Biosimilars Regulatory Expectations & Experiences

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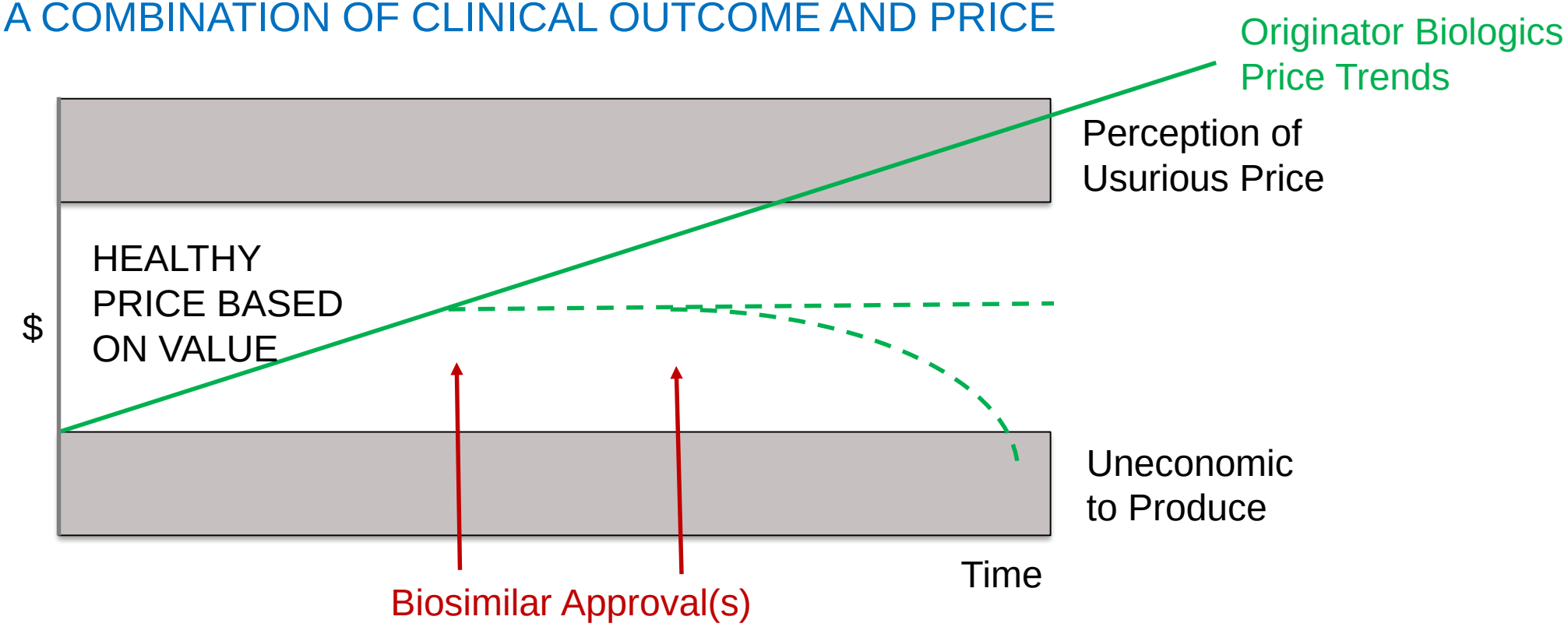
AAM 5Sep18

Outline

- **Context for Biologics and Biosimilar in the US**
- Current Landscape and Future Trends
  - Global Context – plus a bit of history
  - Terminology Reminders
  - The Reference Product Matters
- Future Trends
  - Interchangeability and Switching
- Conclusions

Context: Biosimilars are about additional competition and surety of supply

VALUE IS A COMBINATION OF CLINICAL OUTCOME AND PRICE

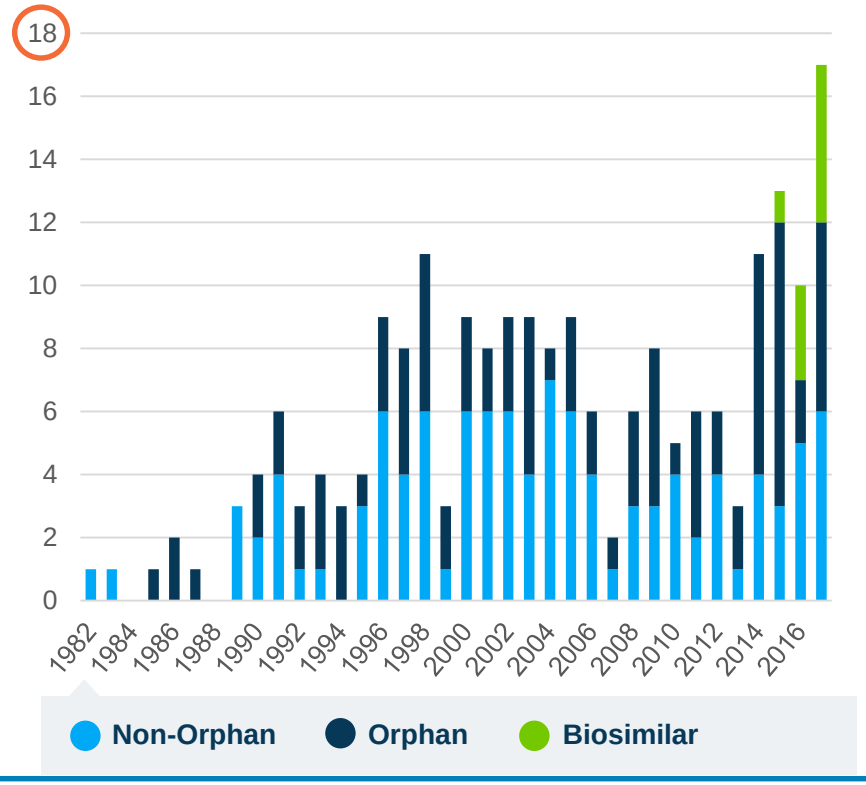


Priority is competition amongst biologics irrespective of the regulatory pathway by which they are approved; FDA Commissioner now an advocate for biosimilars as part of a competitive market[1]

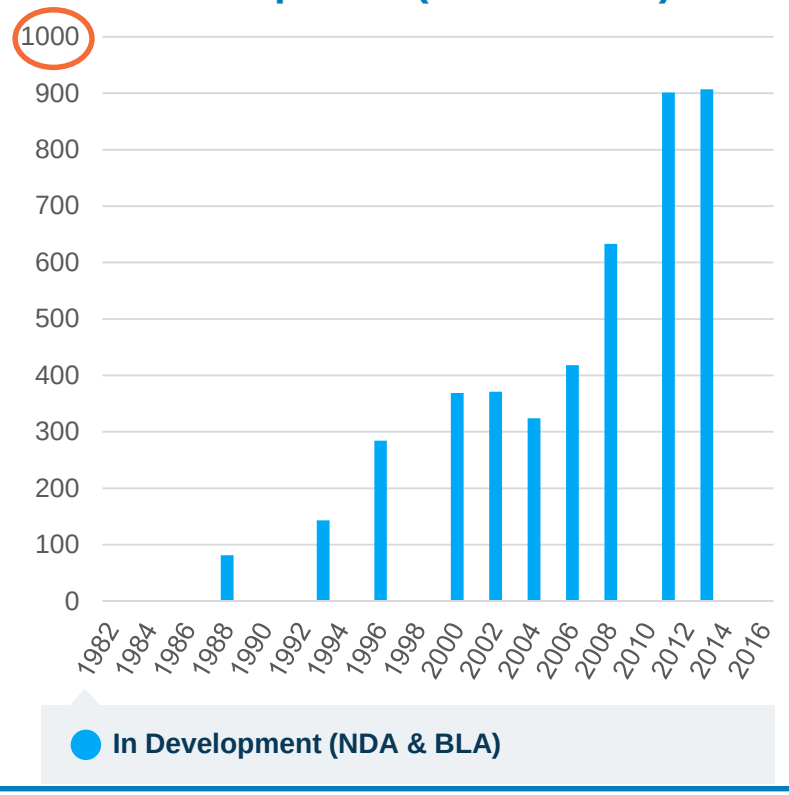
1 *AHIP Capturing the Benefits of Competition for Patients* here 7Mar18, *PCMA Advancing Patient Care Through Competition* here 19Apr18, *Keynote Address by Commissioner Gottlieb to the 2018 FDLI Annual Conference* here 3May18; *Brookings Institution speech* (here and the video here) 18Jul18 plus Biosimilar Action Plan here

Value: US Hosts Major Investment in Biotech – both Originator and Biosimilar

Approvals (NDA & BLA)[1]



In Development (NDA & BLA)[2]

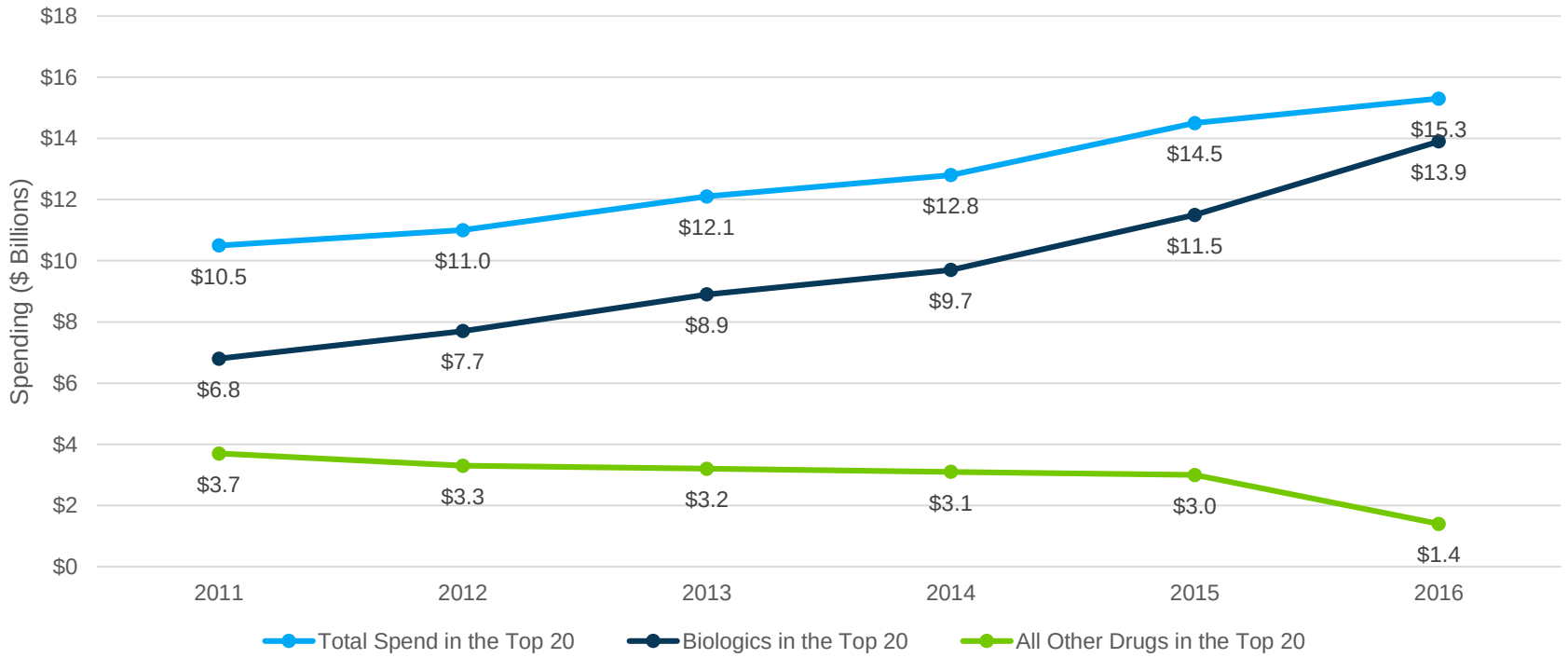


The science is the best it has even been; biotech is offering wholly new approaches to unmet medical needs. Competition based on value is key

FDA. "Drug and Biologic Approval Reports." Not including vaccines and blood products
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/default.htm
PhRMA. "Biotechnology Research Promises to Bolster the Future of Medicine with More Than 900 Medicines and Vaccines in Development." 2013.
http://www.phrma.org/sites/default/files/pdf/biologics2013.pdf, plus previous versions of these reports back to 1988

Late Comer on Biosimilars: Lack of Competition in the US Biologics Market

In 2016, biologics made up 91% of spending on the top 20 Part B

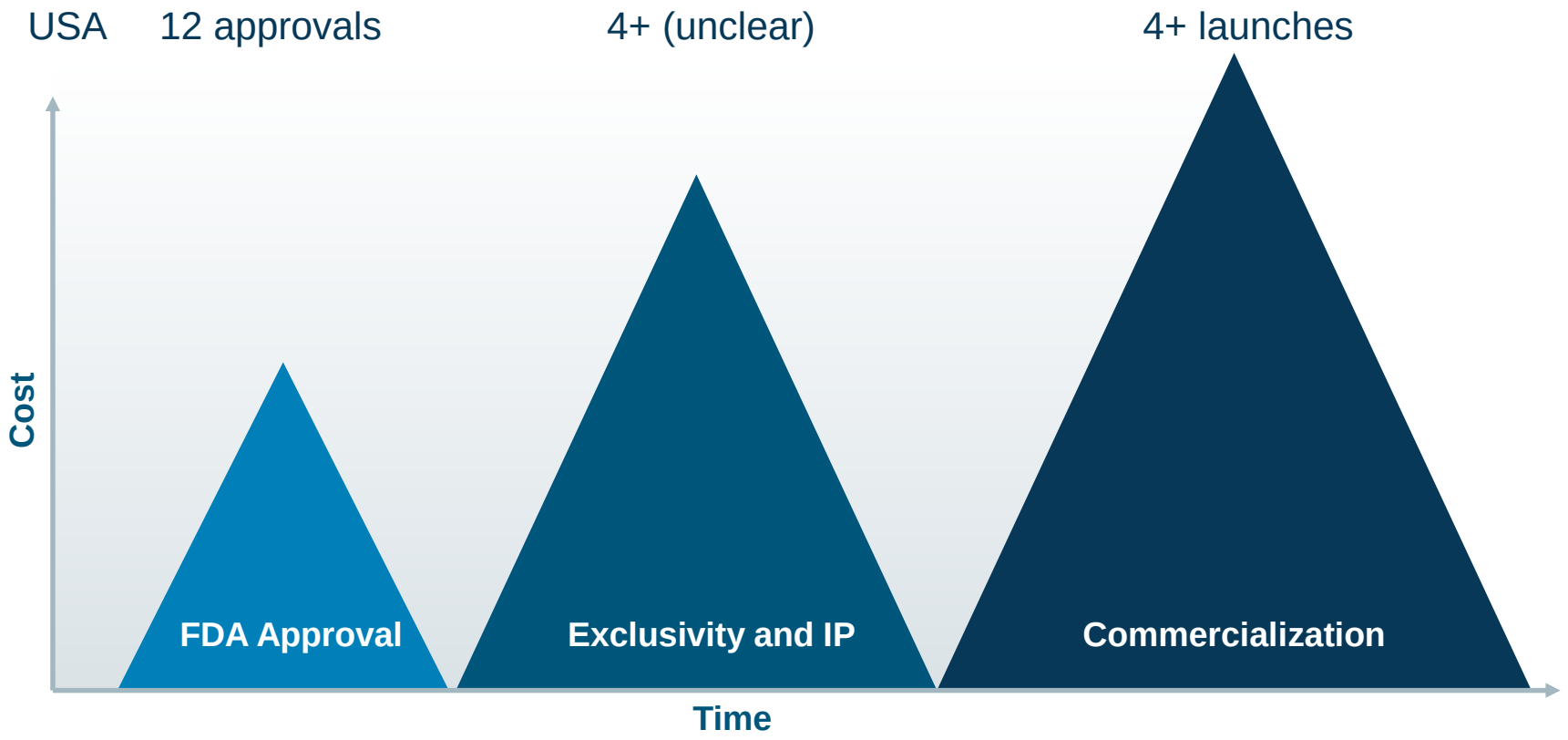


Obstacles to creating a multi-source biologics environment include complexity of development, prescribing patterns, interchangeability, physician reimbursement models, and payer coverage

Avalere Analysis of Medicare Part B and D Drug Spending Data. Available on CMS website: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/MedicarePartB.html.
Avalere: Five Obstacles to Competition, 31May17 http://avalere.com/expertise/life-sciences/insights/five-obstacles-to-competition-in-the-united-states-biologics-market

The Mountainous Challenges for Biosimilars in the US

FDA approval is the first of a series of challenges



Can there be a sustainable multisource specialty market in the US?

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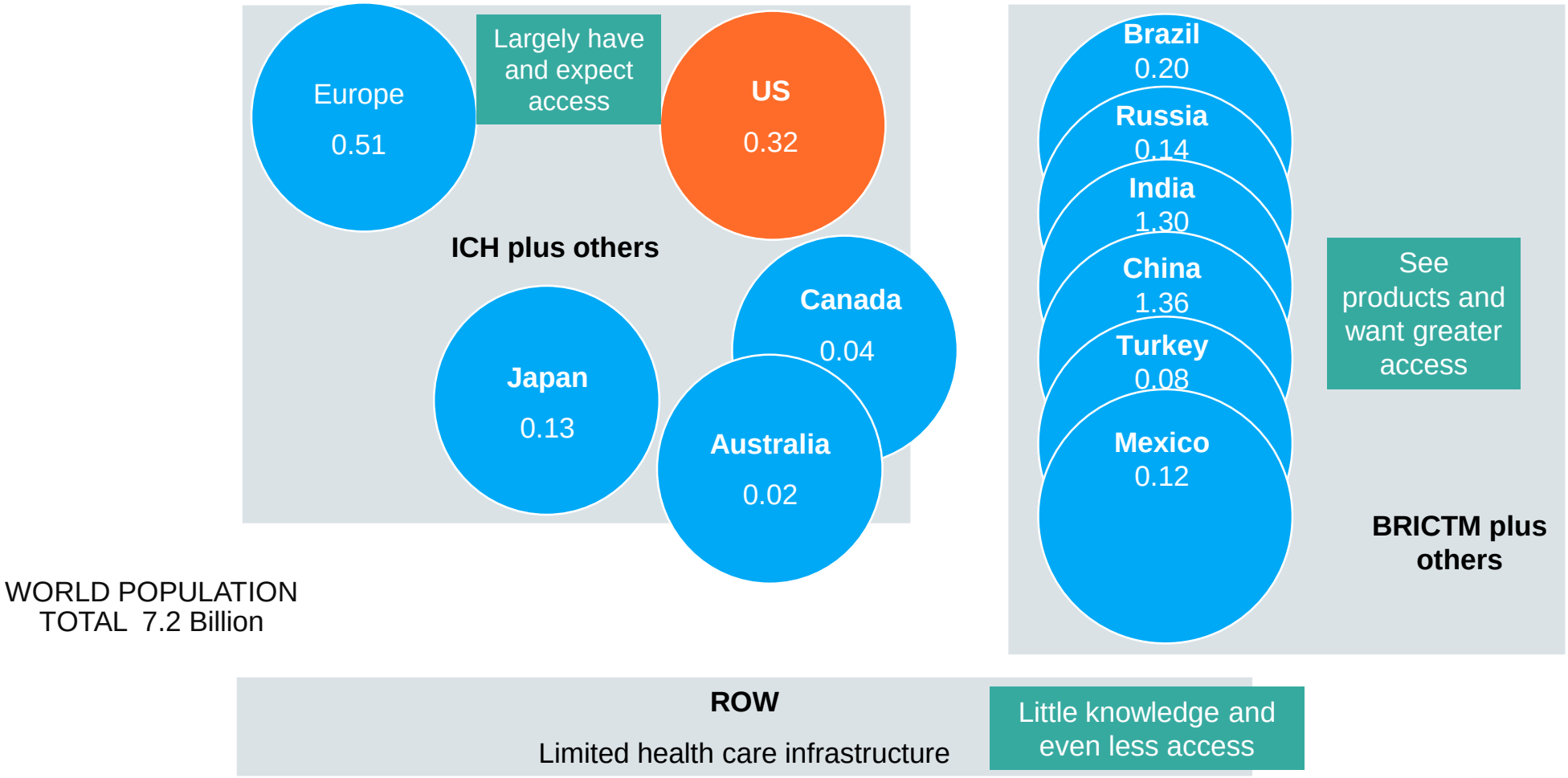
US is ~50% of the market by $ value, yet home to ~5% of the World's Population

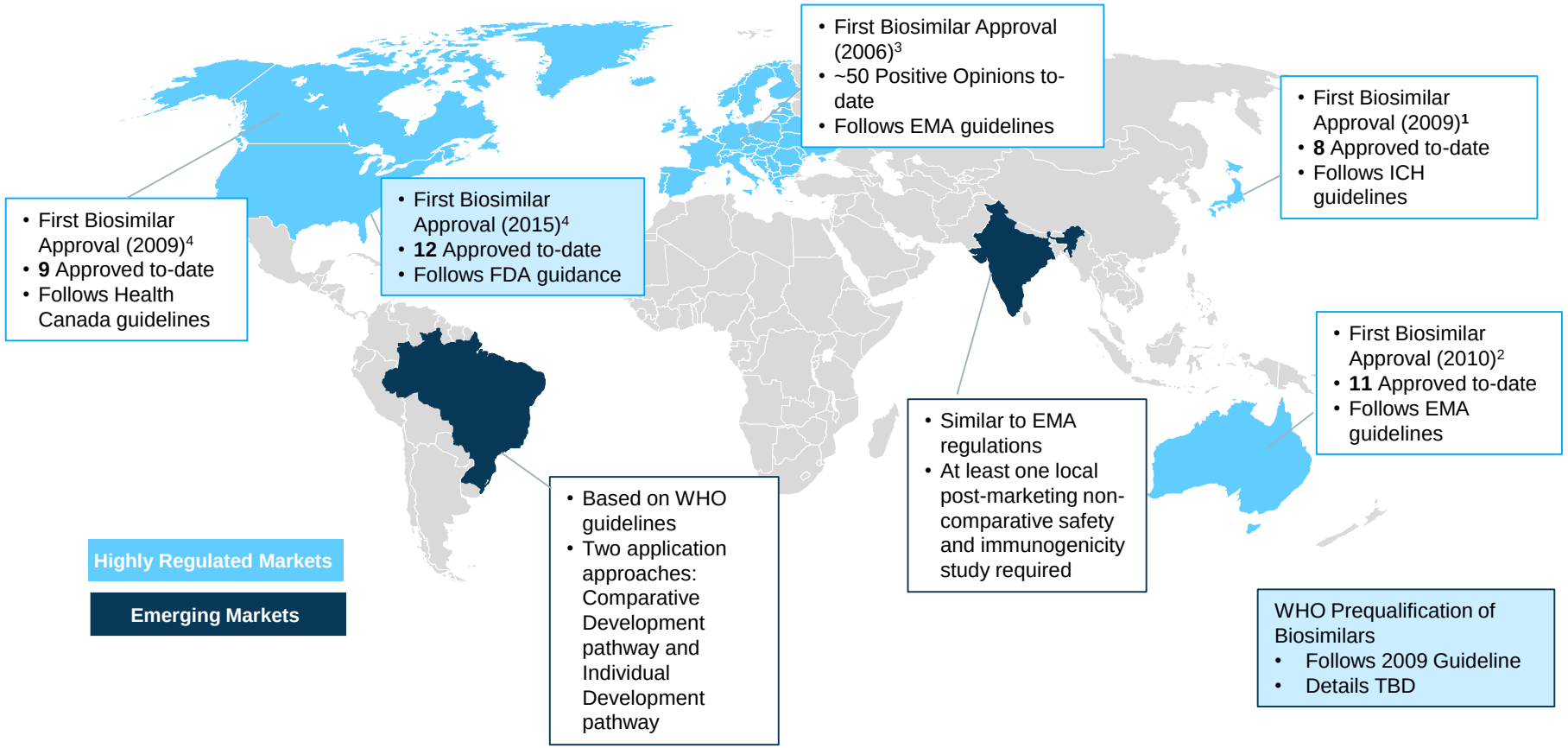


Population Numbers in Billions: http://www.prb.org/pdf14/2014-world-population-data-sheet_eng.pdf

ICH: International Conference on Harmonisation

Biosimilars only Follow Successful Originator Biologics

DEVELOPMENT PROGRAMS ARE INCREASINGLY MULTI-JURISDICTIONAL

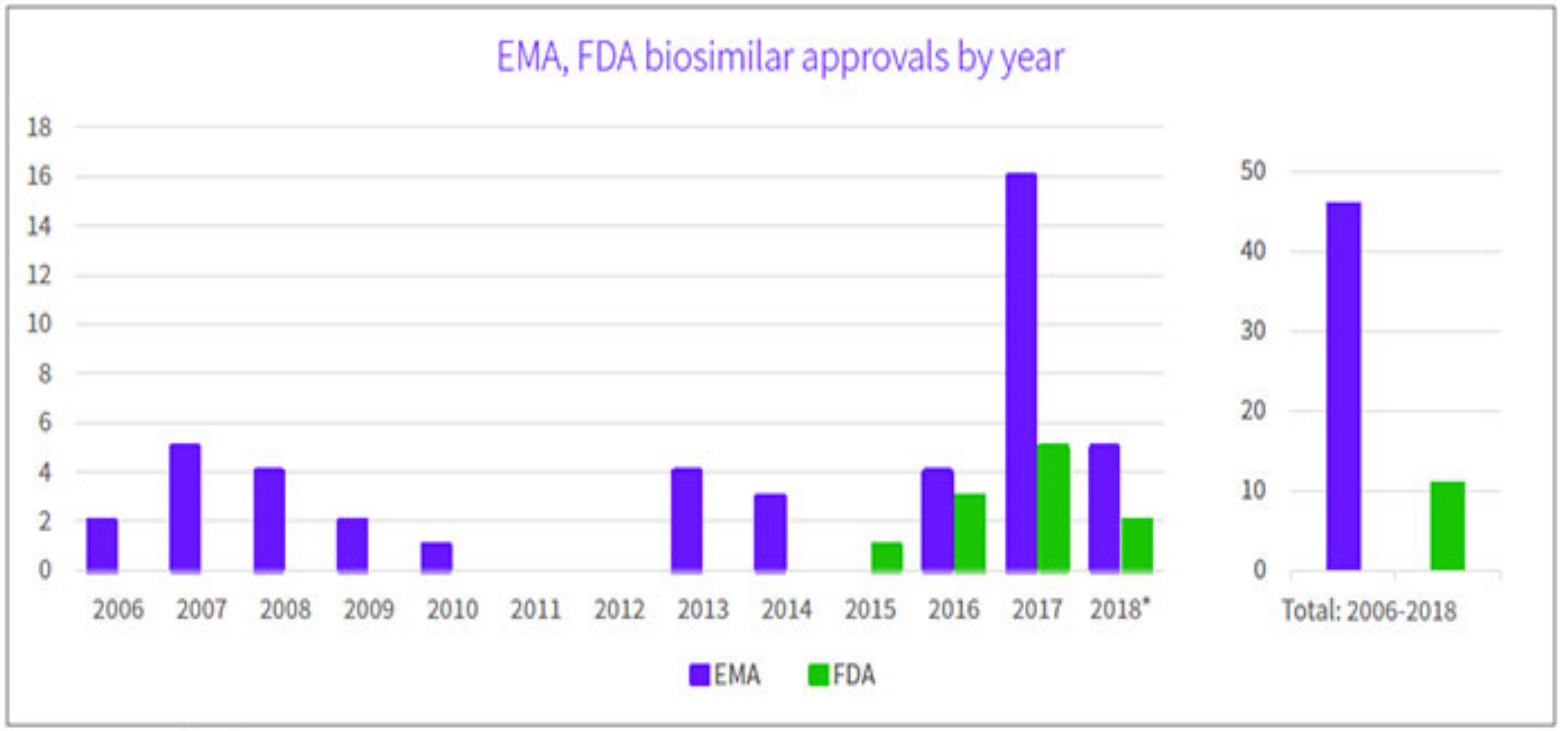


1.http://www.egaevents.org/presentations/2016bios/Daisaku_Sato.pdf and http://www.pmda.go.jp/english/review-services/reviews/approved-information/drugs/0002.html; 2. https://www.tga.gov.au/browse-auspars-active-ingredient; 3. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&mid=WC0b01ac058001d124&searchTab=searchByAuthType&alreadyLoaded=true&isNewQuery=true&status=Authorised&keyword=Enter+keywords&searchType=name&taxonomyPath=&treeNumber=&searchGenericType=biosimilars&genericsKeywordSearch=Submit; 4. http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/drug-med/sbd_smd_2009_omnitrope_113380-eng.php; 5. FDA Purple Book https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM549201.pdf

Avalere

Europe and the US still have Different Biosimilar Approvals

YET US AND EUROPE ARE THE MOST HARMONIZED REGULATORILY



Source: EMA, FDA; *As of June 15

Requirements for different data sets cannot be scientifically justified

BioWorld *Will price competition follow in the wake of incoming U.S. biosimilar wave?* http://www.bioworld.com/content/will-price-competition-follow-wake-incoming-us-biosimilar-wave-0 (accessed 21Jun18)

Biologics are not New – Arguably Much Older than Drugs

BIOLOGICS HAVE A LONG AND WELL-ESTABLISHED REGULATORY HISTORY

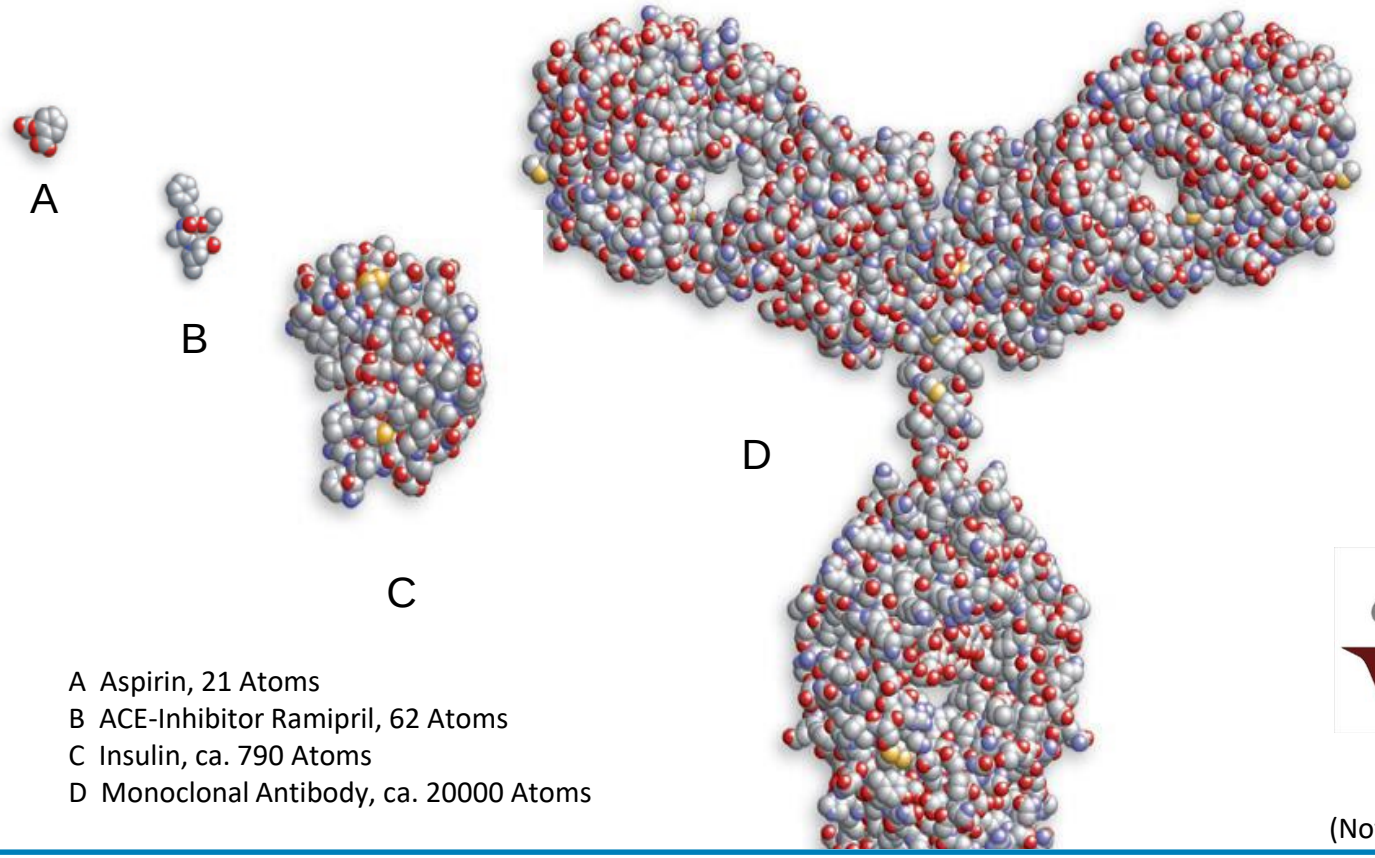
- **Late 18th Century** — First reliable Vaccine –Vaccinia for small pox
- **Early 20th Century** — PHS Act and early naturally-sourced products
- **Mid 20th Century** — Antibiotics
  Globalization of scientific discoveries
  Current good manufacturing practices (cGMPs)
- **Late 20th Century** — Proliferation of blockbuster small molecule drugs
  Emergence of the biotechnology industry
  Beginning of the generic revolution and competition as the stimulus to innovation
  Globalization of manufacturing
  International naming conventions established
  Genome Project (“Big Data”)
- **Early 21st Century** — Patent cliff in the highly regulated markets
  Biotech becoming mainstream
  Multiple special regulatory programs in the highly regulated markets including biosimilars
  Quality is paramount
  Globalization in demands for access

1952 DNA decoded

1975 mAbs

Biologics Vary in Complexity – Even Recombinant Ones

AND MANY ARE COMPLEX MIXTURES THAT VARY BATCH-TO-BATCH AND OVER TIME



A Aspirin, 21 Atoms
B ACE-Inhibitor Ramipril, 62 Atoms
C Insulin, ca. 790 Atoms
D Monoclonal Antibody, ca. 20000 Atoms

"Soup"
(Not drawn to Scale)

Once approved, complexity is no longer a relevant argument

Derived from a slide presented by Brockmeyer Biopharma GmbH Source: VFA 2010

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Working Definitions for Biologics

US HAS THREE OPTIONS - BIOLOGIC, BIOSIMILAR, INTERCHANGEABLE BIOLOGIC;
MOST PLACES HAVE TWO OPTIONS - BIOLOGIC, BIOSIMILAR

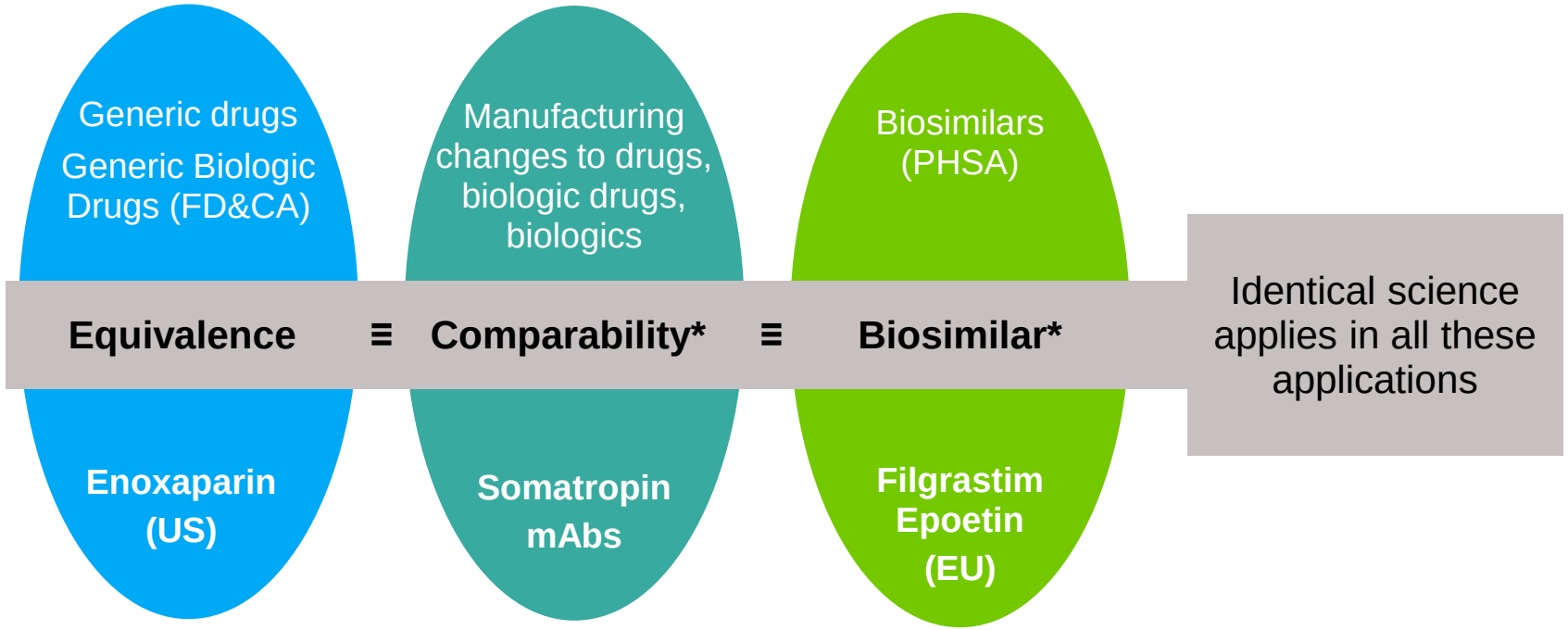
Biologic: Worldwide, a simple and practical definition of a biologic is a product the active ingredient of which is made in a living system

Biosimilar: A biological product that is approved based on a showing that it is highly similar to an already approved biological product, and has no clinically meaningful differences in terms of safety and effectiveness from the reference product

Interchangeable Biologic: FDA designation that switching patients between such products can be made by a pharmacist

In many ways, Biosimilars are to Biologics, as Generics are to Drugs

Consistent Quality for All Biologics is Essential Irrespective of Terminology or Country

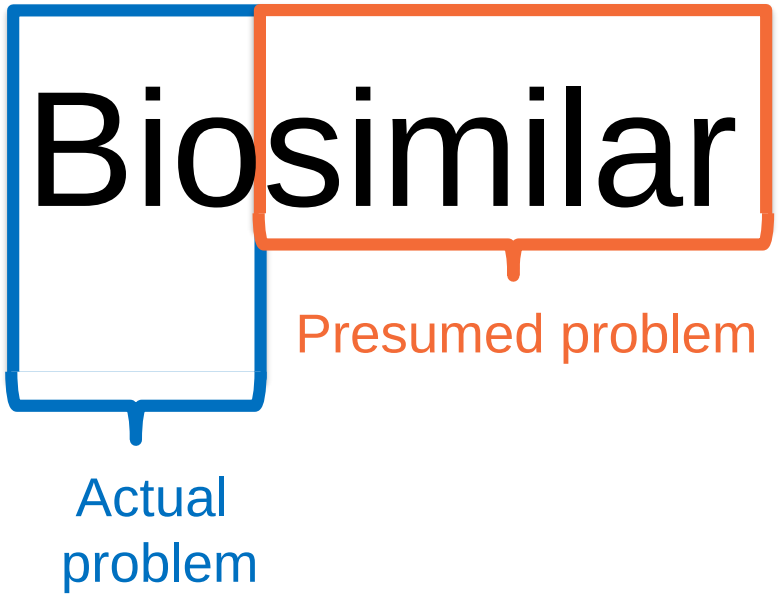


Semantics do not change the underlying regulatory science. Analytical match is distinct from quality. Latter is foundational for ALL medicines in ALL leading markets (CGMP)

***** ICH Q5E Guideline for manufacturing changes defined as “highly similar quality attributes”, BPCIA standard is “highly similar”

The Name Does Not Change the Product in the Tube

SCIENTIFIC AND REGULATORY PRINCIPLES ARE ESTABLISHED FOR ALL BIOLOGICS



Solved by Comparability[1] in 1996, which established the "highly similar" analytical standard as a way to define a biologic

Created through discussions with Ken Williams, Avalere

1. Demonstration of Comparability of Human Biological Products, Including Therapeutic Biotechnology-derived Products April 1996 here

Biosimilars are *ALWAYS* Biologics

LAWS IN DIFFERENT JURISDICTIONS GOVERN REGULATORY AUTHORITIES, HOWEVER **THE SCIENCE IS THE SAME WORLDWIDE**

Economic drivers and the success of biotech were a major reason that biosimilars became the subject of such international attention

- The regulatory science for biologics is well established – often led by FDA
- Regulatory authorities interpret the laws that govern their jurisdiction and these vary considerably:
  - Biosimilars were enabled by the revision to EU overall pharmaceutical laws in 2003
  - WHO issued Guidelines in 2009
  - US modified PHS Act in 2010
  - Canada used a guideline approach (no statutory change)
- Single payer health care systems, expiration of patents and a slightly shorter exclusivity period in Europe also helped biosimilars efforts in those countries to occur sooner

Originator biologics are made and the same product launched in multiple jurisdictions – can the same apply for a biosimilar with or without additional clinical studies?

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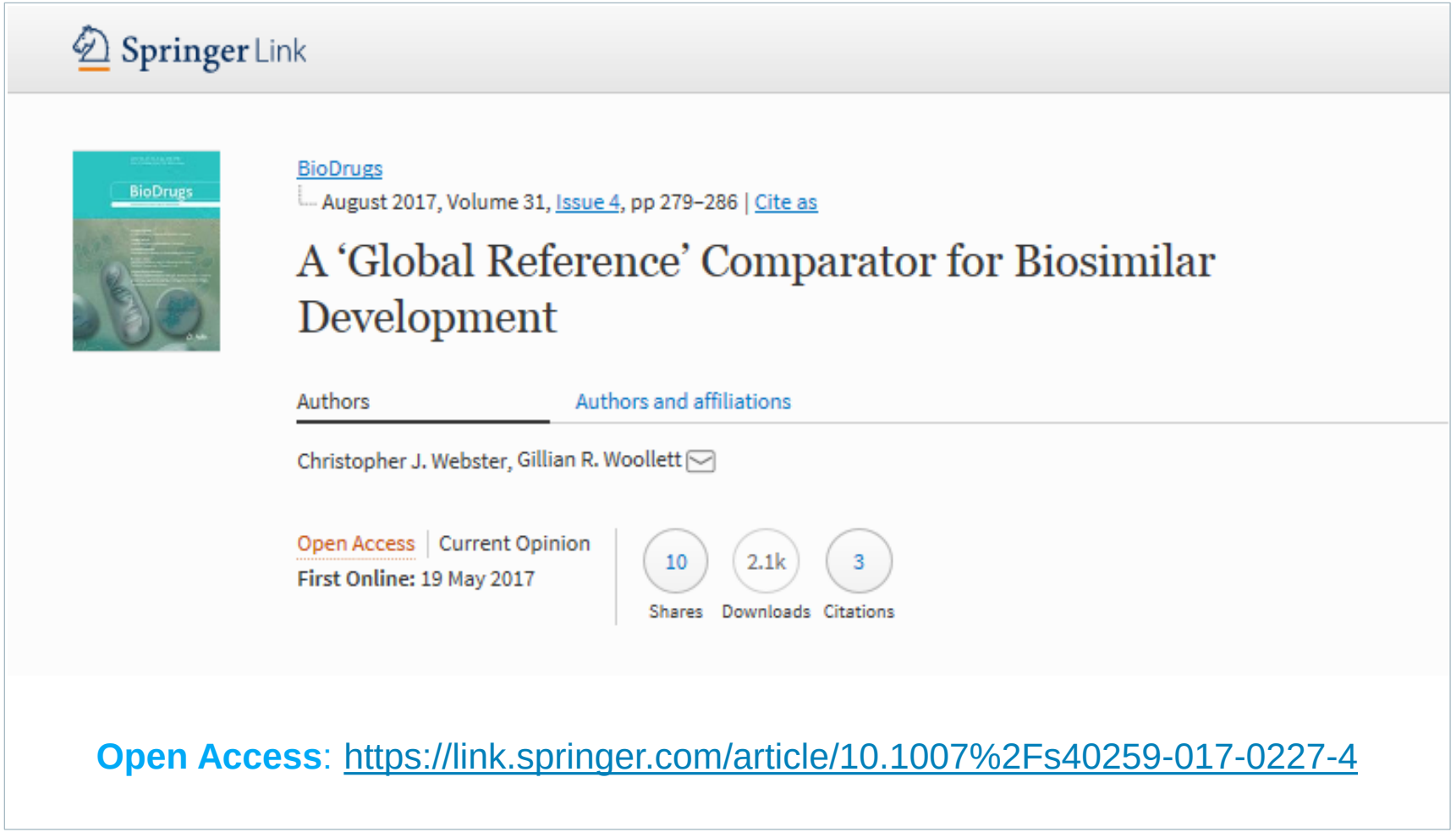
Global Development for Biosimilars is Appropriate – Key to Access and Efficiency



SpringerLink

BioDrugs

August 2017, Volume 31, Issue 4, pp 279–286 | Cite as

A 'Global Reference' Comparator for Biosimilar Development

Authors | Authors and affiliations

Christopher J. Webster, Gillian R. Woollett

Open Access | Current Opinion

First Online: 19 May 2017

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Open Access: https://link.springer.com/article/10.1007%2Fs40259-017-0227-4

If the Reference is the Same Worldwide then Oughtn't the Biosimilar to be Able to Be Too?

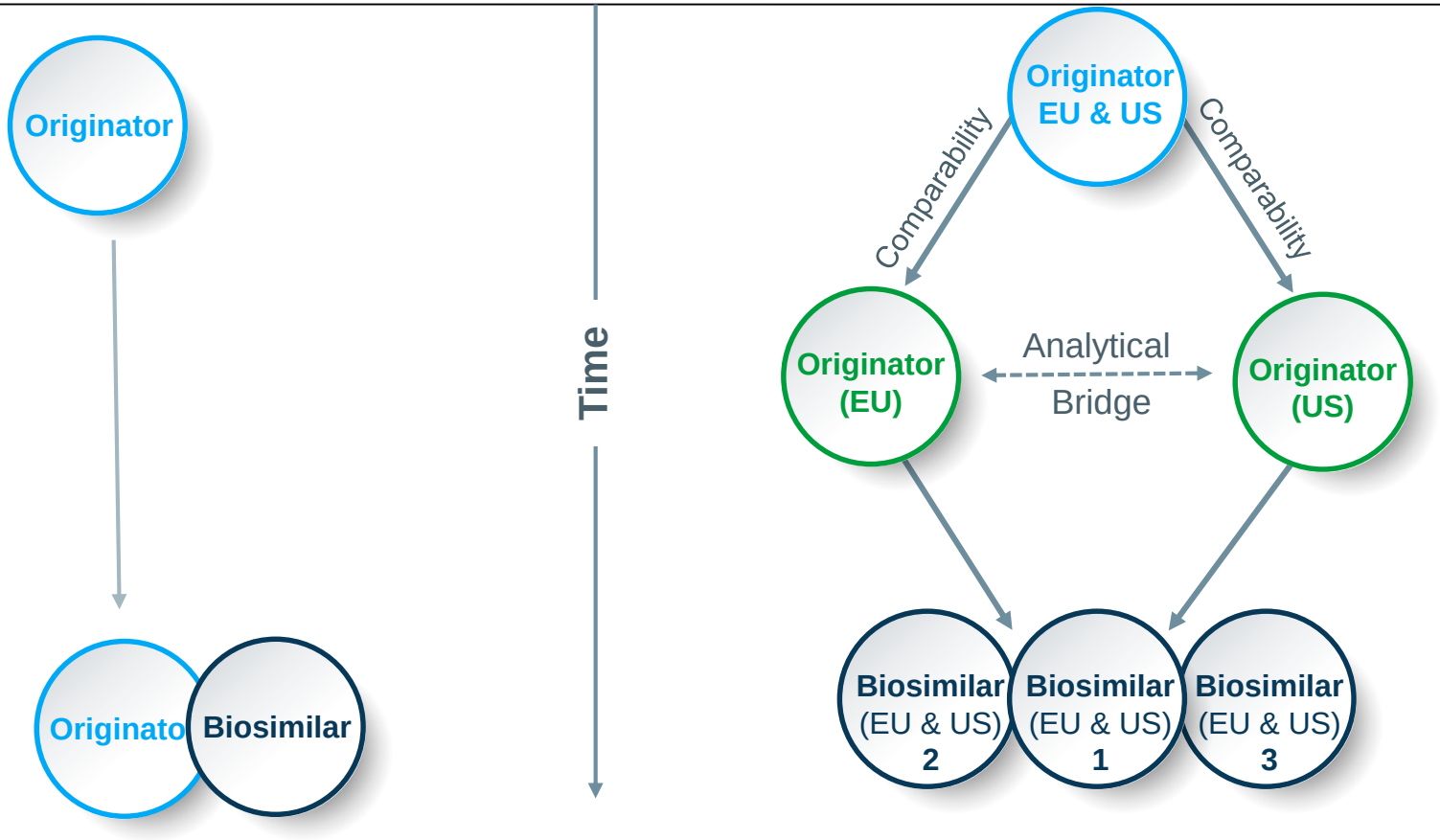
GOAL: MINIMIZE EXCESSIVE REPETITIVE STUDIES THAT PROVIDE NO NEW DATA

Biologic	Trade name	Sponsor	Countries in which 1st approvals were based on the same studies	Studies submitted for 1st approvals in > 1 country	Indications studied
Infliximab	Remicade	Janssen	US, EU, Canada, Australia	T16, T21	Crohn's disease
Etanercept	Enbrel	Amgen	US, EU, Canada, Australia	16.009, 16.014	Rheumatoid arthritis
Adalimumab	Humira	AbbVie	US, EU, Canada, Australia	DE009, DE011, DE019, DE031	Rheumatoid arthritis
Pegfilgrastim	Neulasta	Amgen	US, EU, Canada, Australia	980226, 990749	Febrile neutropenia in treatment of non-myeloid cancers
Bevacizumab	Avastin	Genentech/ Roche	US, EU, Canada, Australia	AVF2107g, AVF0780g	Metastatic colon cancer
Ranibizumab	Lucentis	Genentech	US, EU, Canada, Australia	FVF2598g, FVF2587g, FVF3192g	Age-related macular degeneration

*This is not necessarily a comprehensive list of the countries in which these studies were submitted for licensure of the product

Same Registration Studies = Same Clinical Trials Material = Same Approved Product

Scientifically these Scenarios are the Same



Either one believes in the clinical relevance of analytical similarity or one doesn't – can't use the principle selectively

... And a bridge for one confirms a bridge for all

Manufacturing Changes are Common – Subject to Review in Each Market and Each Biologic becomes “Biosimilar” to Itself

A PRODUCT THAT IS “HIGHLY SIMILAR” HAS THE “SAME” ACTIVE INGREDIENT, AND THE CLINICAL OUTCOME IS EXPECTED TO BE THE “SAME” (see ICH Q5E)

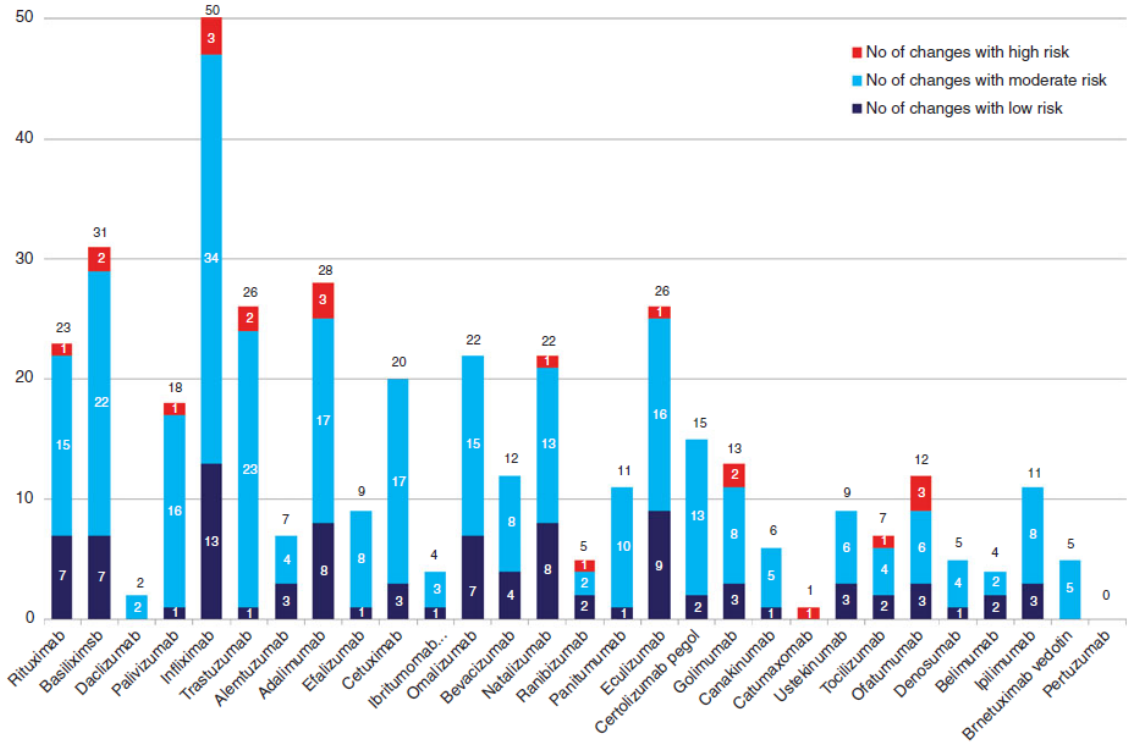


Figure 2. Number of manufacturing changes for monoclonal antibodies in their European Public Assessment Reports according to risk category (during the search period all non-proprietary names relate only to the trade named medicines listed in Table 1).

Each manufacturing change is approved by the regulators in that jurisdiction:

- Complete **extrapolation** between all indications
- **Interchangeability**
- The patient/HCP is not informed of the change because **the label on the product does not change** - the nonproprietary name stays the same when high similarity is established

THE GOOD NEWS: Extensive experience with the reference products among all stakeholders, including regulators, physicians and patients

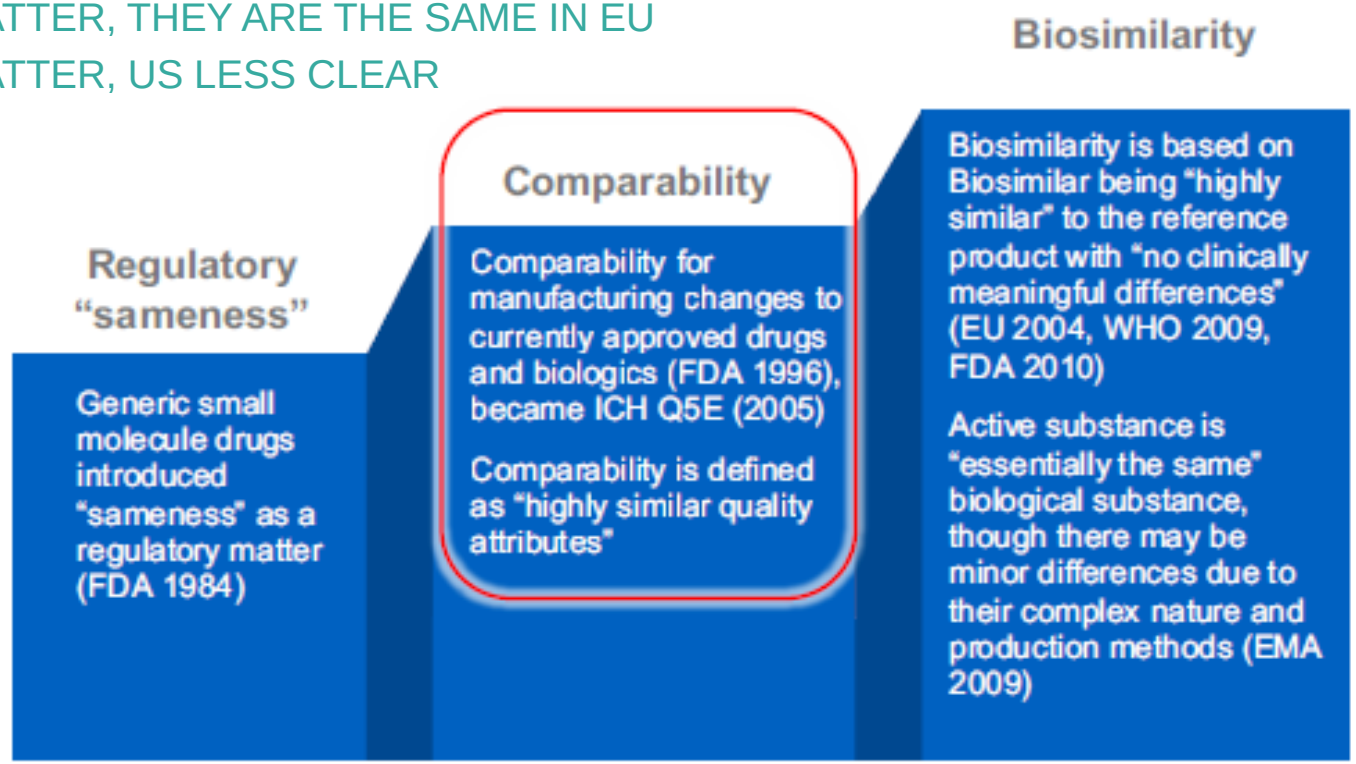
Vezér et al(2016): Authorized manufacturing changes for therapeutic monoclonal antibodies (mAbs) in European Public Assessment Report (EPAR) documents, Current Medical Research and Opinion, DOI: 10.1185/03007995.2016.1145579, available at: http://dx.doi.org/10.1185/03007995.2016.1145579

Comparability and Biosimilarity both Require High Similarity

AS A SCIENTIFIC MATTER, COMPARABILITY AND BIOSIMILARITY ARE THE SAME

AS A REGULATORY MATTER, THEY ARE THE SAME IN EU

AS A REGULATORY MATTER, US LESS CLEAR



Consistency in the application of regulatory science is increasingly important, and core to regulators credibility and consumers trust

McCamish Woollett (2017) "Molecular "Sameness" is the Key Guiding Principle for Extrapolation to Multiple Indications", CPT http://onlinelibrary.wiley.com/wol1/doi/10.1002/cpt.616/full

McCamish & Woollett (2013) The Continuum of Comparability Extends to Biosimilarity CPT http://www.nature.com/doifinder/10.1038/clpt.2013.17

A Proposal to Expedite Biosimilar Development Worldwide[1]

USE OF A 'GLOBAL REFERENCE' COMPARATOR FOR BIOSIMILAR DEVELOPMENT

Based upon the shared development history **a single reference version of the originator biologic may be selected for global biosimilar development** if the following criteria are met:

- The chosen reference has been approved in an ICH compliant jurisdiction (assures comparability);
- The formulation of the chosen reference has the same pharmaceutical form, route of administration, content of active pharmaceutical ingredient (API);
- There is substantial evidence in the public domain that the chosen reference and the local reference product have been approved in their respective jurisdictions on the basis of essentially the same original data.

Supports harmonization of regulations as well as consistency in adoption of same science worldwide – both enhance trust in regulators and biopharma, and are pro-competition

1 Christopher J. Webster, Gillian R. Woollett (2017) ***A 'Global Reference' Comparator for Biosimilar Development*** BioDrugs here

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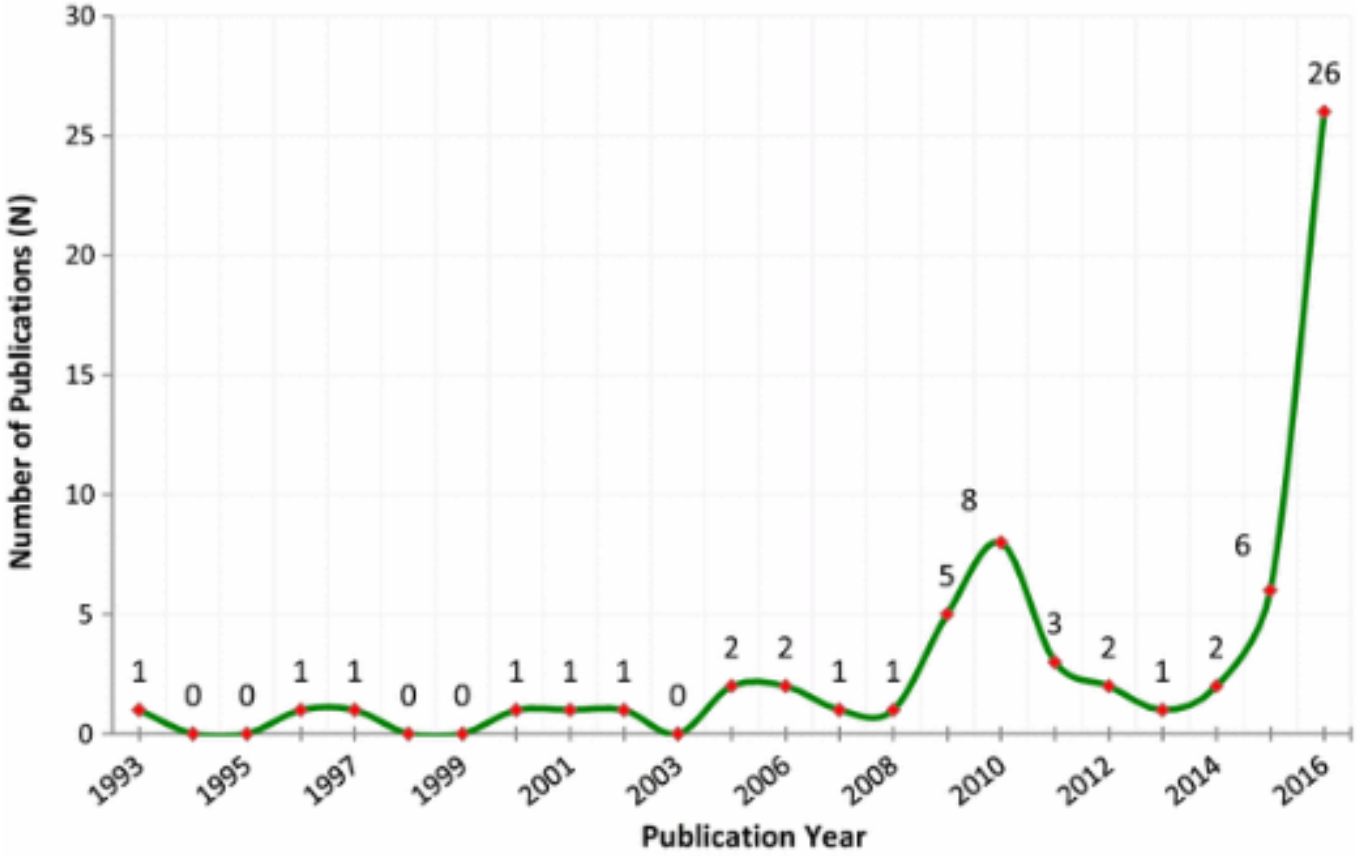
- Clarifying Questions

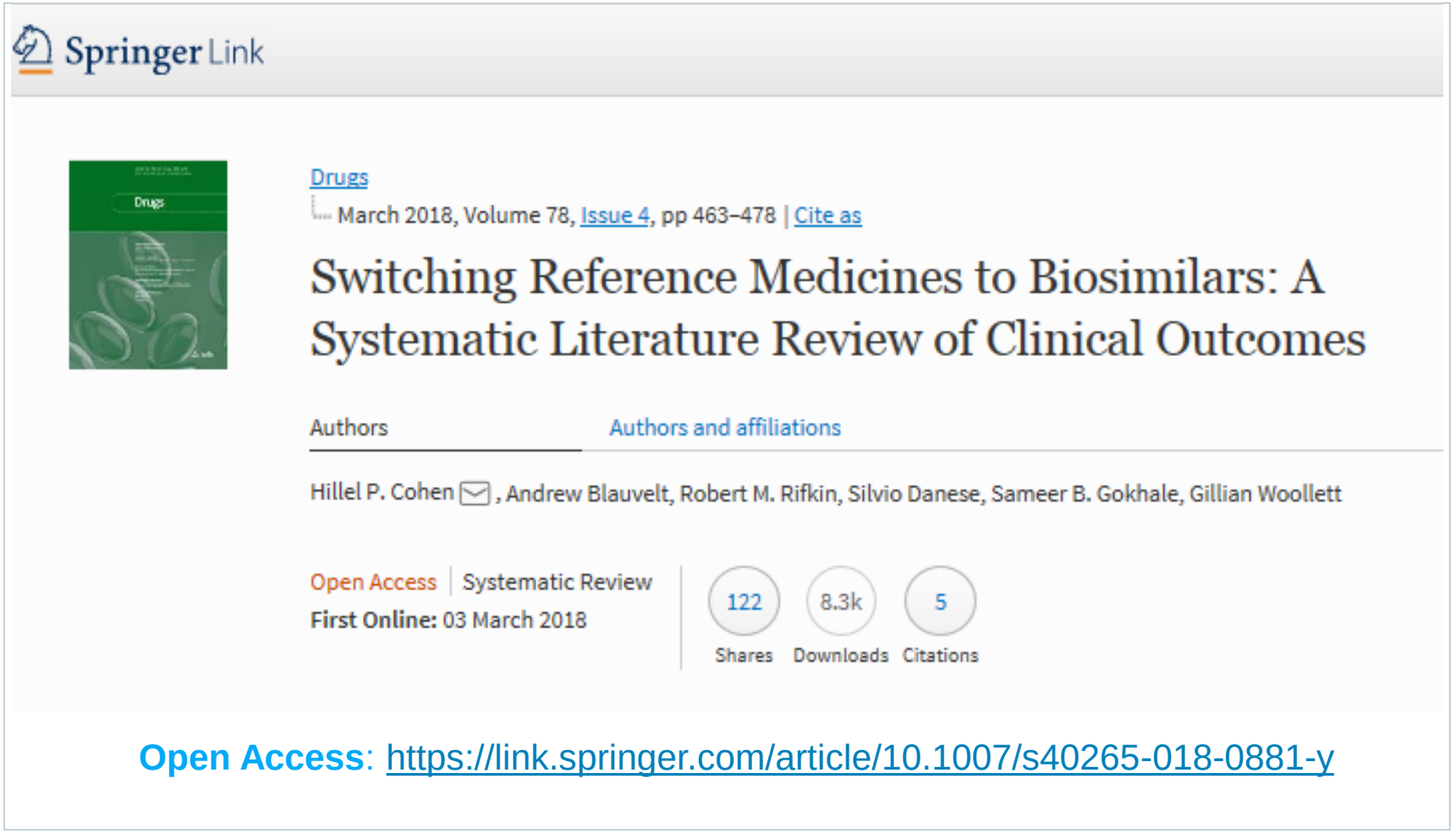
Biosimilars Have Increased the Interest in Switching

SWITCHING BETWEEN BIOLOGICS IS COMMON, COMPARABILITY THE NORM



Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes
https://link.springer.com/article/10.1007/s40265-018-0881-y

Peer Reviewed Reference Paper



Open Access: https://link.springer.com/article/10.1007/s40265-018-0881-y

Why would there be a problem with switching?

BIOSIMILARS SHOULD NO MORE BE EXPECTED TO CAUSE PROBLEMS WHEN A PATIENT IS SWITCHED THAN DO COMPARABLE ORIGINATORS

To confirm this we undertook a systematic literature review:

- Scientific literature (1993 up to 30 June 2017) was reviewed to identify publications that contained primary data on single or multiple switching from reference biological medicines to biosimilars
- A total of **90 studies** were identified involving **seven molecular entities** that treated **14 disease indications**, and **enrolled a total of 14,225 individuals**
- The great majority of studies did not report differences in safety, efficacy, or immunogenicity after a single switch event compared to patients that were not switched. Only a small number (three) of multiple switch studies have been published to date, but likewise no differences were detected

The results suggest a low risk of either a safety concern or a loss of efficacy after switching to a biosimilar. The risk is hypothetical

Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes
https://link.springer.com/article/10.1007/s40265-018-0881-y

Interchangeability – Unique to US Law

Dr. Leah Christl for FDA, said[1] that **FDA agrees with the European regulators' conclusion that biosimilars are interchangeable with their reference[2] for the purpose of physician prescribing.**

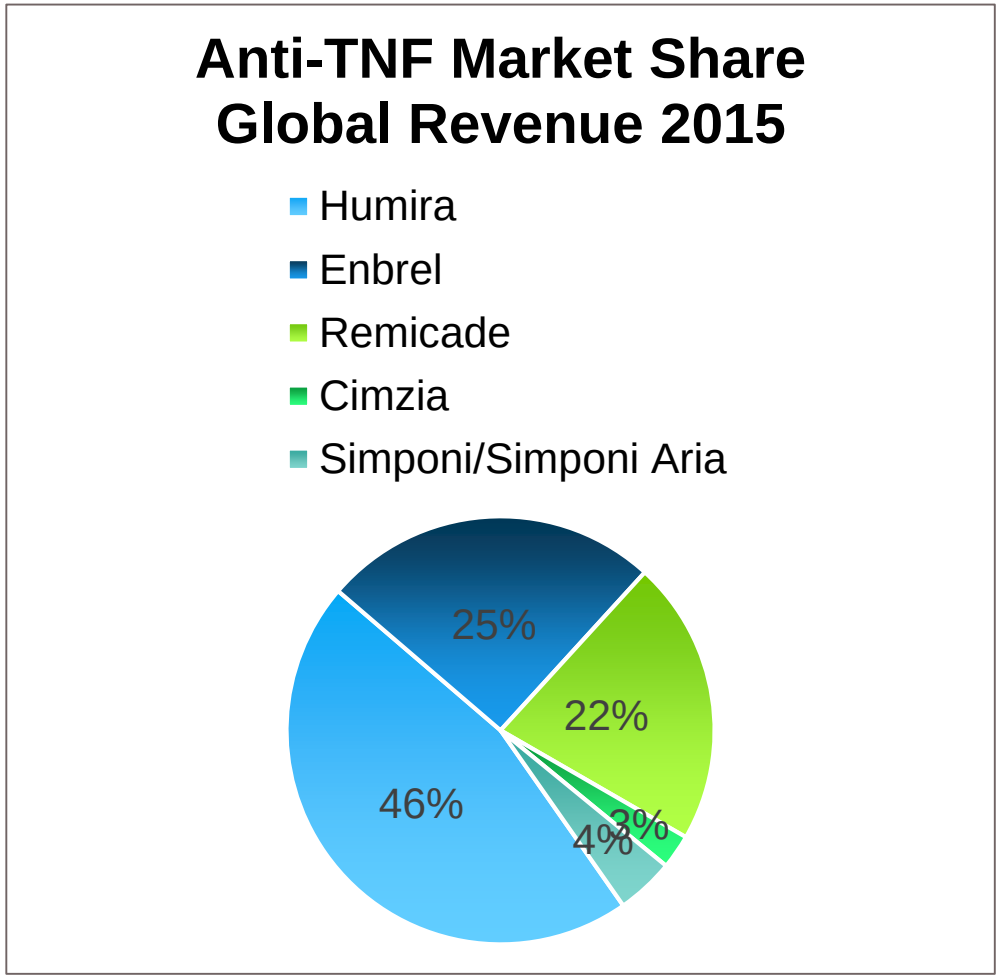
However, she then explained in some detail that interchangeability in the US is a designation **solely for the purposes of substitution by other than the prescriber**. And for such pharmacist substitution the law was clear that an additional designation from FDA was available.

This FDA designation will confirm there being no basis for switching being a safety or efficacy concern. Data showing a problem with switching does not exist[3]

Semantics matter. Nonetheless science-based regulatory consistency is essential to the future potential for harmonization. FDA articulation of principles is key

1 Medicines for Europe, 16th Biosimilars Mtg, London 26-27 April 2018
2 Pekka Kurki et al, *Interchangeability of Biosimilars: A European Perspective* BioDrugs, DOI 10.1007/s40259-017-0210-0
3 Hillel P. Cohen et al *Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes* Drugs. https://link.springer.com/article/10.1007/s40265-018-0881-y

Switching Patients Matters because it Determines the Initial Market for a Biosimilar



Total $30.4 Billion (US $19.5 Billion)

For example: Biosimilars to Remicade®(infliximab)

Initial Global market may be:

- Naïve patients who would otherwise get Remicade®
- All Remicade® market, including established as well as naïve patients = $6.56 Billion
- Entire anti-TNF market (depending on indication) = $30.4 Billion

http://files.shareholder.com/downloads/JNJ/1712315802x0xS200406%2D16%2D71/200406/filing.pdf
http://investors.amgen.com/phoenix.zhtml?c=61656&p=irol-SECText&TEXT=aHR0cDovL2FwaS50ZW5rd2l6YXJkLmNvbS9maWxpbmcueG1sP2lwYWdlPTEwNzQyNzc0JkRTRVE9MCZTRVE9MCZTUURFU0M9U0VDVElPTl9FTlRJUkUmc3Vic2lkPTU3
http://www.abbvieinvestor.com/phoenix.zhtml?c=251551&p=irol-sec#14218269

So Should All Biosimilars be Substitutable (Interchangeable)?

AS A SCIENTIFIC AND CLINICAL MATTER THEY ARE ALREADY COMPARABLE

HOWEVER, as a legal matter, all regulatory authorities are subject to the law of their jurisdiction

NONETHELESS:

- In the US, a biosimilar must be to a single 351(a) originator “standalone” biologic already licensed by FDA – our Proposal answers this with already public information (no “Takings”)
- Analytical comparisons are already accepted cross jurisdictionally; the primary variation has been created by the originator over its own lifetime
- Additional clinical studies lack scientific validity, and therefore ethical validity[1]

Note: Where a biosimilar has already been approved cross-jurisdictionally the bridge has been rebuilt – confirms the validity of our proposal

Local law(s) grant authority to the regulators and will always trump science; but regulators can use their authorities appropriately and courts will usually defer to science

1. Christopher J. Webster, Gillian R. Woollett (2018) Comment here on ***The End of Phase 3 Clinical Trials in Biosimilars Development?*** by Xavier Frapaise here;

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So where is FDA with respect to Biosimilars?

12 BIOSIMILARS APPROVED IN THE US, 4-6 LAUNCHED[1]

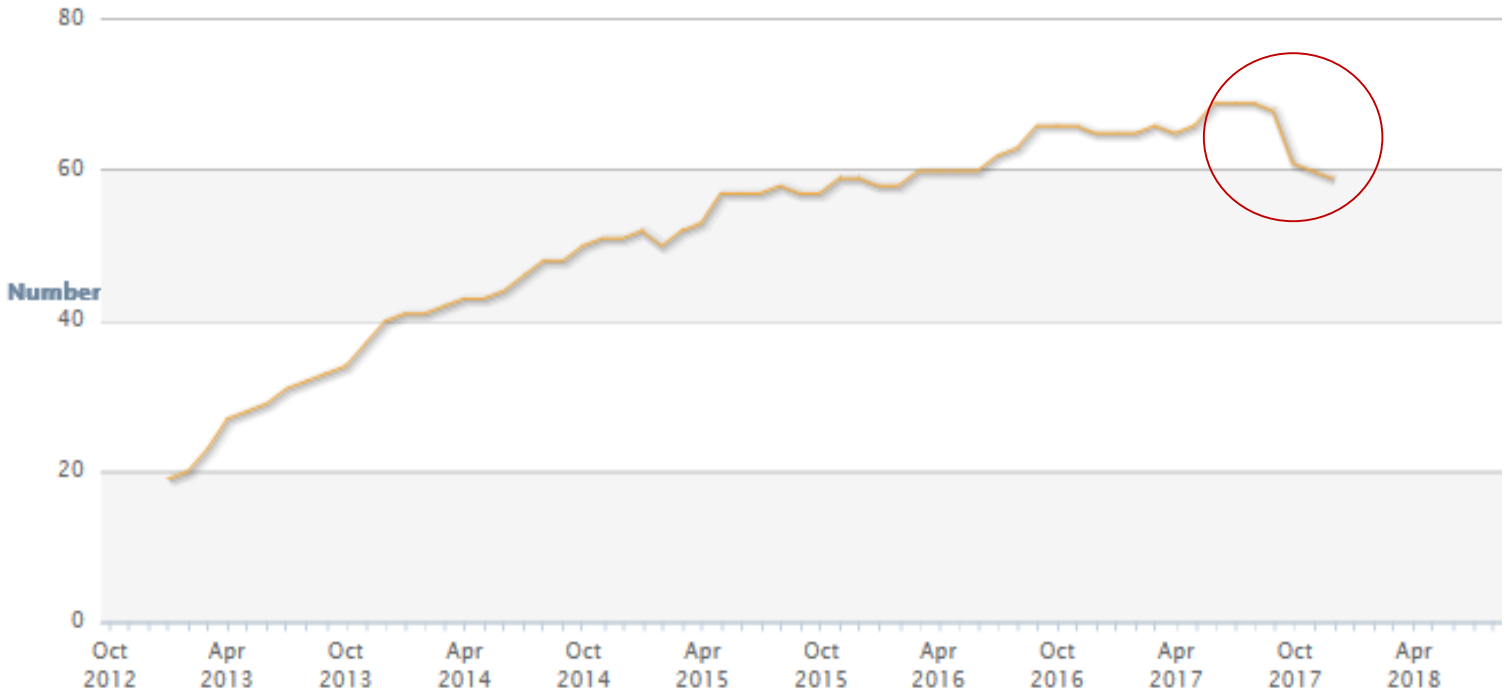
- While FDA approval is far from trivial, it is now perceived as do-able
- An FDA designation of interchangeability, such that other than the prescriber can substitute the biosimilar for its reference, has yet to occur. But it is only relevant to non-physician administered biologics of which there are few
- FDA issued their Biosimilar Action Plan and held Part 15 Hearing (4Sep18)
- EU experience, and that of other highly regulated markets, continues to be positive – no unusual or unexpected adverse events and significant savings
- Emerging markets getting involved as both sponsors and consumers, WHO aspiring to "prequalify" oncology biosimilars, as well as insulins
- FDA Commissioner Gottlieb is engaged on biosimilars[3], and they are now part of the larger competitive, access and drug pricing debate[4]

FDA alone cannot make biosimilars "work" in the US, but can help a lot by only asking for data that is necessary, and countering misinformation

1. By way of comparison EU has 46 positive opinions (as of 4Apr18)
2. Healthy Innovation, Safer Families: FDA's 2018 Strategic Policy Roadmap, Announcement 11Jan18 (here), FDA's 2018 Strategic Policy Roadmap (here)
3. *Capturing the Benefits of Competition for Patients* here 7Mar18, *Advancing Patient Care Through Competition* here 19Apr18, *Keynote Address by Commissioner Gottlieb to the 2018 FDLI Annual Conference* here 3May18
4. HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs here 16May18

Cumulative number of biosimilar development programs at FDA

12 BIOSIMILARS APPROVALS; 4 LAUNCHED; NO INTERCHANGEABLES YET



FDA will be aware of trimming of sponsor biosimilar pipelines once candidates are in the BPD Program, as they are occurring

1 https://www.accessdata.fda.gov/scripts/fdatrack/view/track.cfm?program=cder&status=public&id=CDER-RRDS-Number-of-biosimilar-dev-programs-in-BPD-Program&fy=All

Opportunity 1 – Use Data Cross Jurisdictionally

ALL CLINICAL STUDIES ARE A TAX ON PATIENTS & MUST ADD VALUE

- Clinical studies that are unnecessary are ALWAYS unethical[1]
- Global reference is appropriate where originator approval used same studies[2]

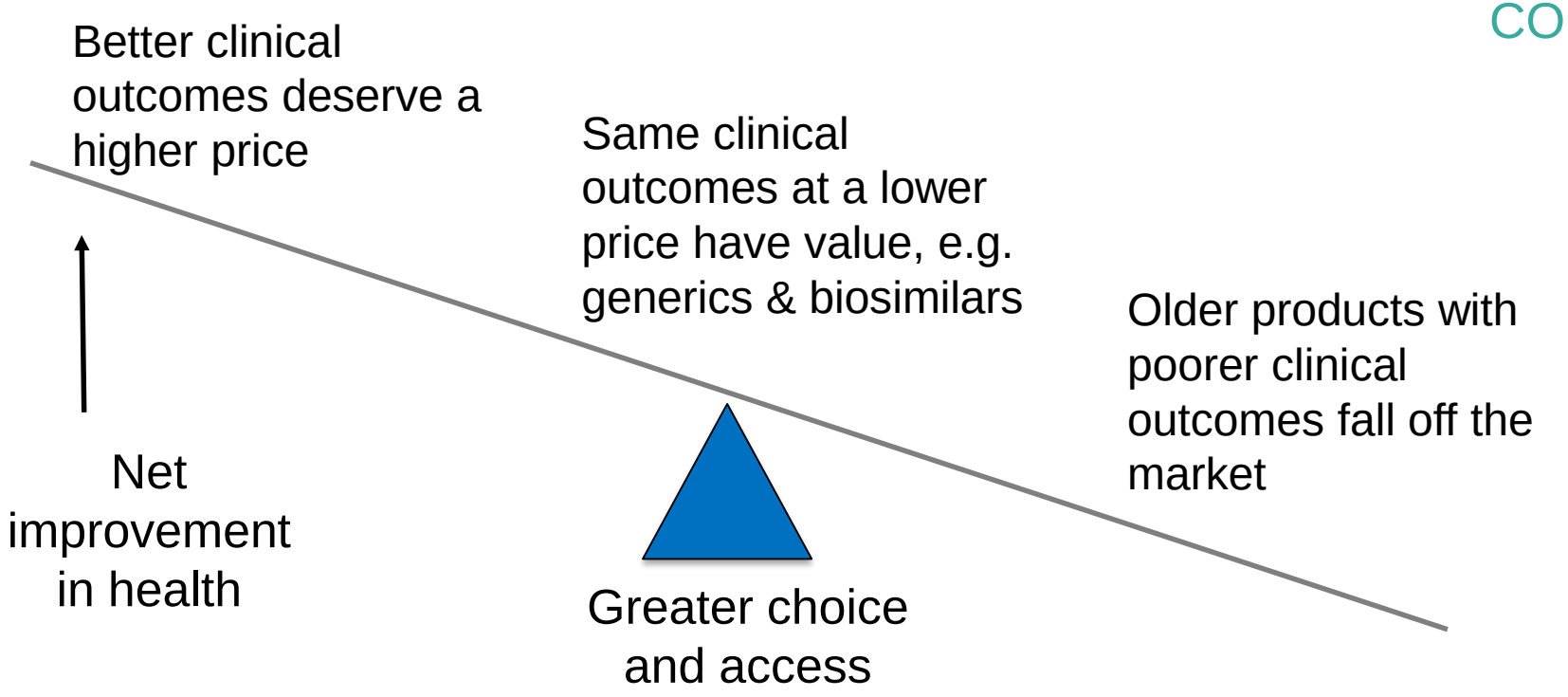
- Harmonization will allow better bigger data set to be achieved more quickly and can supersede local studies Initiatives are already underway, e.g. DQSA (US), 2-D barcodes (EU)[3]
- Pre-agree data cutoffs after which Post Market Surveillance studies can be discontinued reduce costs
- Real World Evidence works everywhere

Studies that provide data upon which actions can be taken in multiple jurisdictions promotes public health – Global reference is achievable TODAY

1. Christopher J. Webster, Gillian R. Woollett (2018) Comment http://link.springer.com/article/10.1007/s40259-018-0297-y on "The End of Phase 3 Clinical Trials in Biosimilars Development?" by Xavier Frapaise https://doi.org/10.1007/s40259-018-0287-0
2. WHO Prequalification presupposes a cross-jurisdictional reference product
3. Pharmacovigilance of Biologics in a Multisource Environment, J Manag Care Spec Pharm. 2017;23(12):1249-5, http://www.jmcp.org/doi/pdf/10.18553/jmcp.2017.23.12.1249

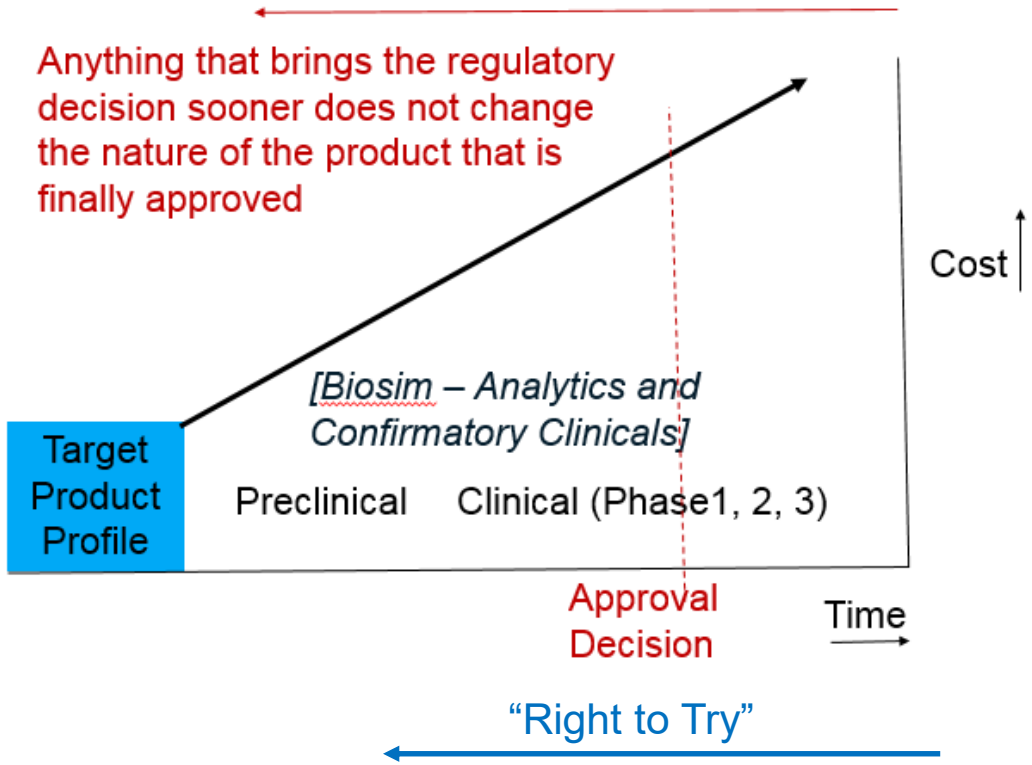
OPPORTUNITY 2 – Payer/ Provider Recognition of Value

VALUE IS A COMBINATION OF CLINICAL OUTCOME AND PRICE CAN VARY BETWEEN COUNTRIES



Foster appropriately coordinated FDA and CMS decision making that can accommodate biosimilars/generics and help attribute value to new products

OPPORTUNITY 3 - Right-Sizing Development for ALL Biologics



All regulatory requests can be hypothesis driven and the data actionable:

- Reduces sponsors need to generate meaningless data, and drain on FDA to review it
- Global data can contribute, including post approval date (aka RWE)
- Harmonization can help concurrent approvals around the world

Support scientifically-meaningful studies, appropriately the minimum necessary for regulatory decision-making; more timely and enables greater competition

Biosimilars Represent a New Development Model

	Estimated Initial Development Costs	Driver of Sales	Value for Prescribers and their Patients
Brand Biologic	$1.4 Billion	Brand Biologic ~~interchangeable~~ **Detailing**	**Brand:** Innovative new medicines, premium prices (high margin) Initial LOW volume
Biosimilar	<$500 Million		**Biosimilars:** Cost to patients will depend on development cost for market access and payor uptake (market share)
Generic Drug	$1-5 Million	Generic Drug Interchangeable **Low Price**	**Generic:** Established products at lower prices (low margin) Initial HIGH volume

Development costs determined by the extent of the studies FDA agrees are needed for approval AND those needed for provider/ patient acceptance

FDA: US Food and Drug Administration

Consumer Confidence in All Medicines Depends on Regulatory Consistency Based on Sound Science

GLOBAL DEVELOPMENT OF ORIGINATOR BIOLOGICS IS AN ACCEPTED NORM

- Both access and affordability of medicines depend on efficient development to accepted clinical standards and norms (e.g. Declaration of Helsinki, ICH[1], IPRF[2])
- High standards can seem unaffordable, but lesser standards unacceptable so leveraging data cross-jurisdictionally is increasingly essential – already the norm for originator medicines and generics
- The highly regulated markets traditionally get the earliest access, but there is increasing intolerance to delayed access for other jurisdictions, especially to biosimilars
- New mechanisms are being sought to facilitate access by minimizing unnecessary repetition of already unnecessary studies, especially clinicals (e.g. WHO Prequalification of Vaccines, and Biosimilars), and regulatory hurdles (e.g. Inspections)

Trust is critical – an essential topic for the discussion. Recent political events highlight reputational risk

1. International Committee for Harmonization http://www.ich.org/home.htm
2. International Pharmaceutical Regulators Forum https://www.i-p-r-f.org/index.php/en/iprf-network/mandate/l

Recap: Biosimilar may mean similar and not the same, but also competition and access to the same clinical outcomes at a lower price

COPIES ARE NOT INHERENTLY BAD…

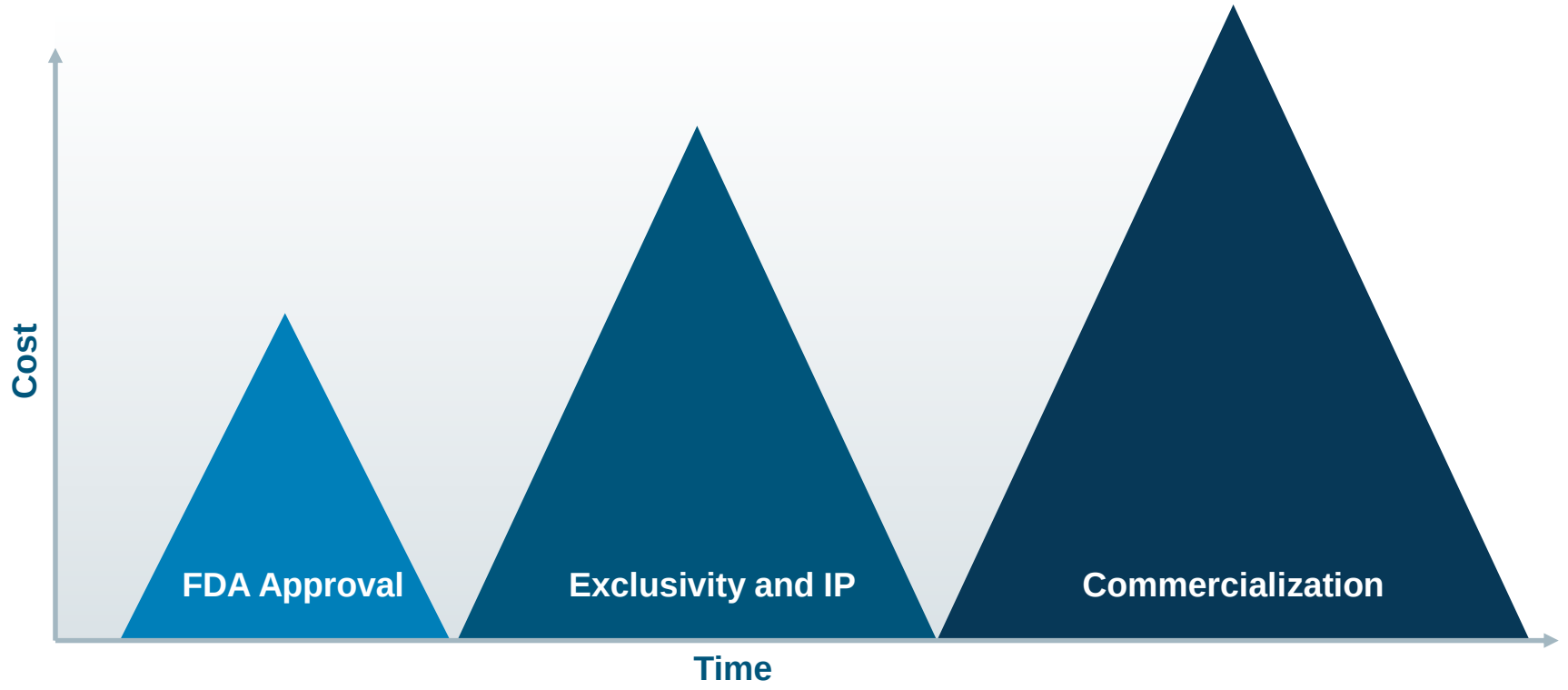
For ALL medicines it is always a matter of trust…

And I would take her kidney or bone marrow or blood any time as fully interchangeable AND substitutable…

The Mountainous Challenges for Biosimilars in the US

FDA approval is the first of a series of challenges

USA 12 approvals 4+ (unclear) 4 launches



Something must change for a sustainable multisource specialty market to emerge in the US

References – so many words, too little action...

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2. Mark McCamish, Gillian Woollett (2013) ***The Continuum of Comparability Extends to Biosimilarity: How Much is Enough and What Clinical data are Necessary?*** CPT here
3. Mark McCamish, John Pakulski, Carlos Sattler, Gillian Woollett (2015) ***Toward Interchangeable Biologics*** CPT here
4. Mark McCamish, Gillian Woollett (2017) ***Molecular "Sameness" is the Key Guiding Principle for Extrapolation to Multiple Indications***, CPT here
5. Christopher J. Webster, Gillian R. Woollett (2017) ***A 'Global Reference' Comparator for Biosimilar Development*** BioDrugs here
6. Sreedhar Sagi, Hillel Cohen, Gillian Woollett (2017) ***Pharmacovigilance of Biologics in a Multisource Environment*** JManag CareSpecPharm here
7. Hillel P. Cohen, Andrew Blauvelt, Robert M. Rifkin, Silvio Danese, Sameer B. Gokhale, Gillian Woollett (2018) ***Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes*** **D**rug here
8. Christopher J. Webster, Gillian R. Woollett (2018) Comment here on ***The End of Phase 3 Clinical Trials in Biosimilars Development?*** by Xavier Frapaise here

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