Advocacy in Biotherapeutics & Cell and Gene Therapies using IAPO’s Fieldbook & Biosimilars Toolkit

Durhane Wong-Rieger
Canadian Organization for Rare Disorders
Introductions

**Durhane Wong-Rieger**  
Chair, IAPO & President, Canadian Organization for Rare Disorders

**May Orfali, MD**  
Executive Director, Global Product Development, Pfizer
Meeting Objectives

• Provide an overview of biosimilars and cell and gene therapies (CGTs)
• Review patient perspectives on biosimilars
• Review the IAPO Advocacy Fieldbook & Biosimilars Toolkit
• Review results from the today’s CGT Survey
• Discuss vision for advocacy in these areas
• Develop patient-centered advocacy plans
## Today’s Agenda

**Biosimilars**

| Presentation: Introduce Biosimilars, Review Patient Perceptions and IAPO Advocacy Toolkit, Scorecard | Durhane Wong-Reiger | 15 minutes |
| Working Session: Develop Advocacy Plans for Patient-Centered Access to Biologic Therapies | All | 20 minutes |

**Cell & Gene Therapies**

| Presentation: Introduce Cell & Gene Therapies (CGT) | May Orfali | 15 minutes |
| Survey: Review CGT Survey Results | Durhane Wong-Reiger | 10 minutes |
| Working Session: Discuss Vision for CGTs, Role of Patient Groups in Advocacy, and Outstanding Needs | All | 15 minutes |
Biosimilars

Durhane Wong-Rieger
Canadian Organization for Rare Disorders
What Are Biosimilars?

- A biosimilar is a biologic medicine that is **highly similar** to an existing approved innovative biological product, known as a **reference product**

- However, **unlike generic medicines** in which the active ingredients are identical to the reference small-molecule drugs, **biosimilars will not be identical to the reference biologics** due to several components, including the **inherent complexity of biologics** and the **proprietary details of the reference product**

- Biosimilars made by different manufacturers **will differ** from the reference product and from each other, **making each biosimilar a unique therapeutic option for patients**
## Key Considerations for Stakeholders

<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
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</table>
| **Regulatory Approval**   | • FDA, EMA, and other national regulatory agencies have established a distinct, abbreviated regulatory approval pathways for biosimilar drugs  
• In order to approve biosimilars, regulators require evidence on similarity, safety, and efficacy, including non-clinical and clinical data |
| **Manufacturing Expertise** | • Because of the complexities of biologics, developing and manufacturing high-quality biosimilars will require manufacturers to have deep scientific and manufacturing expertise |
| **Costs**                 | • Biosimilars are expected to be more affordable therapeutic options but are not expected to generate the same level of cost savings as generics  
• A biosimilar will cost $100-200 million and take 8-10 years to develop, vs. a small-molecule generic which costs $1-5 million and take 3-5 years to develop |
| **Key Topics under Discussion** | • Naming and labeling  
• Pharmacovigilance  
• Traceability  
• Interchangeability/Switching |
| **Key Considerations for Patients** | • Switching from reference product  
• Cost savings and out of pocket costs |
Patient-Centered Access: Scenarios

**NEAR MONOPOLY**
(Current and New Innovators OR Biosimilar Only with Gainshare)
Little Choice
Moderate to High Budget

**OPEN FORMULARY**
(No prescriber or patient penalties or incentivized switch)
Much Choice
Moderate to High Budget

**INCENTIVIZED SWITCH**
(Forced Biosimilar Switch with Price Competition or Tender)
Little Choice + Biosimilar Switching
Low Budget (if No Rebate to User)

**OPEN MARKET**
(Innovator and Similar Biologics Competitively Priced & Supported)
Much Choice
Moderate to Low Budget

**Budget Impact**

**Patient Choice**
Patients: Level of Knowledge

**Biosimilars as compared to original biologic...**

- **Differ in effectiveness**
  - Agree: 77%
  - Neither: 13%
  - Disagree: 10%

- **Differ in adverse events**
  - Agree: 77%
  - Neither: 13%
  - Disagree: 10%

- **2 Biosimilars similar to each other**
  - Agree: 29%
  - Neither: 19%
  - Disagree: 52%

- **Biosimilar is generic copy**
  - Agree: 35%
  - Neither: 13%
  - Disagree: 52%

**Choosing original vs. similar biologic...**

- **Choose original even if costlier**
  - Agree: 83%
  - Neither: 11%
  - Disagree: 6%

- **New patients may start biosimilar**
  - Agree: 29%
  - Neither: 19%
  - Disagree: 52%

- **Expect no difference in switching**
  - Agree: 18%
  - Neither: 23%
  - Disagree: 60%

- **Ok switch biologic & biosimilar**
  - Agree: 15%
  - Neither: 30%
  - Disagree: 56%
Patients: Willingness to Switch

<table>
<thead>
<tr>
<th>Monitoring in real-world use is a key requirement</th>
<th>50%</th>
<th>50%</th>
<th>50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>If tracked for effectiveness and adverse events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If each biosimilar is monitored separately</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If each biosimilar has unique name</td>
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</table>

<table>
<thead>
<tr>
<th>Patients should be engaged in informed discussion</th>
<th>65%</th>
<th>70%</th>
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<tr>
<td>If physician discusses biosimilar use</td>
<td></td>
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<tr>
<td>Automatic substitution for prescribed original</td>
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<tr>
<th>Cost differential has some impact</th>
<th>30%</th>
<th>30%</th>
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<tbody>
<tr>
<td>If biosimilar is cheaper</td>
<td></td>
<td></td>
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<tr>
<td>If personal pay difference (is high)</td>
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IAPO Advocacy Fieldbook

Contents: Theory, Guidelines, and Tools for better advocacy
Sections: Advocacy Principles; Step-by-Step; Tools; and Skills

HOW TO USE THIS FIELDBOOK

WELCOME TO THE ADVOCACY FIELDBOOK
This Advocacy Fieldbook provides theory, guidelines, and tools to help you and your group advocate for a particular issue and get your voice heard. The Fieldbook serves as a companion to the advocacy workshops or can be used as a stand-alone resource.

The Fieldbook is organized in four sections: Advocacy Principles; Advocacy Step-by-Step; Advocacy Tools; and Advocacy Skills.

We suggest that you read the Advocacy Principles section at your convenience and use it as a reference source when you are starting to do advocacy. The Advocacy Step-by-Step section is intended to be your guide to helping you define the issue, get support, and plan your advocacy actions. The Advocacy tools are individual “how-to” packages that include an explanation of what the tool is, how and when to use it, as well as templates and samples.

The development of this Advocacy Field Book was funded by a grant from Novartis. Additionally, the workshops and other testing opportunities were supported by Aymds,FromBody, and Novartis.

Download Online: https://www.iapo.org.uk/advocacy-fieldbook
IAPO Biosimilar Advocacy Toolkit

**Briefing Paper on Biological and Biosimilar Medicines**

**Quick Guide on Biological and Biosimilar Medicines**

**Fact Sheet 1: Introduction & Definitions**

**Fact Sheet 2: What Are Biologics & Biosimilars?**

Download Online: [https://www.iapo.org.uk/biosimilars-toolkit](https://www.iapo.org.uk/biosimilars-toolkit)
IAPO Biosimilar Advocacy Toolkit

**Fact Sheet 3:** How are biosimilars regulated?

**Fact Sheet 4:** Pharmacovigilance

**Fact Sheet 5:** What Can Patient Orgs Do?

**Booklet for Patient Groups & Other Resources**

Download Online: [https://www.iapo.org.uk/biosimilars-toolkit](https://www.iapo.org.uk/biosimilars-toolkit)
**IAPO Biosimilar Advocacy Toolkit**

<table>
<thead>
<tr>
<th>Fact Sheet 6: Role of HCP in Talking to Patients</th>
<th>Fact Sheet 7: Regulator Capacity for Biologics</th>
<th>Fact Sheet 8: WHO Biosimilar Guidelines</th>
</tr>
</thead>
</table>

Download Online: [https://www.iapo.org.uk/biosimilars-toolkit](https://www.iapo.org.uk/biosimilars-toolkit)
Biosimilar Scorecard: Questions to Help Patients Talk to Doctors

**ISSUE: PERSONAL BIOLOGIC EXPERIENCE**

4. Can I get the biologic that I feel is best suited to me personally?

<table>
<thead>
<tr>
<th>Support Biosimilar</th>
<th>No Preference</th>
<th>Support Original Biologic</th>
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**ISSUE: ABILITY TO TREAT**

3. If I am taking a medication that is the same level of benefit for me, can I be switched to another medication that is similar?

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**ISSUE: EVIDENCE OF SAFETY AND EFFECTIVENESS**

1. Is there evidence that the same biological causes the same reactions?

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**ISSUE: CHOICE OF ORIGINAL BIOLOGIC OR BIOSIMILAR**

5. If my drug plan lists the biosimilar as the “preferred” biologic, how can I still get the original biologic?

- If I am being dispensed the biosimilar only because it costs less, I am willing to pay the difference to get the original biologic
- I have no or little experience with the original biologic so I do not object to starting with the biosimilar
- I will be taking the biologic only for a short period of time and do not object to taking the biosimilar
- I am concerned that if I take a biosimilar I could be switched to another different biosimilar which is considered similar to the original biologic but not similar to my biosimilar
- I am concerned that if I am taking a biosimilar (based only on lower cost), I will not get access to improved versions of the original biologic or better biologics when they become available
- I believe drug plans should make biosimilars and original biological equally available if they are similar in price

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Total: [ ] [ ] [ ]
Questions?
Cell & Gene Therapies

May Orfali, MD
Pfizer
FDA & Gene Therapy: Current State
Current Gene Therapy Programs

Indications Addressed by Gene Therapy Clinical Trials

- Cancer diseases 64.6% (n=1590)
- Monogenic diseases 10.5% (n=259)
- Infectious diseases 7.4% (n=182)
- Cardiovascular diseases 7.4% (n=178)
- Neurological diseases 1.8% (n=45)
- Ocular diseases 1.4% (n=34)
- Inflammatory diseases 0.6% (n=14)
- Other diseases 2.3% (n=56)
- Gene marking 2% (n=50)
- Healthy volunteers 2.2% (n=54)

The Journal of Gene Medicine, © 2017 John Wiley and Sons Ltd

www.wiley.co.uk/genmed/clinical
What Is A Gene?

- The **basic physical and functional unit** of heredity
- Composed of **DNA**
- Each person has **2 copies** of every gene
- **Small differences in sequence** of copies causes each person to have unique features
- Changes in gene sequence are called **mutations** – they can have very serious consequences
What Is Gene Therapy?

• A technique using **genes to treat or prevent disease** – genes are inserted into a patient’s cells instead of using drugs or surgery

• Approaches to gene therapy include:
  • **Replacing a mutated gene** that causes disease with a healthy copy of the gene
  • **Inactivating, or “knocking out,” a mutated gene** that is functioning improperly
  • **Introducing a new gene** to help fight a disease

• Gene therapy is **a promising treatment option for a number of diseases** (e.g., inherited disorders, some cancers, and certain viral infections)

• Gene therapy is **currently only being tested** for the treatment of **diseases that have no other cures**
How Does Gene Therapy Work?

- Gene therapy is designed to introduce *genetic material into cells* to compensate for abnormal genes or to make a beneficial protein.

- If a mutated gene causes a necessary protein to be faulty or missing, gene therapy may be able to introduce a normal copy of the gene to restore the function of the protein.

- A gene that is inserted directly into a cell usually does not function - instead, a *carrier called a vector* (such as a modified virus) is genetically engineered to deliver the gene.
1902: British physician Archibald Garrod deduced that an inherited disease called alkaptonuria was caused by a mutation that breaks a specific, but then-unknown metabolic enzyme.

1957: Biochemist Vernon Ingram first to pinpoint the exact molecular cause of a genetic disease: he discovered the specific molecular defect in the hemoglobin protein of people afflicted by sickle-cell disease.

1990s: Scientists had developed the capability to make replacements for damaged genes ~ the most obvious delivery vehicles were viruses.

1999: Major setback for gene therapy, when 18 year old Jesse Gelsinger with OTD died in gene therapy trial that led to the initiation of a robust safety oversight system in place to protect patient safety.
## Cutting Edge Development

### 2 Cancer Targeted Gene Therapies Approved by FDA

<table>
<thead>
<tr>
<th><strong>Avoids the virus risk by altering the gene outside the body:</strong></th>
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<tbody>
<tr>
<td>• T-cells (part of the immune system) are removed from the cancer patient</td>
</tr>
<tr>
<td>• In a lab setting, a gene that targets cancer cells is engineered into the patient’s T-cells</td>
</tr>
<tr>
<td>• These T-cells are infused back into the patient, where they replicate and engineered gene helps the T-cells target cancer cells</td>
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### Gene Therapy in Dermatology: Life Saver

<table>
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<tr>
<th><strong>Similar approach used in a last-ditch treatment effort</strong></th>
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<tbody>
<tr>
<td>• A seven-year-old child, Hassan, suffered from a severe genetic skin disease due to damage to a gene needed to anchor the skin in place</td>
</tr>
<tr>
<td>• When he arrived at the hospital, he had lost &gt;80% of outer skin layer</td>
</tr>
<tr>
<td>• Working with a small sample of the boy's skin cells, a team of German and Italian doctors corrected the gene mutation and then used the cells to grow sheets of replacement skin in the lab</td>
</tr>
<tr>
<td>• After a series of surgical grafts, Hassan now has healthy, genetically corrected skin over almost his entire body</td>
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</table>
Recent Accomplishments

Dec: In two small trials published in December, viruses successfully delivered gene therapy to the blood cells of patients suffering from the two major types of hemophilia.

Nov: Study published that showed a different virus—optimized to target the central nervous system—successfully delivered a replacement gene into cells of 18 children suffering from spinal muscular atrophy, a neurodegenerative disease that is almost always fatal by age two. At 20 months, all 18 children were doing well.

Mar: Report published that showed another type of virus was used in gene therapy administered to a 13-year-old boy suffering from sickle-cell disease. Fifteen months after treatment, he was largely free of symptoms.
What Are Risks of Gene Therapy?

- Current research is **evaluating the safety and efficacy of gene therapy** as a treatment option.
- Several studies have already shown that this approach can have **very serious health risks**, such as toxicity, inflammation, and cancer.
- Because the techniques are relatively new, some of the risks may be **unpredictable**.
- However, medical researchers, institutions, and regulatory agencies are **working to ensure that gene therapy research is as safe as possible**.
Potential Ethical Issues

Because gene therapy involves making changes to the body’s set of basic instructions, it raises many unique ethical concerns, e.g.,:

• Will the high costs of gene therapy make it available only to the wealthy?
• Could the widespread use of gene therapy make society less accepting of people who are different?
• How can “good” and “bad” uses of gene therapy be distinguished?
• Who decides which traits are normal and which constitute a disability or disorder?
• Should people be allowed to use gene therapy to enhance basic human traits such as height, intelligence, or athletic ability?
Ethical Issues: Germline Therapy

- Current gene therapy targets body cells such as bone marrow or blood cells, which **cannot be passed on** to a person’s children.

- **Germline gene therapy** is when egg and sperm cells (germ cells) are targeted, which would allow the inserted gene to be passed on to future generations.

- Germline gene therapy is **controversial** - long term risks are unknown and unborn people cannot choose treatment.

- The U.S. Government **does not allow federal funds to be used for research** on germline gene therapy in people.
Today’s CGT Survey Results

Durhane Wong-Reiger
### Results from Today’s CGT Survey

#### Number of Respondents

<table>
<thead>
<tr>
<th>Question</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>How informed are you about cell and gene therapy?</td>
<td>• Most people are only a “little informed”</td>
</tr>
</tbody>
</table>
| Who do you trust for source of information on cell and gene therapy?    | • Scientific media is most trusted, followed by physicians  
                              • Patient organizations are somewhat trusted  
                              • Other sources (e.g., public and social media, family and friends) are also used but less trusted |
| Would you recommend a family member or friend for a CGT clinical trial? | • Half (50%) said yes  
                              • Half (50%) said maybe                             |
## Results from Today’s CGT Survey

<table>
<thead>
<tr>
<th>Agreement</th>
<th>Opinion Statements</th>
</tr>
</thead>
</table>
| **Very high agreement** | • I believe cell and gene therapies are important new approaches to treat serious diseases and should be made available as soon as possible  
|                  | • Patients with serious conditions requiring life-long therapy should be given the option of cell or gene therapy if it offers a potential cure for the condition  
|                  | • Like heart, liver or other transplants, patients should be triaged (prioritized) to receive cell or gene therapy based on individual need and not ability to pay |
| **Medium - high agreement** | • Therapy that changes a person’s cellular or genetic makeup (DNA) raises ethical, moral, or religious questions that need to be addressed  
|                  | • Patients should have an option to purchase “cell/gene therapy” insurance that would give them priority access  
|                  | • Health systems should pay for cell and gene therapies now even if they are costly so they will be available to more patients later |
| **Low - med agreement** | • I think cell and gene therapies should not be available to the general patient population until the long-term benefits and risks have been proven  
|                  | • I feel cell and gene therapies should only be used for life-threatening situations when there are no other alternatives  
|                  | • Stem cell therapies, including bone marrow transplantation, are not available to most patients because of the lack of matched donors; genetically modifying a person’s own stem cells and genes are important life-saving alternatives |

**Number of Respondents**: 32
# Results from Today’s CGT Survey

<table>
<thead>
<tr>
<th>KNOWLEDGE ASSESSMENT</th>
<th>CORRECT ANSWERS &amp; YOUR RESPONSES:</th>
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<tbody>
<tr>
<td><strong>4. TRUE or FALSE Questions</strong></td>
<td></td>
</tr>
<tr>
<td>Each person has a unique set of genes</td>
<td>TRUE</td>
</tr>
<tr>
<td>Humans share about 99.9% of the same DNA</td>
<td>TRUE</td>
</tr>
<tr>
<td>Genetic disorders are always inherited from one or both parents</td>
<td>FALSE</td>
</tr>
<tr>
<td>In order for a child to have a genetic disorder, both parents must carry a copy of the defective gene</td>
<td>FALSE</td>
</tr>
<tr>
<td>Many people who are left-handed also have symptoms of dyslexia (reading difficulties); this association led to the discovery that they are caused by the same genetic abnormality</td>
<td>TRUE</td>
</tr>
<tr>
<td>Identical triplets always have the same DNA</td>
<td>TRUE</td>
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<tr>
<td>Some genetic mutations protect against disease</td>
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<td>Some genetic mutations cause disease in men but have little or no effect in women</td>
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</tr>
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<td>A male who has a sex-linked genetic disorder (on the X-chromosome) will have inherited the disease</td>
<td>TRUE</td>
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Mostly correct
Some correct
Mostly incorrect
Results from Today’s CGT Survey

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<tr>
<td><strong>5. Hereditary genetic disorders</strong></td>
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<tr>
<td>Cystic Fibrosis</td>
<td>Yes</td>
</tr>
<tr>
<td>Hemophilia</td>
<td>Yes</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Down’s Syndrome</td>
<td>Yes</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Sometimes</td>
</tr>
<tr>
<td>High Cholesterol</td>
<td>Sometimes</td>
</tr>
<tr>
<td>HIV</td>
<td>No</td>
</tr>
<tr>
<td>Tuberculosis (TB)</td>
<td>No</td>
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</tbody>
</table>

Mostly correct
Some correct
Mostly incorrect

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Questions?
Contact Us

For any questions, please contact:

**Durhane Wong-Rieger**
President & CEO, Canadian Organization for Rare Disorders
p: 416-969-7435 | m: 647-801-5176
Durhane@sympatico.ca

**May Orfali, MD**
Executive Director, Global Product Development Rare Diseases, Pfizer Inc.
p: 647-694-5276
May.Orfali@pfizer.com
Thank you