The era of biological medicines

Since their first use in the 1980s, biological medicines (including biosimilar medicines) have grown to become an indispensable tool in modern medicine. Worldwide, millions of patients have already benefited from approved biological medicines, but what exactly are they, and how are they produced?\textsuperscript{1,2}

Biological medicines have revolutionized the treatment of many disabling and life-threatening diseases

- Biological medicines:
  - include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapies, tissues, and recombinant therapeutic proteins
  - are highly specific and targeted medicines
  - help to treat or prevent many rare and severe diseases, including:
    - Cancers
    - Arthritis
    - Psoriasis
    - Inflammatory digestive disorders
    - Growth disorders
    - Diabetes

Biological medicines contain one or more active substances made by or derived from a biological source\(^1\)

- Since their first use in the 1980s, biological medicines have grown to become an indispensable tool in modern medicine\(^2\)

### Timeline

- **1980s**: The first biological medicinal products produced by DNA recombinant techniques were approved\(^2\)
- **1986**: Monoclonal antibody receives first FDA approval\(^3\)
- **1998**: First biological medicine for rheumatoid arthritis is introduced\(^4\)
- **2006**: Europe approves first biosimilar medicine\(^5\)
- **2014**: By 2014, over 245 biological medicines had been approved in the EU and US, representing 166 different active substances\(^6\)

### References

2. Kinch MS. Drug Discov Today 2015;20:393–8;
Biological medicines are predominantly larger and more complex than chemically synthesized medicines

<table>
<thead>
<tr>
<th>Type of molecule</th>
<th>Chemically synthesized medicine</th>
<th>Growth hormone</th>
<th>Antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of molecule</td>
<td>Small molecule</td>
<td>Protein (without sugars)</td>
<td>Glycoprotein (variable sugars)</td>
</tr>
<tr>
<td>Synthesis</td>
<td>Chemical</td>
<td>Bacterial</td>
<td>Mammalian</td>
</tr>
<tr>
<td>Uniformity</td>
<td>Single substance</td>
<td>Single main substance</td>
<td>Mixture of variants</td>
</tr>
<tr>
<td>Size</td>
<td>21 atoms (aspirin)</td>
<td>3000 atoms (HGH)</td>
<td>&gt;20,000 atoms (mAb)</td>
</tr>
</tbody>
</table>

The complexity of biological medicines is such that they cannot usually be synthesized by conventional methods.

Abbreviations: HGH, human growth hormone; mAb, monoclonal antibody.
Producing biological medicines tends to be more complex than producing chemically derived medicines\textsuperscript{1,2}

The inherent variability of living organisms and the manufacturing process result in the biological medicine displaying a certain degree of variability (‘microheterogeneity’)\textsuperscript{1}

A biological medicine is a mixture of closely related variants of the same protein

- The living organisms used to make biological medicines are naturally variable
- An inherent degree of minor variability (‘microheterogeneity’) is thus normally present in biological medicines
- Microheterogeneity is also present within and/or between batches of the same biological medicine
- The degree of variability must fall within a range agreed upon by the health authority to ensure consistent safety and efficacy
- Strict controls are always in place during manufacturing to ensure batch-to-batch consistency, and that the differences do not affect safety or efficacy

Summary: The era of biological medicines

Biological medicines contain one or more active substances made by or derived from a biological source\(^1\)

The complexity of biological medicines is such that they cannot usually be synthesized by conventional methods\(^2\)

The variability of the living organisms contributes to microheterogeneity\(^3\)

Microheterogeneity is normal, and seen within or between different batches of the same biological product\(^4\)

Strict controls during manufacturing ensures safe and effective biological medicines\(^4\)

Biological medicines have grown to become an indispensable tool in modern medicine\(^5\)