THE EVOLUTION OF BIOSIMILAR MARKETS:

Key elements for long-term sustainability of the healthcare ecosystem

ISPOR 2022 Global HEOR Conference

Forum brought to you by the ISPOR Special Interest Group on Biosimilars

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<table>
<thead>
<tr>
<th>Name</th>
<th>Title and Affiliation</th>
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<tbody>
<tr>
<td>Cate Lockhart</td>
<td>PharmD, PhD, Executive Director, BBCIC</td>
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<td>Murray Aitken</td>
<td>MBA, Executive Director, IQVIA Institute for Human Data Science</td>
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<td>Jackie Vanderpuye-Orgle</td>
<td>PhD, Vice President. Advanced Analytics, HEOR and RWE, Parexel International (US)</td>
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<td>MA, Vice President of Advocacy and Access, Arthritis Foundation</td>
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<td>Teresa Barcina</td>
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Conflicts of Interest Statements

- **Cate Lockhart**, PharmD, PhD. Executive Director at Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)
  
  No conflicts of interest to disclose

- **Murray Aitken**, MBA. Executive Director at IQVIA Institute for Human Data Science
  
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- **Jackie Vanderpuye-Orgle**, PhD. Vice President, HEOR and RWE at Parexel International (US)
  
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- **Anna Hyde**, MA. Vice President of Advocacy and Access at Arthritis Foundation
  
  No conflicts of interest to disclose

- **Teresa Barcina**, PharmD. PhD researcher at the Faculty of Pharmaceutical Sciences in KU Leuven (MABEL Fund)
  
  No conflicts of interest to disclose
AIM OF TODAY’S FORUM

- Share insights on the role biosimilar medicines play in supporting the long-term sustainability of the healthcare ecosystem
- Reflect on learnings extracted from the use of biosimilars in the U.S.
- Identify elements that may undermine the sustainability of off-patent biologic/biosimilar markets
- Provide a multistakeholder perspective on elements necessary to ensure sustainable markets
AGENDA

- U.S. Perspective (Lockhart)
- IQVIA Sustainability Framework (Aitken)
- Multistakeholder Objectives (Vanderpuye-Orgle)
- Patient Advocate’s Perspective (Hyde)
It’s Time for a Poll!

What is your work environment? Please select:

a) Industry
b) Regulatory agency/HTA agency
c) Clinical practice/hospital/managed care/pharmacy management
d) Academia
e) Other
Cate Lockhart

U.S. Perspective
Who are the stakeholders for biosimilars in the United States?

- Payers
- Prescribers
- Health Systems
- Manufacturers
- Other Healthcare Providers
- Regulators
- Patients
U.S. PERSPECTIVE – TRASTUZUMAB SUCCESS

PERCENT NEW USERS PER 100k ELIGIBLE MEMBER-YEARS

2016: 98.1%
2017: 97.0%
2018: 97.3%
2019: 92.7%
2020: 59.4%

Other HER2I
Trastuzumab-anns
Trastuzumab

Note: For 2020, data up to 2/29/20 were analyzed. Data at the beginning of the year may reflect different utilization compared to the rest of the year due to coverage changes.

Adapted from Nam YH, et al. Poster presented at: AMCP Nexus 2021; October 19-21, 2021; Denver, CO.
U.S. PERSPECTIVE – ADALIMUMAB JAIL BREAK

Adalimumab Biosimilars

Adalimumab Reference
(Humira®)
U.S. PERSPECTIVE

Medical Benefit vs Pharmacy Benefit
2018 Survey

<table>
<thead>
<tr>
<th>Specialty Pharmacy</th>
<th>Managed Care / PBM</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 120)</td>
<td>(n = 180)</td>
</tr>
</tbody>
</table>

300 Surveys Collected

2020 Survey

<table>
<thead>
<tr>
<th>Specialty Pharmacy</th>
<th>Managed Care / PBM</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 24)</td>
<td>(n = 150)</td>
<td>(n = 163)</td>
</tr>
</tbody>
</table>

337 Surveys Collected

2021 Survey

<table>
<thead>
<tr>
<th>Health Plan</th>
<th>PBM</th>
<th>IDN</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 33)</td>
<td>(n = 9)</td>
<td>(n = 9)</td>
</tr>
</tbody>
</table>

51 Surveys Collected

PBM = Pharmacy Benefit Manager
IDN = Integrated Delivery Network


Hydery et al. Presented at AMCP Nexus 2021, Denver, CO.
**U.S. PERSPECTIVE**

Q. WHAT ARE THE MOST DIFFICULT BARRIERS IN BIOSIMILAR ADOPTION?

<table>
<thead>
<tr>
<th></th>
<th>Most Challenging</th>
<th>2nd</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescriber Concerns</td>
<td>16%</td>
<td>45%</td>
<td>13%</td>
</tr>
<tr>
<td>Pricing/Contracting Issues</td>
<td>22%</td>
<td>35%</td>
<td>14%</td>
</tr>
<tr>
<td>Lack of Clarity on Substitution/Interchangeability</td>
<td>17%</td>
<td>36%</td>
<td>23%</td>
</tr>
</tbody>
</table>

Q. WHAT CHALLENGES DO YOU ANTICIPATE FOR PHARMACY BENEFIT BIOSIMILARS VS MEDICAL BENEFIT?

<table>
<thead>
<tr>
<th></th>
<th>Most Challenging</th>
<th>2nd</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula Management</td>
<td>35%</td>
<td>16%</td>
<td>22%</td>
</tr>
<tr>
<td>Need Interchangeability</td>
<td>33%</td>
<td>25%</td>
<td>14%</td>
</tr>
<tr>
<td>Lack of Clarity on Substitution</td>
<td>8%</td>
<td>29%</td>
<td>24%</td>
</tr>
</tbody>
</table>

Hyder et al. Presented at AMCP Nexus 2021, Denver, CO.
Q: FOR PATIENTS WHOSE CONDITIONS ARE TREATED ON REFERENCE BIOLOGICS, SWITCHING TO A BIOSIMILAR PRODUCT IS SAFE AND EFFECTIVE

<table>
<thead>
<tr>
<th>Year</th>
<th>Strongly Agree</th>
<th>Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021 (N=51)</td>
<td>51%</td>
<td>41%</td>
</tr>
<tr>
<td>2020 (N=337)</td>
<td>47%</td>
<td>40%</td>
</tr>
<tr>
<td>2018 (N=300)</td>
<td>32%</td>
<td>52%</td>
</tr>
</tbody>
</table>

Hydery et al. Presented at AMCP Nexus 2021, Denver, CO.
### 2020 (n = 337)

**Q. WHAT STRATEGIES ARE MOST LIKELY TO OVERCOME BARRIERS TO BIOSIMILAR ADOPTION?**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Most Important</th>
<th>2nd</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescriber education on switching studies</td>
<td>39%</td>
<td>52%</td>
<td>7%</td>
</tr>
<tr>
<td>Clear FDA guidance on substitution</td>
<td>54%</td>
<td>36%</td>
<td>10%</td>
</tr>
<tr>
<td>Formulary policies for treatment-naïve patients</td>
<td>39%</td>
<td>48%</td>
<td>10%</td>
</tr>
<tr>
<td>Prescriber education on RWE</td>
<td>34%</td>
<td>52%</td>
<td>10%</td>
</tr>
</tbody>
</table>

### 2021 (n = 51)

**Q. WHAT ARE THE MOST IMPORTANT SOLUTIONS TO HELP OVERCOME BARRIERS TO ADOPTION OF PHARMACY BENEFIT BIOSIMILARS?**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Most Important</th>
<th>2nd</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>RWE - switching</td>
<td>31%</td>
<td>27%</td>
<td>20%</td>
</tr>
<tr>
<td>State laws/regs-substitution</td>
<td>35%</td>
<td>18%</td>
<td>10%</td>
</tr>
<tr>
<td>RWE - effectiveness</td>
<td>20%</td>
<td>25%</td>
<td>22%</td>
</tr>
<tr>
<td>RWE - safety</td>
<td>6%</td>
<td>5%</td>
<td>29%</td>
</tr>
</tbody>
</table>

## Q. FACTORS THAT WOULD HELP DRIVE BIOSIMILAR ADOPTION

<table>
<thead>
<tr>
<th>Factor</th>
<th>Most Important</th>
<th>2nd</th>
<th>3rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost Savings</td>
<td>65%</td>
<td>22%</td>
<td>4%</td>
</tr>
<tr>
<td>Interchangeability</td>
<td>27%</td>
<td>33%</td>
<td>8%</td>
</tr>
<tr>
<td>More Safety and Efficacy Data</td>
<td>6%</td>
<td>14%</td>
<td>18%</td>
</tr>
<tr>
<td>Prescriber Understanding</td>
<td>2%</td>
<td>18%</td>
<td>20%</td>
</tr>
<tr>
<td>Regulatory Clarity</td>
<td>10%</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Patient Understanding</td>
<td>2%</td>
<td>12%</td>
<td></td>
</tr>
</tbody>
</table>

2021 (n = 51)  
Hydery et al. Presented at AMCP Nexus 2021, Denver, CO.
Q. BIOSIMILARS HAVE PROVIDED MEANINGFUL COST SAVINGS

2021 (N=51)

- Agree Completely: 29%
- Agree Very Much: 29%
- Agree Somewhat: 35%
- Do Not Agree Much/At All: 6%

2021 (n = 51)

Hydery et al. Presented at AMCP Nexus 2021, Denver, CO.
• Interchangeability studies
• Switching studies
• HC resource utilization and cost implications
• Real-world evidence
• Models
• Clinical operations

• Clear regulatory guidance on substitution
• Formulary management
• Expanded Medicare/Medicaid policies
• Reduced cost sharing for patients
According to managed care pharmacy professionals, which of the following is NOT among the most important solutions to overcoming barriers to biosimilar adoption?

a) Real-world evidence on product switching
b) Clarity on laws and regulations regarding product substitution
c) Real-world evidence on safety and effectiveness of biosimilars
d) More clinical trials
Murray Aitken

Methodologies to Evaluate Sustainability Risks
Biosimilar sustainability improves **patient access** and **physician prescription choice** of **safe and high-quality biologic medicines**, in a framework that considers the **needs of all stakeholders** (patient, healthcare professionals / providers, and manufacturers), provides a means to **manage existing healthcare budgets** while safeguarding a **healthy level of competition** and **supply**.

Source: IQVIA Institute for Human Data Science, Advancing Biosimilar Sustainability in Europe, 2018
Criteria for the sustainable market

ACCESS TO BIOLOGICS
1. Significant increase to biologics since biosimilar entry*

REGULATORY AND PMA
2. Regulatory and PMA pathway: ensuring timely access to biosimilars following EMA approval
3. Treatment guidelines: recommending biosimilar use
4. Switching and substitution policies: at physicians’ discretion while preventing automatic pharmacy substitution

COMPETITIVE PRESSURE
5. Level of competition: high level of competition with multiple players
6. Pricing rules and dynamics: prices driven by competition only
7. Procurement: systems which support competition and drive uptake in the market

INCENTIVES
8. Patient benefits: effective benefits encouraging biosimilar use
9. Provider and prescriber benefits: effective benefits supporting biosimilar usage
10. Awareness and education: strong awareness of biosimilar benefits and sustainable practices across stakeholder groups

*Defined as >25% increase in DDD per capita
# Sustainability scorecard metric definitions

<table>
<thead>
<tr>
<th>POLICY AREA</th>
<th>METRIC</th>
<th>SUSTAINABILITY MEASURE (5: sustainable; 1: not sustainable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory environment and clinical guidelines</td>
<td>• Time from EMA approval to first biosimilars sales</td>
<td>• Biosimilar average time to first sales from EMA approval: 5: 0-5 months; 4: 5–8 months; 3: 8-11 months; 2: 11-14 months; 1: &gt;14 months</td>
</tr>
<tr>
<td></td>
<td>• Treatment guidelines for biosimilar use</td>
<td>• 5: Multiple publications and guidelines on recommended biosimilar use; 4: Some publications on recommended biosimilar use; 3: Acceptance of EMA guidelines/ no official position on biosimilars or papers to support use; 2: Against biosimilar use; 1: Strongly against biosimilar use</td>
</tr>
<tr>
<td></td>
<td>• Physician switching policies</td>
<td>• Is a switch to biosimilar allowed at physician’s discretion? 5: Yes; 3: Switching not allowed from biosimilar to biosimilar; 1: No</td>
</tr>
<tr>
<td></td>
<td>• No biologic pharmacy substitution</td>
<td>• Is biologic pharmacy substitution allowed in the retail and hospital prescription setting? 5: No; 3: With limitations/no stringent enforcement; 1: Yes</td>
</tr>
<tr>
<td>Awareness and education</td>
<td>• Comprehensive training / education for patient</td>
<td>• 5: Comprehensive training or education provided in a country, or historic acceptance; 3: in between; 1: No training or education provided in a country</td>
</tr>
<tr>
<td></td>
<td>• Comprehensive training / education for physician</td>
<td></td>
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</table>

## Purchasing mechanisms

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<table>
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<tbody>
<tr>
<td>Time from tender award to delivery</td>
<td>• 5: 4-6 months; 3: 2-4 months; 1: &lt;2 months or &gt;6 months</td>
<td></td>
</tr>
<tr>
<td>Number of winners</td>
<td>• Total number of active winners in a country: 5: Consistently award multiple winners; 3: Usually a single winner, but more would be allowed 1: Strictly single winner</td>
<td></td>
</tr>
<tr>
<td>Winner decision criteria beyond price</td>
<td>• 5: Yes, the most economically advantageous tender offers win; 3: Some, but limited; 1: None beyond price</td>
<td></td>
</tr>
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</table>
Unique footprints of markets

Source: IQVIA PMR analysis and MIDAS data Q4 2020
Notes: Analysis includes national level perspectives only. Regional breakdown is included within the appendix for 3 regions for both Italy and Spain where areas within the analysis may differ to the national picture.
Methodologies to assess sustainability risk

- Definition of biosimilar sustainability requires multi-stakeholder considerations.
- Criteria that are measurable in a combination of quantitative and qualitative assessments can be applied at a country or sub-national level to assess sustainability.
- Markets have unique characteristics and sustainability profiles that change over time.
- Sustainability risk should also be linked to measures of biosimilar penetration and concentration, pricing dynamics and patient access levels.
How applicable are the discussed sustainability elements to the U.S. market environment? Please rate (scale 1-10):
In your experience, what approaches are being pursued by policy-makers to improve the level of sustainability?
Biosimilars market sustainability and the healthcare ecosystem
“…not everyone means the same thing when they speak about ‘sustainable health care’.” [Muzyka et al. 2014]

There are various schools of thought but there are also common themes across stakeholders

### Elements of a sustainable healthcare ecosystem

**Long-term strategic perspectives and innovation**
- Keeping financial costs under control
- Enacting enabling policies with long-term perspectives
- Advancing effective therapies and improving services

**Disease prevention and health promotion**
- Emphasizing comprehensive patient-centered primary care and chronic disease management
- Fostering a satisfactory environment for healthcare workforce

**Quality**
- Defining and tracking appropriate quality standards and performance indicators
- Facilitating health equity and parity
- Investing in advancements in data infrastructure and digital solutions

**Institutionalization of social and ecological environmental concerns**
- Addressing broader socio-economic and cultural determinants of health
- Addressing environmental contributing factors
- Understanding interdependencies

**Institutional accountability and individual responsibility**
- Prioritizing transparency in decision making and driving efficiencies
- Empowering patients and enabling them to take ownership of their health
Through lower-priced therapies and more treatment options, biosimilars may result in:

- More people treated
- Earlier treatment
- Better adherence

**Drivers include**
- Safety
- Efficacy
- Effectiveness
- Reimbursement
- Stakeholder perceptions
  - Competition
  - Prices
  - Market share

**Health system sustainability**

**Competition**

**Expanded access**

**Cost savings**

**Headroom for innovation**
Estimates of the benefits of the biosimilars in the US

Potential for significant health system savings

- US cost savings of $54 bill from 2017 – 2026
- About 3% of total estimated biologic spending
- Range of $24 bill - $150 bill depending on:
  - Biosimilar price relative to reference biologic
  - Market share
- Potential savings per biologic class will depend on:
  sales, degree of competition, and timing of entry

The promise of biosimilars and the benefits to the healthcare ecosystem can only be attained if we have a thriving and sustainable biosimilars market with a level playing field

Biosimilars have the potential to positively impact healthcare systems and budgets. To realize this potential, stakeholders need to balance competition and supply chain security to foster a sustainable biosimilars market. There is significant variation in the policies for pricing, procurement, and use of biosimilars in the EU.

To establish a multistakeholder definition of biosimilar market sustainability. To further identify components of a sustainable biosimilar market. To identify drivers and risks of a sustainable biosimilar market.

A modified Delphi process
11 participants (1 patient advocate, 1 oncologist, 1 rheumatologist, 2 hospital pharmacists, 2 procurement pharmacists, 1 national payer, 2 policy advisers, 1 manufacturer)
7 European countries

Stage 1: Brainstorming
Participants contributed initial views by email and telephone, with reference to stimulus materials

Stage 2: Structured feedback on themes
Feedback on statements derived from participant responses to the brainstorming process

Stage 3: Facilitated roundtable discussion
Anonymised feedback from stage 2 collated and used during facilitated discussion
A multistakeholder definition of biosimilar market sustainability

- A sustainable biosimilar market means that ...
  "All stakeholders, including patients, benefit from appropriate and reliable access to biological therapies. Competition leads to a long-term predictable price level, without compromising quality, while delivering savings that may be reinvested."

Three key components:

- Delivers tangible and transparent benefits to the healthcare system
- Addresses the needs of all stakeholders
- Requires collaboration across stakeholders

Drivers and risks: Competition and incentives

1. Competition is more effective for achieving long-term predictable price level than regulation

2. There needs to be incentives for investment in future biosimilars

3. Governments and pricing bodies need to drive incentives
- Biosimilars have a key role in facilitating a sustainable health system both directly and indirectly.

- In principle health system sustainability is feasible but there is a lot of work that needs to be done:
  - Drive a consensus on how sustainability is defined for the different archetypes of health systems
  - Identify drivers/levers to facilitate sustainability and optimal pathways for collaboration within health systems
Efficiency of treatments will probably lead to higher costs and contribute to financial instability in the long run.

- a) True
- b) False
Anna Hyde

A patient advocate’s perspective on sustainability
Patients are a critical stakeholder in driving biosimilars uptake

- Patient perception and comfort is derived from:
  - Their health care provider
  - FDA stamp of approval
  - Peer-to-peer support and real-world evidence
What is the value proposition to the patient?

- Lower out-of-pocket costs
- Lower administrative burden

Which can benefit the entire system through

- Direct benefits such as lower drug costs overall and greater access, leading to greater medication adherence
- Indirect benefits such as greater employee presenteeism
Understanding barriers to help drive uptake

- Our data show that patients may not take a biosimilar if:
  - They do not know about them or are unfamiliar
  - Their doctor has not talked about biosimilars as a treatment option
  - They fear biosimilars will not work as well and have concerns about interchangeability
  - They may not have easy access through their formulary or the out-of-pocket cost is not significantly lower
Combining our data with what else we know is happening in the market…

**Barriers to uptake fall into four main categories:**

1. A lack of incentives to the patient
2. Communication bias or misinformation
3. Inherent fear of “the new”
4. Formulary access challenges
What are the needs moving forward?

- Education and communication that is tailored to where the patient is in their disease journey and flows through the health care provider
- Consensus around terms and phrases we use for biosimilars
- Communication around transitions that emphasizes buy-in and bottom-up feedback
- Realization of the value proposition
- Patient engagement through the drug development process
According to your experience, please rank the relevance of the following barriers to biosimilars uptake:

a) Lack of incentives to the patient
b) Communication bias or misinformation
c) Inherent fear of “the new”
d) Formulary access challenges
Thank You!
Sign up to join our Special Interest Group!

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3. Select “Special Interest Groups”
4. Click on “Biosimilars”
5. Select “Join a Special Interest Group”

Join our meeting today!
National Harbor 10-11 | 12:45 – 13:15 PM

>For more information about our group email
biosimilarsig@ISPOR.org