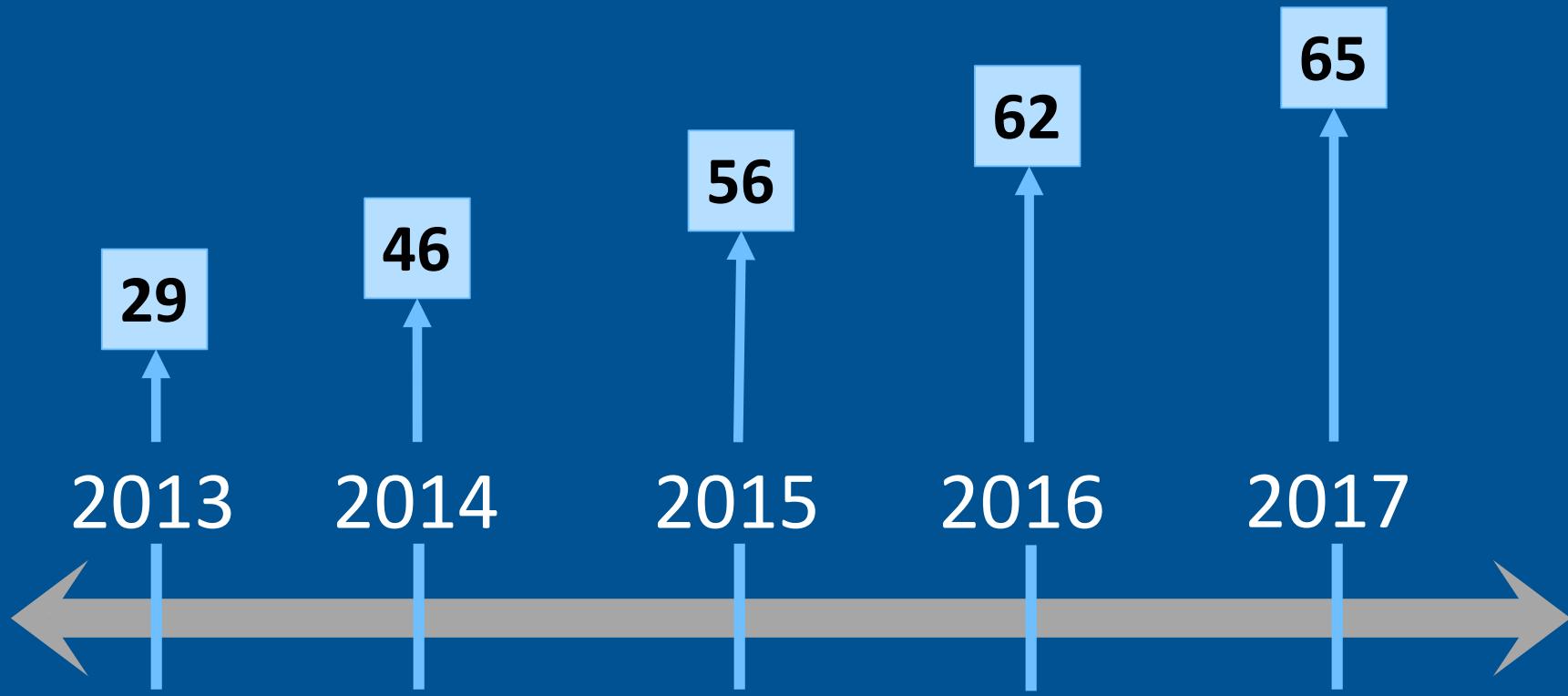
# Biosimilars in Development in the U.S.

**NUMBER of PRODUCTS in**
**FDA's BIOSIMILAR DEVELOPMENT PROGRAM**




www.fda.gov

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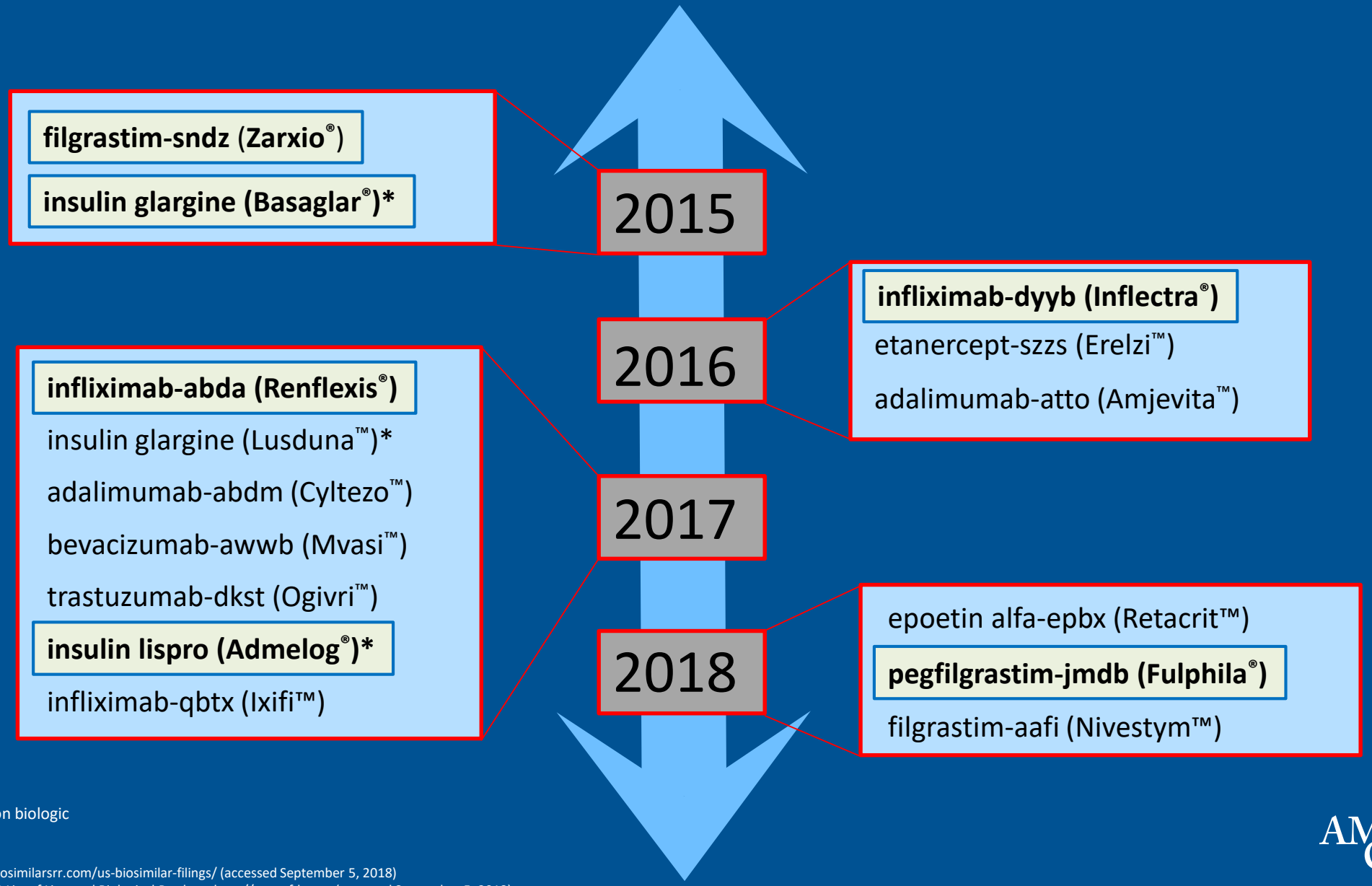
# Biosimilars Approved in US – as of September 2018




*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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# Biosimilars Approved by EMA – as of September, 2018

| Year of EMA Approval | Biosimilar Product | Reference Product | Number of Products |
|---|---|---|---|
| 2006 | Somatropin | Norditropin® | 2 |
| 2007 | Epoetin alfa | Epogen® | 3 |
| 2007 | Epoetin zeta | Retacrit® | 2 |
| 2008/2009/2010/2013/2014 | Filgrastim | Neupogen® | 9 |
| 2013/2014 | Follitropin alfa | Gonal-f® | 2 |
| 2013/2016/2018 | Infliximab | Remicade® | 4 |
| 2014/2017/2018 | Insulin glargine | Lantus® | 3 |
| 2016 | Enoxaparin sodium | Lovenox® | 2 |
| 2016/2017 | Etanercept | Enbrel® | 2 |
| 2017/2018 | Adalimumab | Humira® | 8 |
| 2017 | Insulin lispro | Humalog® | 1 |
| 2017 | Rituximab | Rituxan® | 6 |
| 2017 | Teriparatide | Forteo® | 2 |
| 2017/2018 | Trastuzumab | Herceptin® | 4 |
| 2018 | Bevacizumab | Avastin® | 1 |
| 2018 | Pegfilgrastim | Neulasta® | 2 |

TOTAL APPROVALS
= 53*

*3 were withdrawn in 2011, 2012, and 2016

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European Medicines Agency. www.ema.europa.eu (accessed May 8, 2018)
Generics and Biosimilars Initiative. http://gabionline.net/Biosimilars/General/Biosimilars-approved-in-Europe. (accessed September 7, 2018)

# Biosimilars: U.S. Market Access and Utilization

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# Current Utilization Patterns in the U.S.

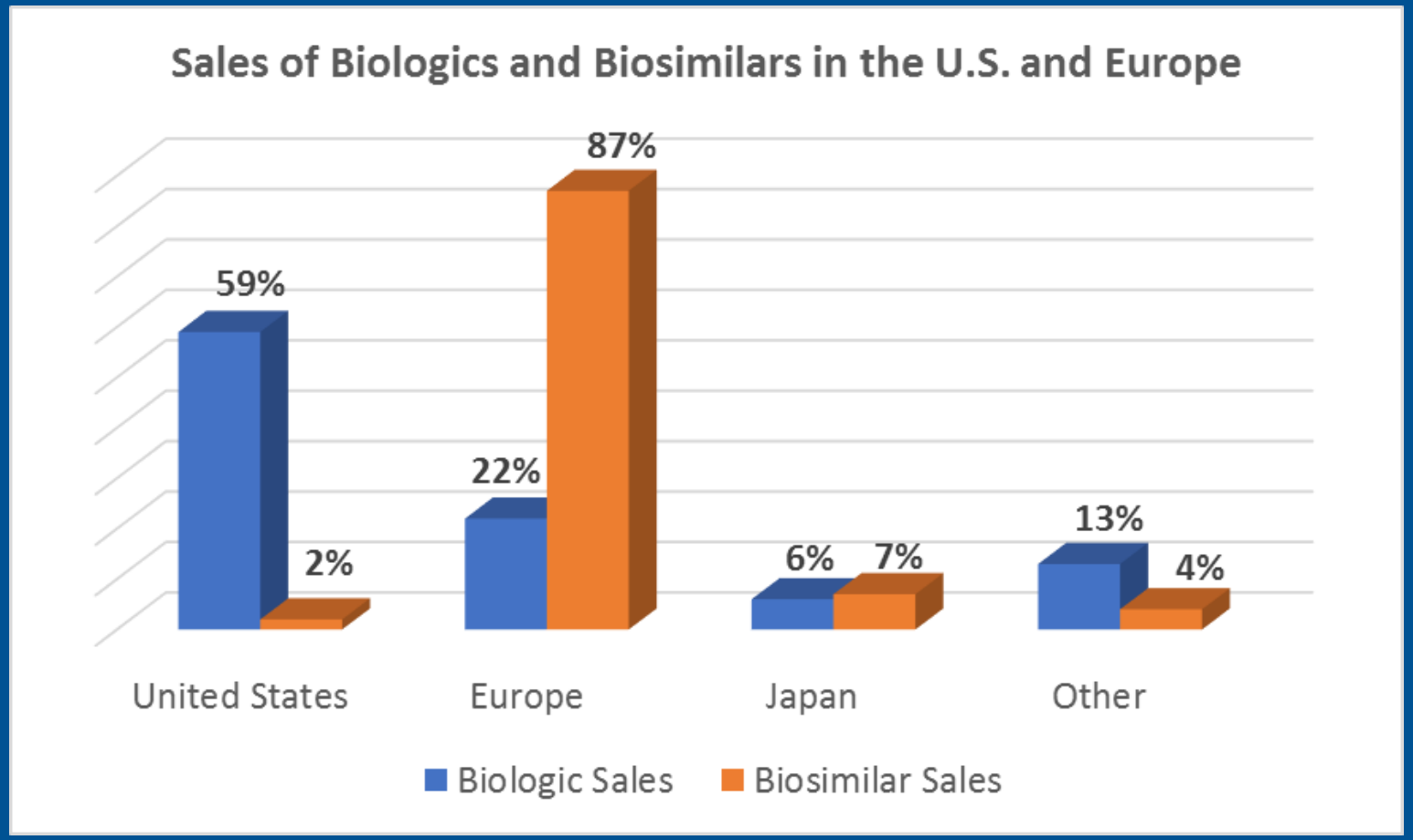
## 2017

filgrastim-sndz (Zarxio®) → 22% of filgrastim sales

infliximab-dyyb (Inflectra®) → 1.6% of infilximab sales

https://www.statista.com/statistics/869873/percentage-neupogen-sales-loss-to-biosimilars/
https://accessiblemeds.org/sites/default/files/2018-02/Doug%20Long.pdf
https://www.pacificresearch.org/wp-content/uploads/2018/06/PolicyObstaclesFweb.pdf

# 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

# Factors Influencing U.S. Biosimilar Utilization

1. Regulatory
2. Business Decisions
3. Uncertainty

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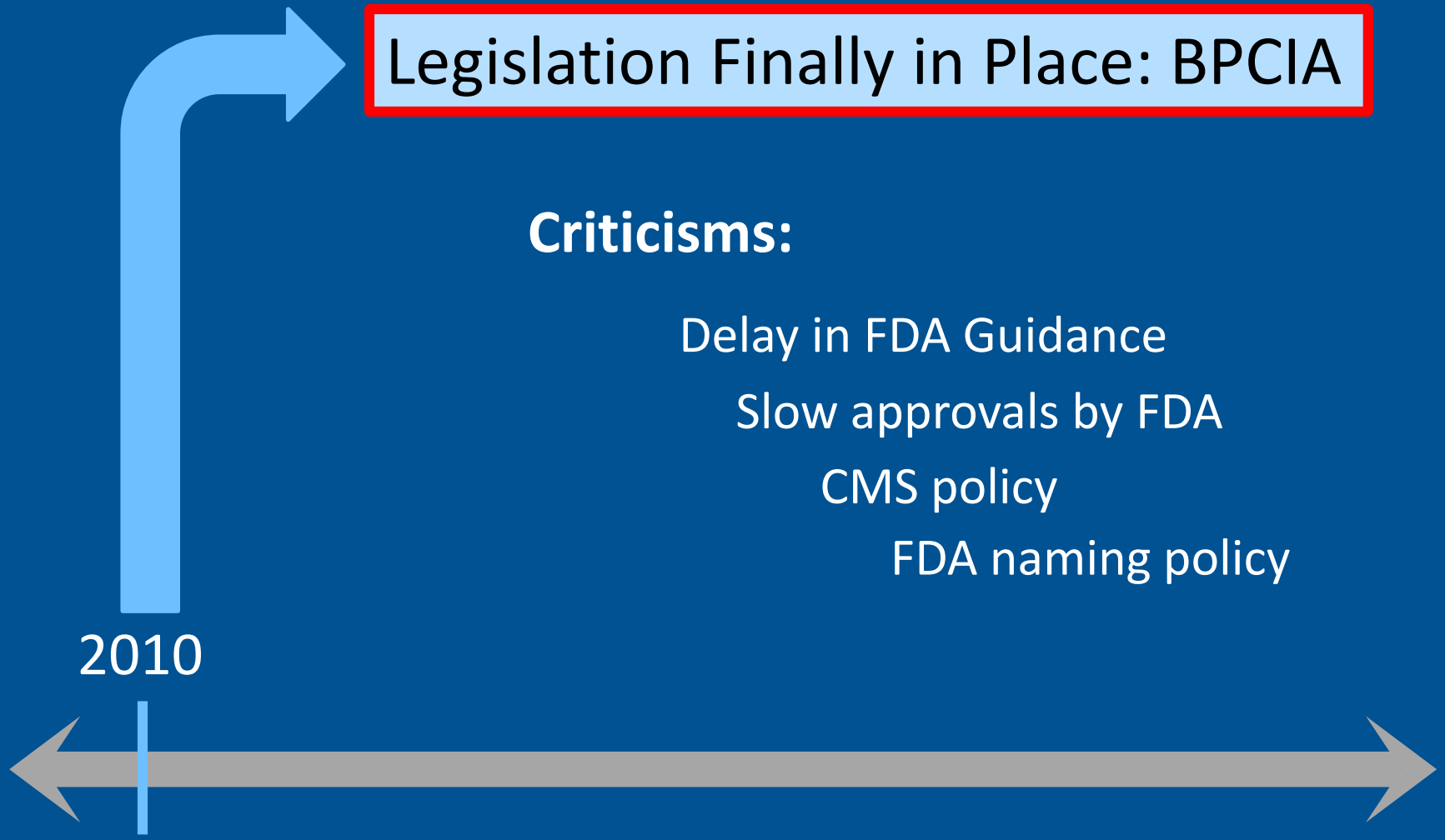


www.fda.gov

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

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# FDA Biosimilars Action Plan (BAP)

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 payers; 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

# Factors Influencing U.S. Biosimilar Utilization

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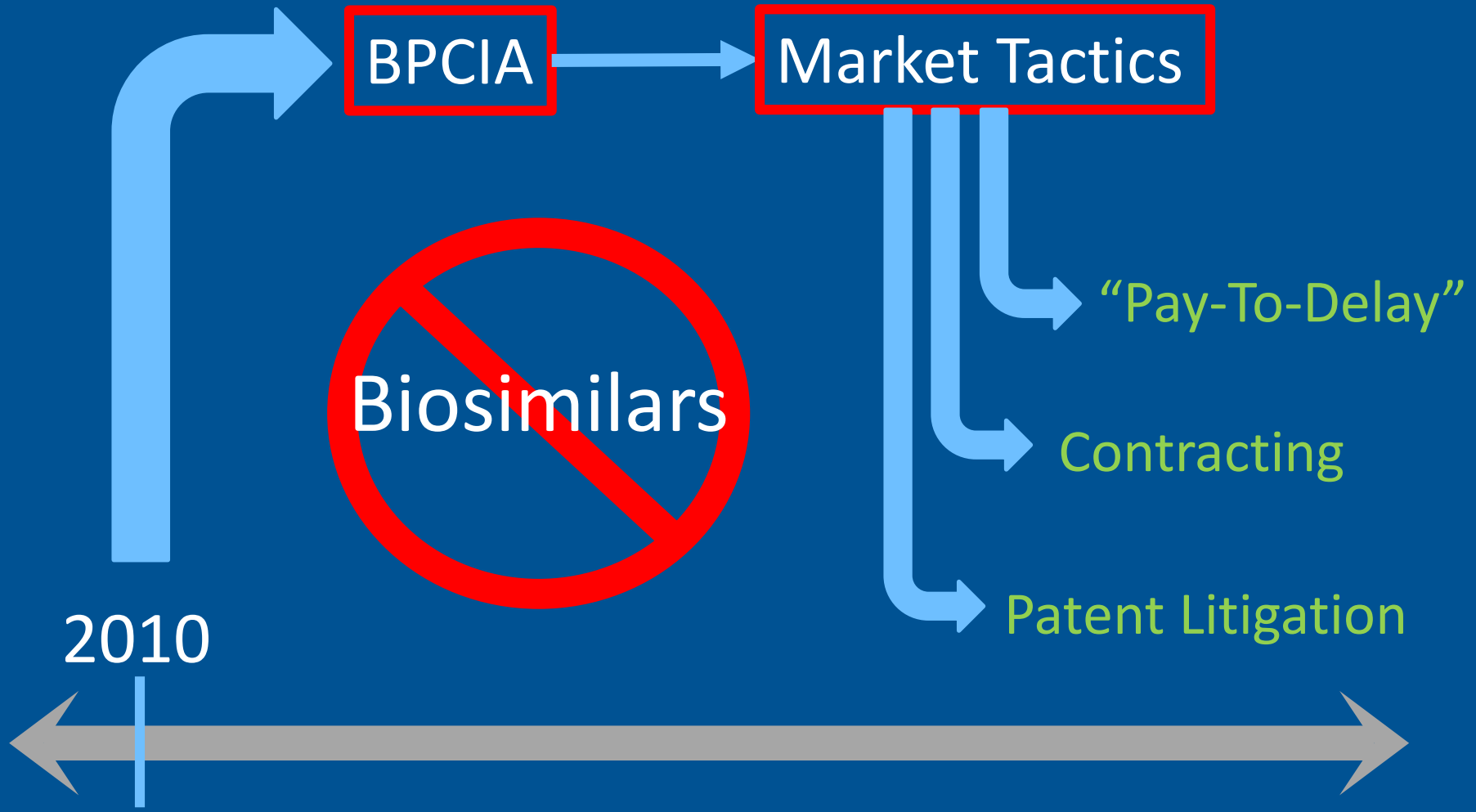
# Factors Influencing U.S. Biosimilar Utilization

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# Factors Influencing U.S. Biosimilar Utilization

1. Regulatory
2. Business Decisions
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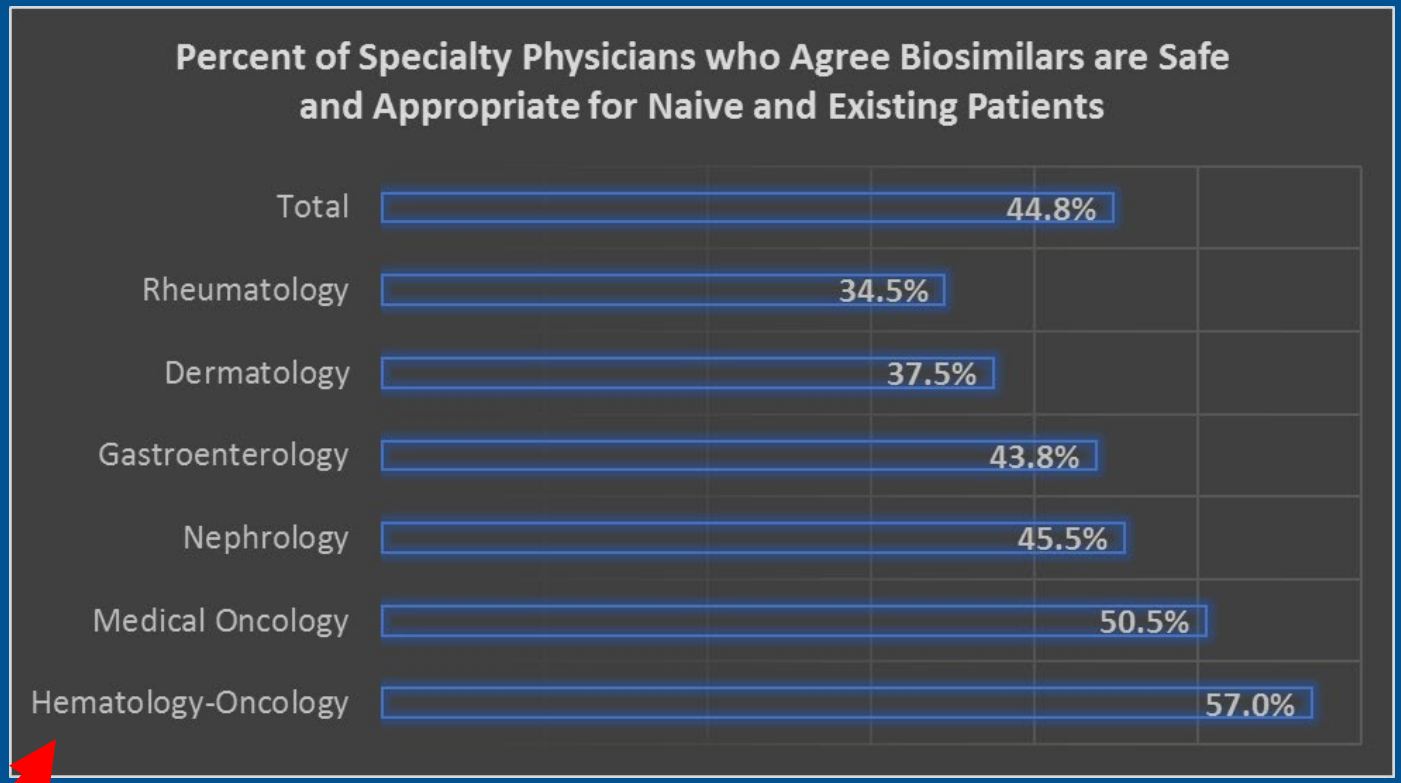
# Factors Influencing U.S. Biosimilar Utilization

## 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….

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# Factors Influencing U.S. Biosimilar Utilization

## Uncertainty - Patients

Jacobs et al. **Patient attitudes and understanding about biosimilars: an international cross-sectional survey**. *Patient Preference and Adherence* 2016;10:937-948.

| | Biologics | | | Biosimilars | | |
|---|---|---|---|---|---|---|
| | Basic awareness | No knowledge | Currently use | Basic awareness | No knowledge | Currently use |
| Patient (n=635) | 30% | 33% | 18% | 9% | 54% | 2% |
| Patient advocate (n=245) | 47% | 10% | 29% | 20% | 31% | 9% |
| General public (n=250) | 11% | 57% | N/A | 6% | 70% | N/A |

- Basic awareness = Defined as reporting at least a general impression of biologics or knew the term “biologic” or “biosimilars”.
- **N = 3,198** patients with inflammatory diseases or cancer that could be treated with available biosimilars
- 38.8% from US.

Note: ”Caregiver” category (N = 111) not included in this table
Not all categories sum to 100% due to rounding

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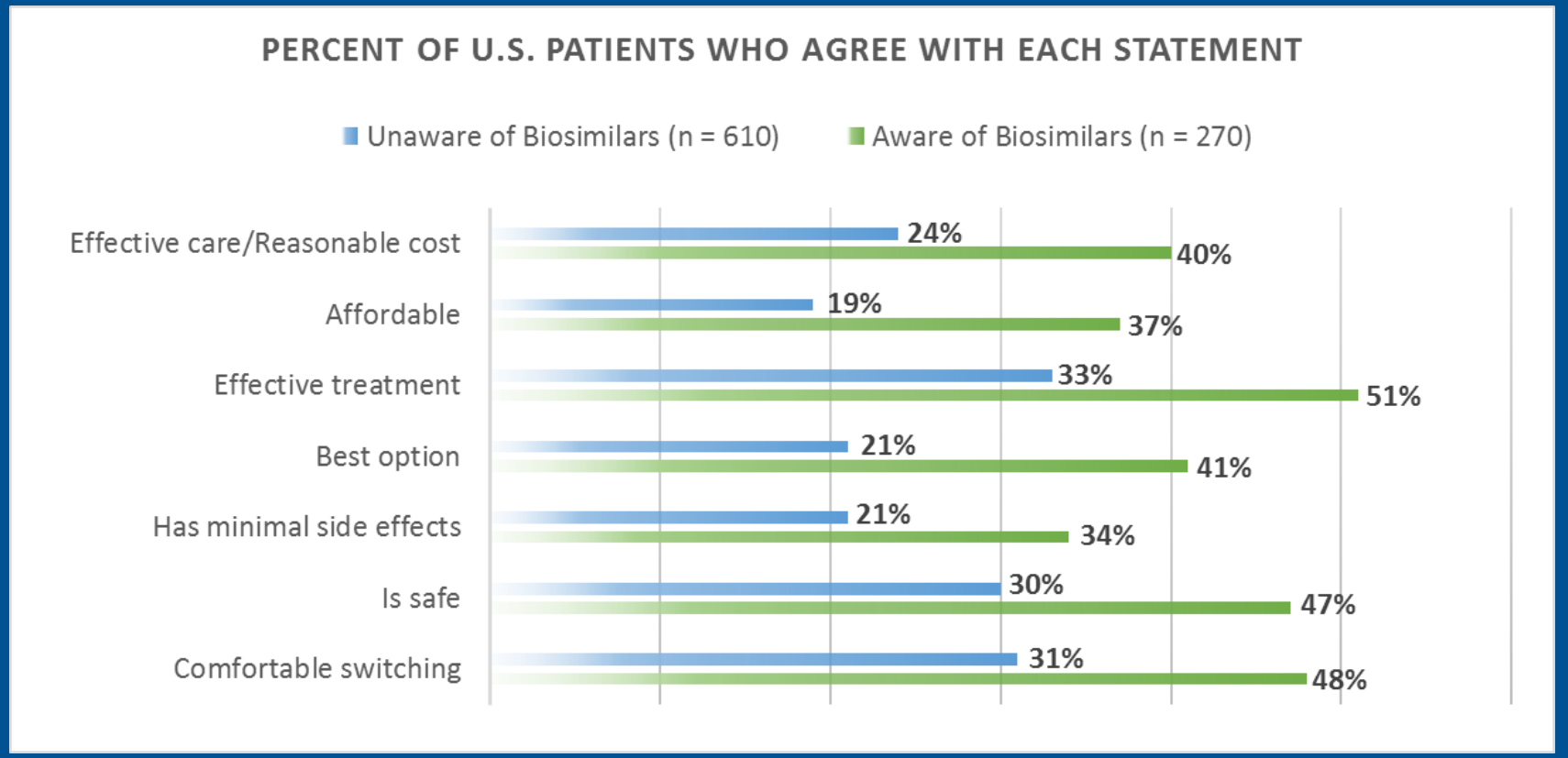
# Factors Influencing U.S. Biosimilar Utilization

## Uncertainty - Patients

Adapted from: Jacobs et al. **Patient attitudes and understanding about biosimilars: an international cross-sectional survey**. *Patient Preference and Adherence* 2016;10:937-948.




- Basic awareness = Defined as reporting at least a general impression of biologics or knew the term “biologic” or “biosimilars”.

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# Factors Influencing U.S. Biosimilar Utilization

**Medical Specialists' Attitudes to Prescribing Biosimilars**
*Pharmacoepidemiol Drug Saf* 2017;26(5):570-577.

**Subjective Complaints as the Main Reason for Biosimilar Discontinuation After Open-Label Transition from Reference Infliximab to Biosimilar Infliximab**
*Arthritis Rheumatol* 2018;70(1):60-68.

Barsell et al. **A Survey Assessment of US Dermatologists' Perception of Biosimilars**
*J Drugs Dermatol* 2017;16(6):6122-615.

….and others

Post-approval studies evaluating comparative safety and effectiveness will be critical to generating real-world evidence to inform clinical practices and policy decisions

OPPORTUNITY FOR EDUCATION

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# Biosimilars: Data Sources for Decision-Makers

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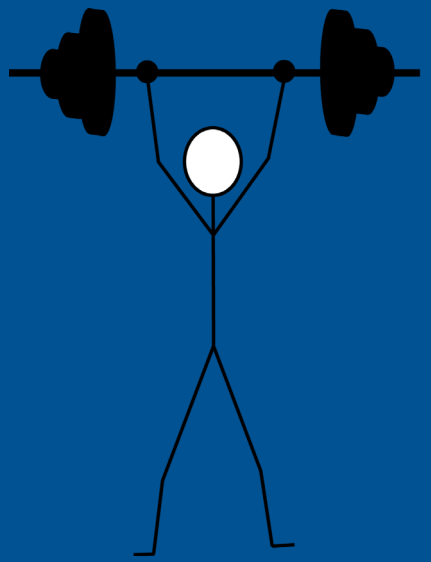
# Data Source – Clinical Trials

## Strengths:

Randomized Controlled Trials (RCTs) = **GOLD STANDARD**

Carefully designed to **reduce**:

**BIAS**
**CONFOUNDING**
**PLACEBO EFFECT**



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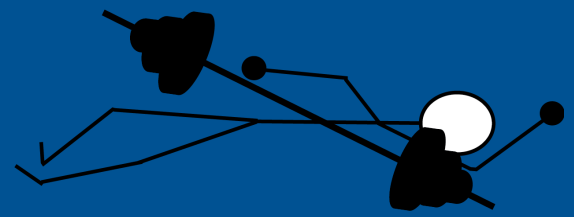
Hannan EL. *J Am Cardiol Intv*. 2008;1(3):211-217.

# Data Source – Clinical Trials

## Limitations:

- May not be sufficient to address all relevant questions
- Exclude potentially large segments of the population
- Cover a limited length of time, often very short
- Do not often reflect normal clinical settings
- Very Expensive



Greenfield. *Value in Health* 2017;20:1023-4.
Jarow, et al. *JAMA* 2017;318(8):703.

# Origins in the Gap in Evidence

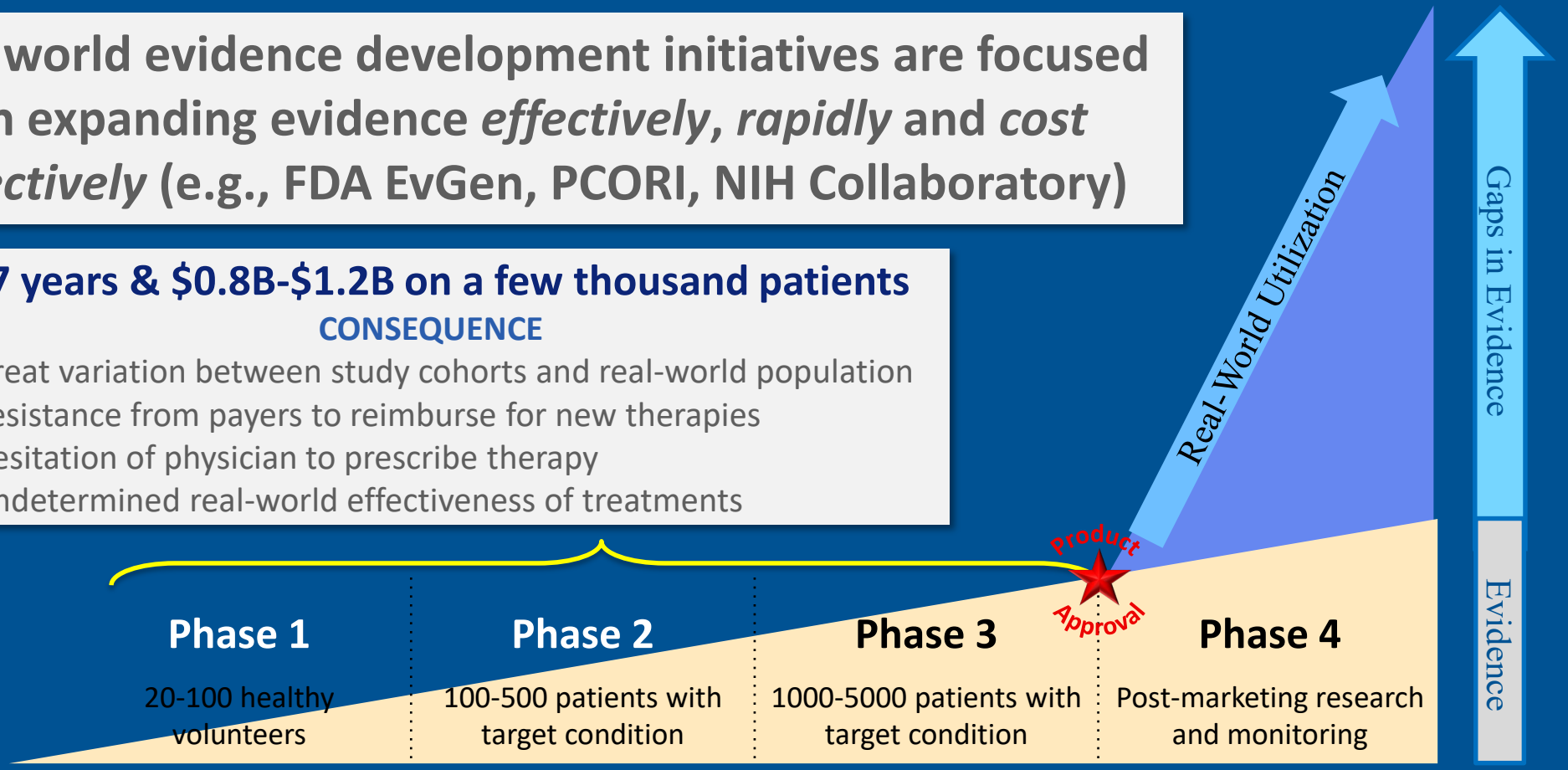
## Real-world utilization quickly outpaces available clinical evidence

**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

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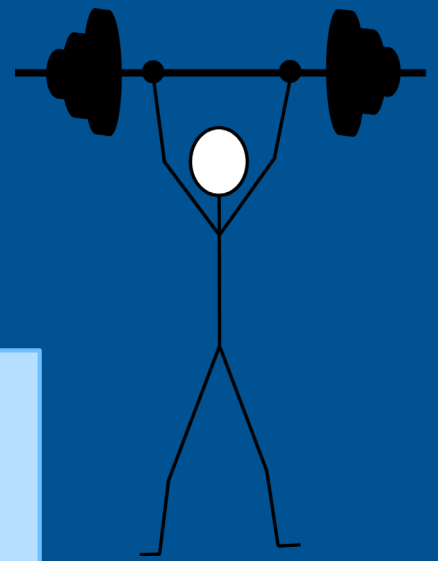
# Data Sources – Real World Evidence (RWE)


**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

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# 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
- Data provide rich source of information for patient safety evaluations



*Platt R, et al. Pharmacoepidemiol Drug Saf. 2012 Jan;21 Suppl 1:1-8.*

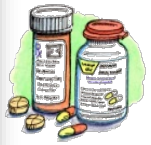
# Bob's Story

| Demographic | | | | |
|---|---|---|---|---|
| **Coverage** | **PatID** | **Birth Date** | **Sex/Race** | **ZIP Code** |
| Harvard Pilgrim Health Care | 5291321 | 07/29/63 | M/Unknown | 02119 |


Lives in Boston, MA

Has appendectomy

Diagnosed with hypertension



Routine Office Visit

| Encounter | Dispensings | Encounters | Encounter | Dispensings | Encounter |
|---|---|---|---|---|---|
| • 1/1/2011 **Office Visit** • **Dx:** Influenza with pneumonia | • 1/1/2011 • **Rx:** Antibiotic | • 3/15/2012 **Emergency Department** • **Px:** appendectomy<br>• 3/15/2012-3/18/2012 **Hospital** Inpatient stay | • 12/11/12 **Office Visit** • **Dx:** Hypertension | • 12/11/12 • **Rx:** Anti-hypertensive | • 10/31/13 **Office Visit** • **Dx:** Hypertension |

2011 2012 2013 2014

Bob is a 47-50 year old male with 1,035 days of observed time

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# ISPOR/ISPE Task Force on RWE - Recommendations

- **Define study** (questions and purpose)
  - *Exploratory*
  - *Hypothesis evaluating treatment effectiveness* (HETE)
- **Public posting** of **study protocol** and **analysis plan**
- **Publish** **study results** (or post on website)
- **Enable** **replication** (same data and analyses)
- **Confirm important findings** (2nd data source & population)
- **Publicly address** **methodologic criticism** after publication
- **Include** **key stakeholders** in design, conduct & dissemination

Berger et al. *Value in Health* 2017;20:1001-8

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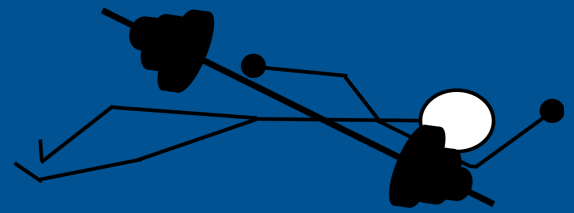
# Real World Evidence

## 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



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


# BBCIC: One Approach to Real-World Evidence Generation

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# BBCIC - Background


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

# BBCIC Purpose: Why the BBCIC Is Needed

**Generics saved the US well over $1.6 trillion in past decade** *but it took 20 years.*

–Generics are safe and effective, resulting in increased patient access to critical medications.

–Slow generic uptake influenced by anecdotal reports that got wide press coverage.

–Lingering uncertainty among physicians and patients about safety and comparability.

Physician survey, 2011 → ***GENERICS*** → 23% – concern about efficacy
50% – concern about quality

Physician survey, 2015 → ***BIOSIMILARS*** → 78% – very concerned about safety/immunogenicity

Shrank et al. Ann Pharmacotherapy, 2011;45(1):31-8.
http://www.gastro.org/press_releases/2015/7/29/national-survey-reveals-gastroenterologists-views-on-biosimilar-drugs

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# BBCIC Surveillance – Leveraging Sentinel Capabilities

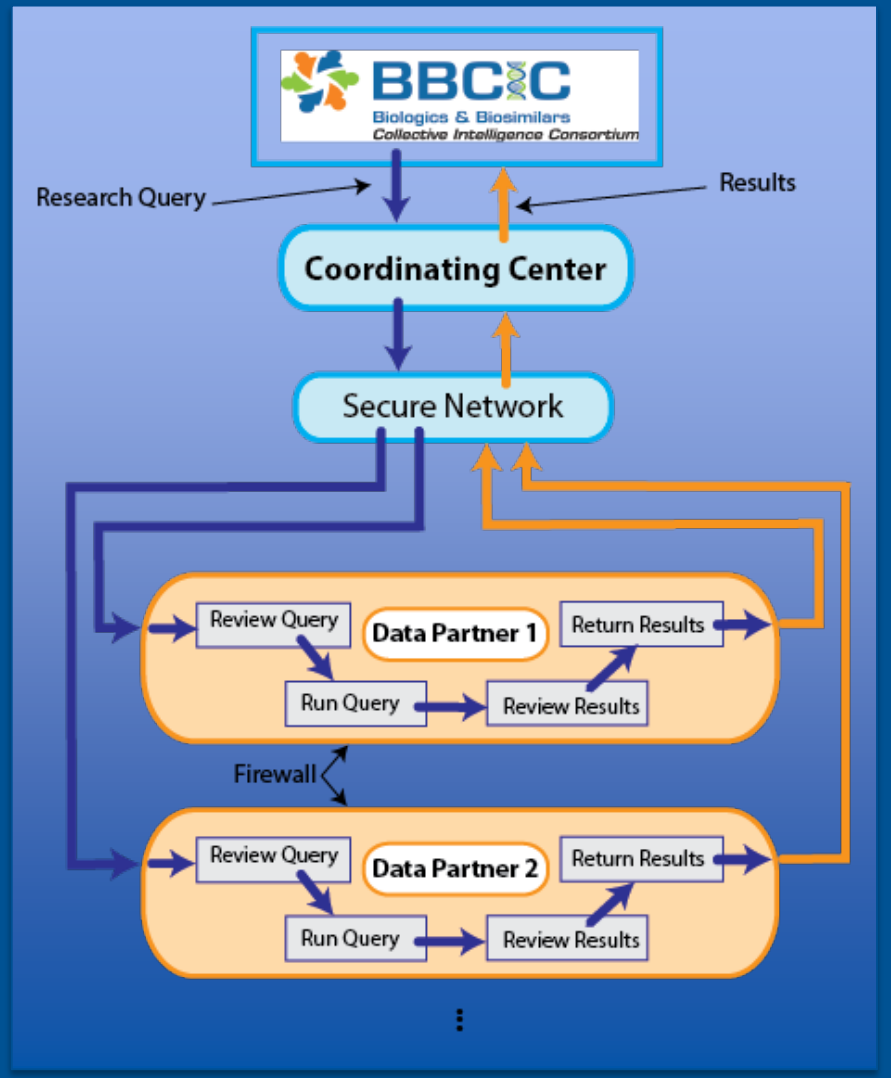
**The AMCP BBCIC strategy provides a unique opportunity for Managed Care to support public knowledge of biologic and biosimilar drugs with robust science.**

**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 ~150 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*

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# 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

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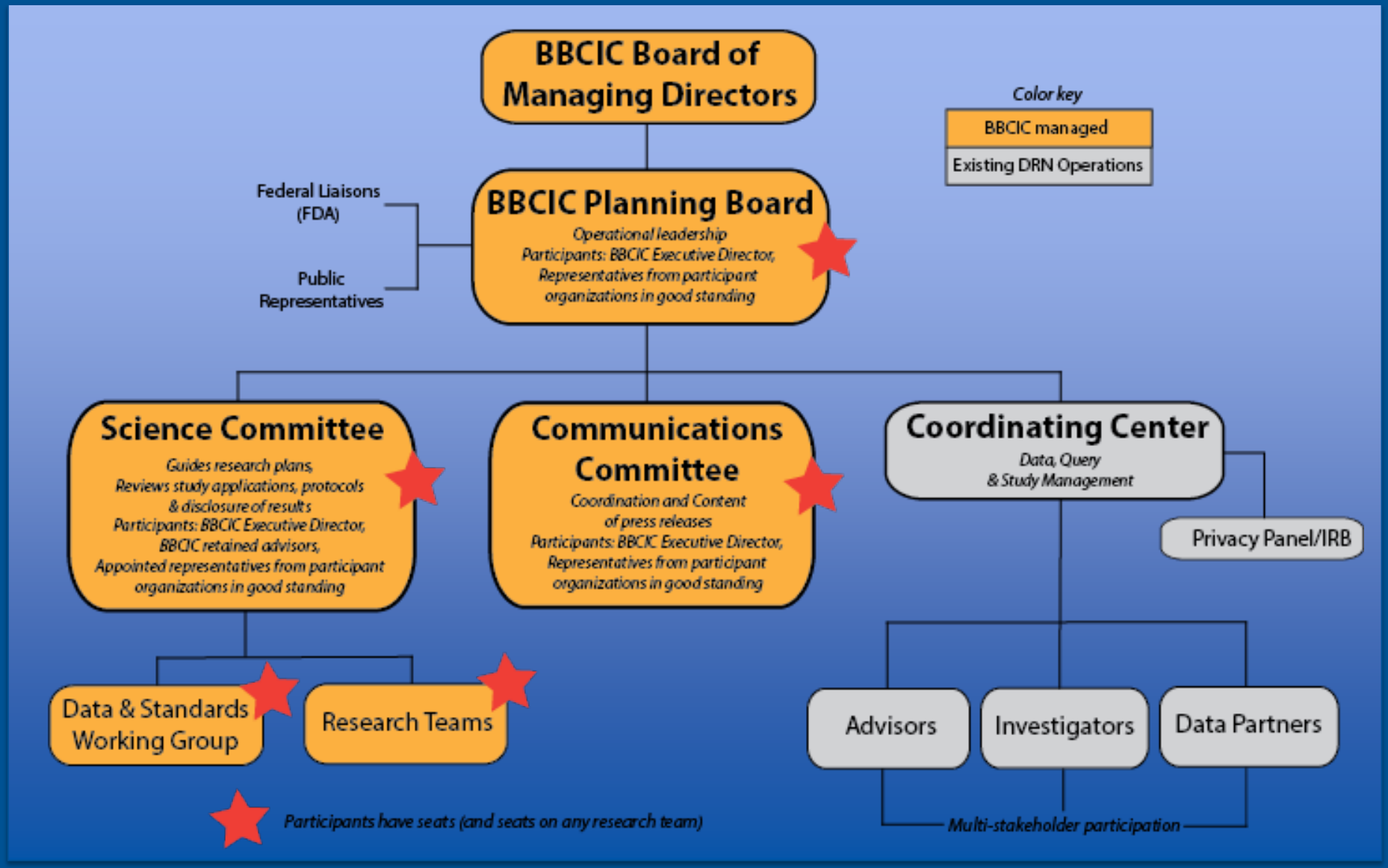
# BBCIC Governance Overview




*AbbVie*
*Aetna*
*Amgen*
*Anthem*
*Apobiologix*
*Boehringer*
*Express Scripts KP*
*Washington*
*Harvard Pilgrim*
*HealthPartners*
*HOPA*
*Henry Ford*
*Merck*
*Momenta*
*Optum*
*Pfizer*
*Sandoz*
*Sanofi*

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# BBCIC Partner Organizations

**Coordinating Center**

Harvard Pilgrim Health Care Institute

**Data and scientific partners**

- HealthCore
- Anthem
- HOPA
  Hematology/Oncology Pharmacy Association
- Health Care Systems Research Network
  HealthPartners, Henry Ford Health System
- Kaiser Permanente Washington Health Research Institute
- Harvard Pilgrim Health Care
- Aetna
- Optum
- Express Scripts

**Convened by**

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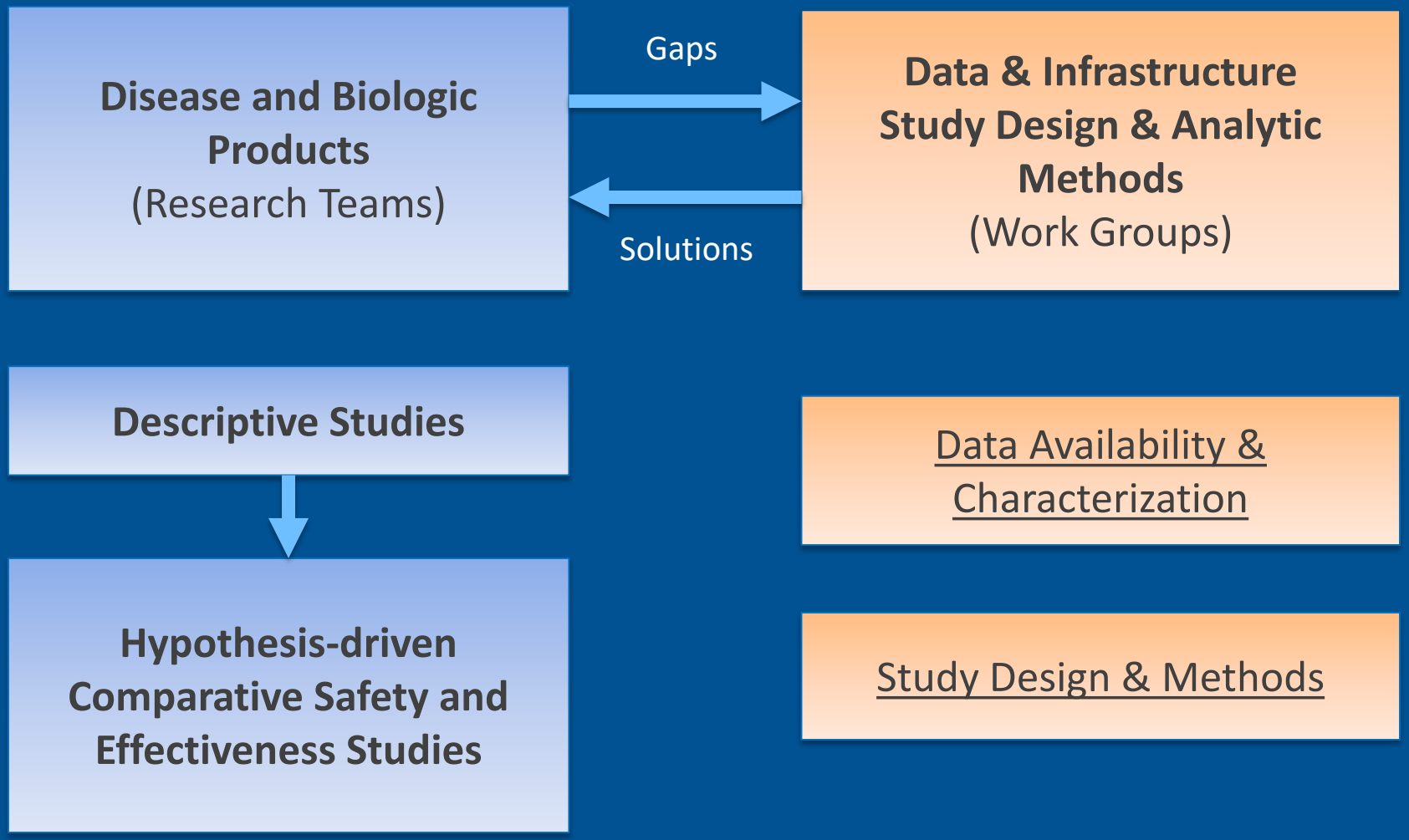
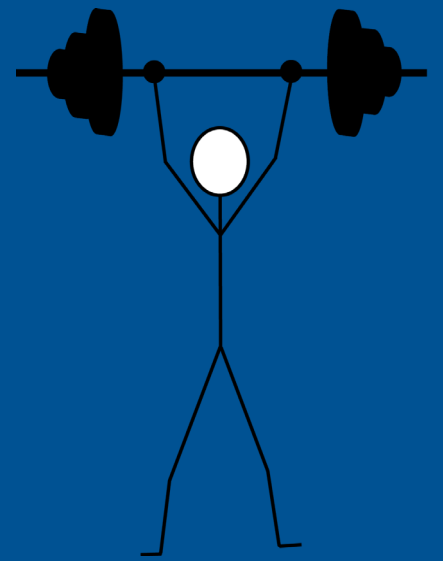
# BBCIC Scientific Operations



# Strengths of BBCIC

- **Stakeholders** play an active and extensive role
- **Focus** on biologic class and diseases for new biosimilars
- **Descriptive analysis**
  - To understand patients, disease, treatments, outcomes
  - To understand data, methods, gaps, possible solutions
- **Comparative analysis**
  - Both safety and effectiveness
  - All biosimilars for originator biologic
- **Active surveillance**
- **Leverage Sentinel**



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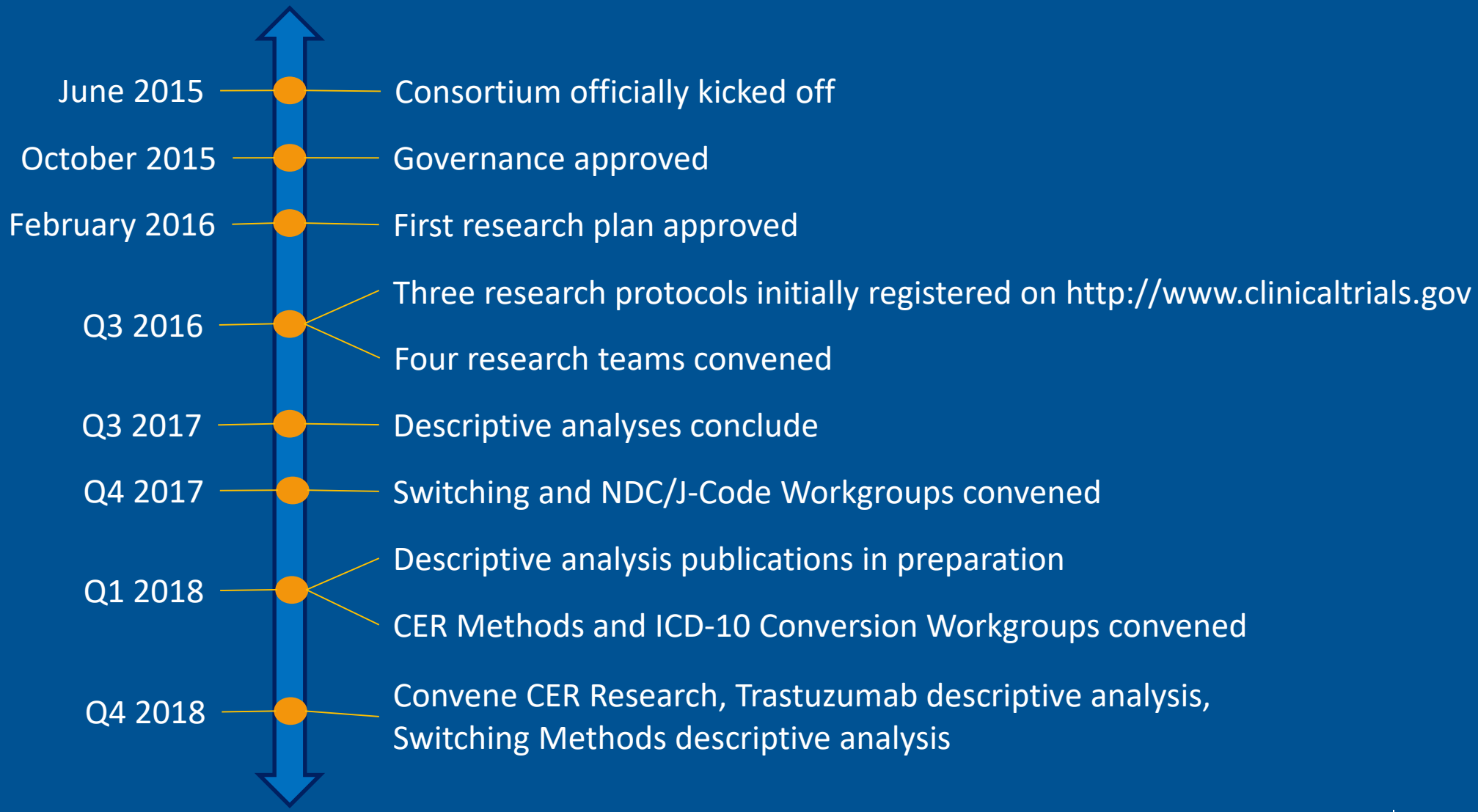
# BBCIC Progress to Date

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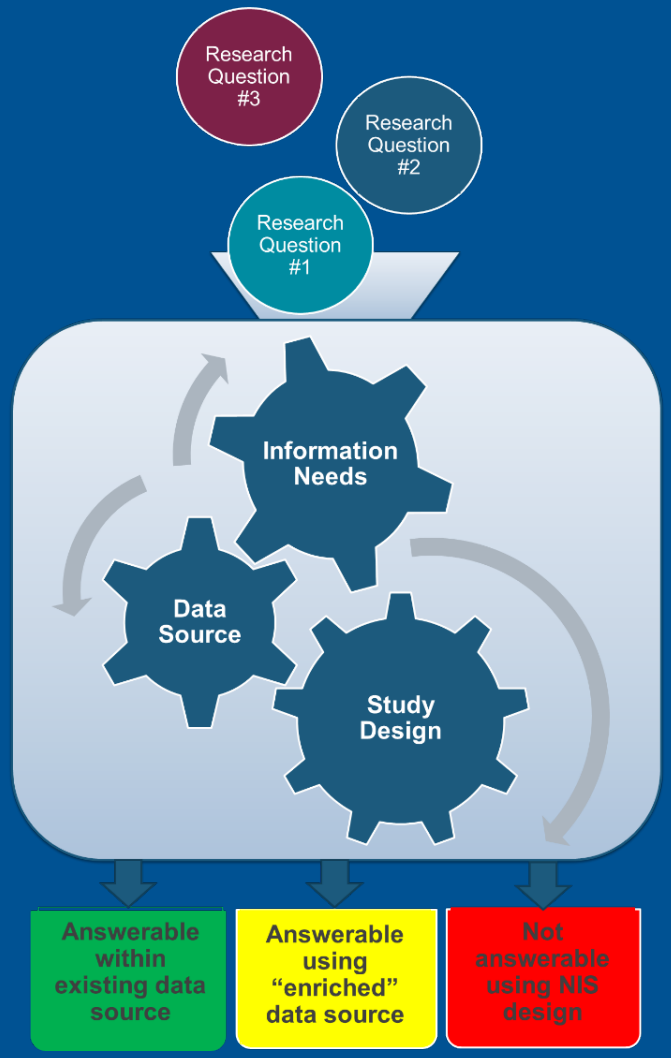
# BBCIC 2017-2019: Lines of inquiry

- 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

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# 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**
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# Descriptive Analysis Research Teams

**In 2016, the BBCIC Science Committee convened 4 research teams to conduct descriptive analyses using the BBCIC DRN**

| Project | Disease Indications | Drugs |
|---|---|---|
| **Insulins** | • Diabetes | Insulin |
| **Colony Stimulating Factors (G-CSF)** | • Febrile Neutropenia risk reduction in non-myeloid malignancies treated with myelosuppressive anti-cancer drugs associated with febrile neutropenia | Filgrastim (Neupogen), PEG-filgrastim (Neulasta), TBO-filgrastim, filgrastim-sndz (Zarxio) |
| **Anti-Inflammatories** | • Rheumatoid Arthritis<br>• Psoriasis<br>• Psoriatic Arthritis<br>• Ankylosing Spondylitis<br>• Ulcerative Colitis<br>• Crohn's Disease | Adalimumab (Humira), infliximab (Remicade),infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), rituximab (Rituxan), tocilizumab (Actemra), abatacept (Orencia), etanercept (Enbrel), certolizumab (Cimzia), golimumab (Simponi), ustekinumab (Stelara), secukinumab (Cosentyx), natalizumab (Tysabri), golimumab (Simponi) |
| **Erythropoeitin-Stimulating Agents (ESA)** | • Anemia (CKD, Hemodialysis) | Epoetin alfa (Epogen, Procrit) darbepoetin alfa (Aranesp), methoxy polyethylene glycol-epoetin beta (Mircera) |

# Descriptive Analysis Research Teams

**In 2016, the BBCIC Science Committee convened 4 research teams to conduct descriptive analyses using the BBCIC DRN**

| Project | Objective | Outcomes |
|---|---|---|
| **Insulins** | Describe treatment patterns and outcomes of adult patients with diabetes who use long-acting (LAI) or intermediate-acting (NPH) insulin | (1) major cardiac events, combined; severe hypoglycemic events; (2) A1C baseline and follow-up |
| **Colony Stimulating Factors (G-CSF)** | Descriptive analysis G-CSF use in breast or lung cancer patients who received chemotherapy with Grade III or IV neutropenic-risk. | (1) rate of hospitalizations; (2) severe neutropenia; anaphylaxis; combined measure of bone pain, glomerulonephritis, capillary leak syndrome, hyperleukocytosis and splenic rupture. |
| **Anti-Inflammatories** | Describe treatment patterns and outcomes of patients with autoimmune diseases receiving biologic treatments | Serious infections requiring hospitalization. |
| **Erythropoeitin-Stimulating Agents (ESA)** | Assess the feasibility of currently available BBCIC data to conduct a study of ESA biosimilars and innovators in hemodialysis (HD) patients. | Chronicity of HD among patients; similarity of population of HD patients described by USRDS |

- 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.

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# Descriptive Analysis – Lessons Learned

**OVERALL:**

- **The BBCIC DRN is robust and reliable for large-scale observational studies**
- **Additional methods and data sources are being incorporated to enrich the data and capabilities of the BBCIC**

| Project | Challenges | Lessons Learned/Solutions |
|---|---|---|
| **Insulins** | • Design Considerations | • Coding algorithms for diagnosis inconsistency<br>• Careful attention to episode gap length<br>• Alternative methods for patient adherence |
| **G-CSF** | • Exposures<br>• Outcomes | • Broader inclusion criteria<br>• Careful attention to covariates and clinical outcome measures |
| **Anti-Inflammatory** | • Outcomes | • Clinical effectiveness measures are difficult to identify from administrative claims<br>• Pilot to link PRO and clinical measures to claims<br>• Include linked EMR + claims data sources |
| **ESA** | • Data Sources | • Data sources with adequate patient numbers |

# BBCIC - Progress

- What we have **DONE**
- What we are **DOING**
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# Lessons Learned - Infrastructure Improvements

## Data Improvements

- Address multiple gaps identified in descriptive analyses
- Pilots with Patient Reported Outcomes from MTM or Specialty Pharmacy providers
- Pilots with mobile health patient reported outcomes tied longitudinally to the Common Data Model

## Add Data Partners

- Cancer Research Network
- Medicare ESRD Full data set
- Anthem HealthCore Integrated Research Environment (HIRE)
- ASCO CancerLinQ

## Expand Common Data Model

- Outcomes measures

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# Workgroups

**In 2017, the BBCIC Science Committee convened 4 workgroups to develop best practices in research methodology and a platform for future studies**

| Project | Challenges Addressed | Study Goal |
|---|---|---|
| **Switching** | • Design Considerations | Treatment of switching/sequencing as a covariate/confounder in BBCIC CER studies |
| **CER Methods** | • Design Considerations | Develop best-practices based on current methodology for conducting observational comparative-effectiveness research |
| **NDC / J-Code** | • Exposures<br>• Outcomes | Investigate the extent to which NDCs are being supplied on physician-office claims |
| **ICD-10 Mapping** | • Exposures<br>• Outcomes | In preparation for future descriptive and CER projects, ICD-9 codes are being mapped to ICD-10 codes to allow utilization of data both before and after October 2015. |

# BBCIC - Progress

- What we have **DONE**
- What we are **DOING**
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# Upcoming BBCIC Research - 2019

## COMPARATIVE EFFECTIVENESS

### G-CSF

First BBCIC CER study to compare the G-CSF originator biologic to available biosimilars in the US. The Research Team is expected to kickoff in Q4 of 2018 and research will commence in earnest by the end of the year.

### Insulins

The topic of a PCORI grant application.

## DESCRIPTIVE ANALYSIS

### Trastuzumab Descriptive Analysis

We anticipate research will commence research in Q1 2019.

## METHODS

### Switching Methods Descriptive Analysis

The next phase of the Switching Methods Workgroup. This study will include an in-depth discussion of best practices for study design, and a descriptive analysis to test study designs in the BBCIC DRN.

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# BBCIC Future Directions

## Expanded Research Scope

- Priority research in current and emerging BIOSIMILARS
- We are the BIOLOGICS and Biosimilars Collective Intelligence Consortium
- Opportunities for drug class or disease level research

## Expanded Partnerships

- Pursuing partnerships to leverage resources for specific projects
- Seeking new participating members (manufacturers, managed care, PBMs, research organizations, data partners)

## Expanded Data Capabilities

- Adding new data sources to enrich the BBCIC DRN
- Exploring inclusion of patient-reported and clinical data with administrative claims

## Expanded Communications Plan

- PUBLICATIONS!!
- Increased public exposure to research programs and results

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# Anticipated Publications in 2019

## ❑ Methods and Infrastructure

- CER Methods Systematic Review
- CER Methods Best-Practices and Recommendations
- ICD-9 to ICD-10 Mapping
- NDC/J-Code Patterns and Implications in Physician Claims
- Switching Patterns Descriptive Analysis

## ❑ Observational Research

- Descriptive Analyses: Insulins, Anti-Inflammatories, G-CSF, ESA
- G-CSF: Design of a CER Study
- G-CSF: Preliminary Results
- Trastuzumab: Design of a Descriptive Analysis
- Trastuzumab: Preliminary Results

# Practical Application of BBCIC Research

## WHAT WE PROVIDE:

**REAL-WORLD EVIDENCE**

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

**EDUCATION**

Source of **education** for stakeholders

## WHAT WE NEED:

**ENGAGEMENT**

- Health Plans
- Pharmacy Benefit Managers
- Patients
- Prescribers and Healthcare Practitioners
- Manufacturers

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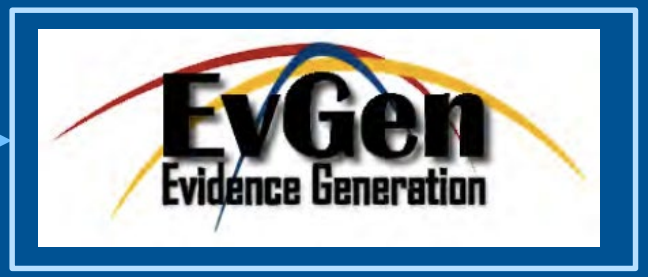
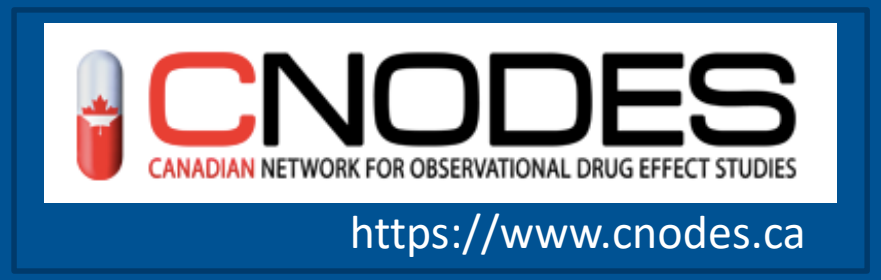
# Sources of Post-Marketing Data

# Rapidly Evolving Landscape


https://fda.gov






https://www.cnodes.ca


https://pcornet.org

# Sources of Post-Marketing Data for BIOSIMILAR Research

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# Post-Marketing Research - BIOSIMILARS


To date the only multi-stakeholder, multi-source research consortium dedicated to proactive surveillance of safety and effectiveness of **biosimilar products and reference biologics** in the United States

# POST-TEST

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# LQ1: Which of the following were barriers to generic drug adoption and utilization in the United States?

a. An unexpected side effect of the Hatch-Waxman Act that facilitated “pay-to-delay” arrangements
b. A 1988-1989 investigation resulted in convictions of FDA officials, manufacturers, and consultants for bribery
c. Patients and prescribers were uncomfortable with generic drugs
d. All of the above

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# LQ2: Which of the following is a LIMITATION of clinical trial data?

a. Designed to reduce confounding and bias
b. Potentially excludes large segments of the population who may be treated with the drug in real-world practice
c. Provides evidence that assesses safety and efficacy of the drug to support regulatory requirements
d. All of the above

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d. All of the above

**LQ3: Data produced from research by organizations such as the Biologics and Biosimilars Collective Intelligence Consortium could be used to inform treatment and coverage decisions.**

a. True
b. False

**LQ3: Data produced from research by organizations such as the Biologics and Biosimilars Collective Intelligence Consortium could be used to inform treatment and coverage decisions.**

a. True
b. False

# LQ4: There are multiple organizations conducting post-marketing surveillance specifically on biosimilars and their reference biologics in the United States

a. True
b. False

# LQ4: There are multiple organizations conducting post-marketing surveillance specifically on biosimilars and their reference biologics in the United States

a. True
b. False

# QUESTIONS?

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