

Chapter 1

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?^{1,2}

Biological medicines¹ 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



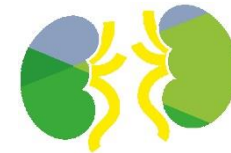
Inflammatory
digestive
disorders



Growth
disorders



Diabetes



Nephrology

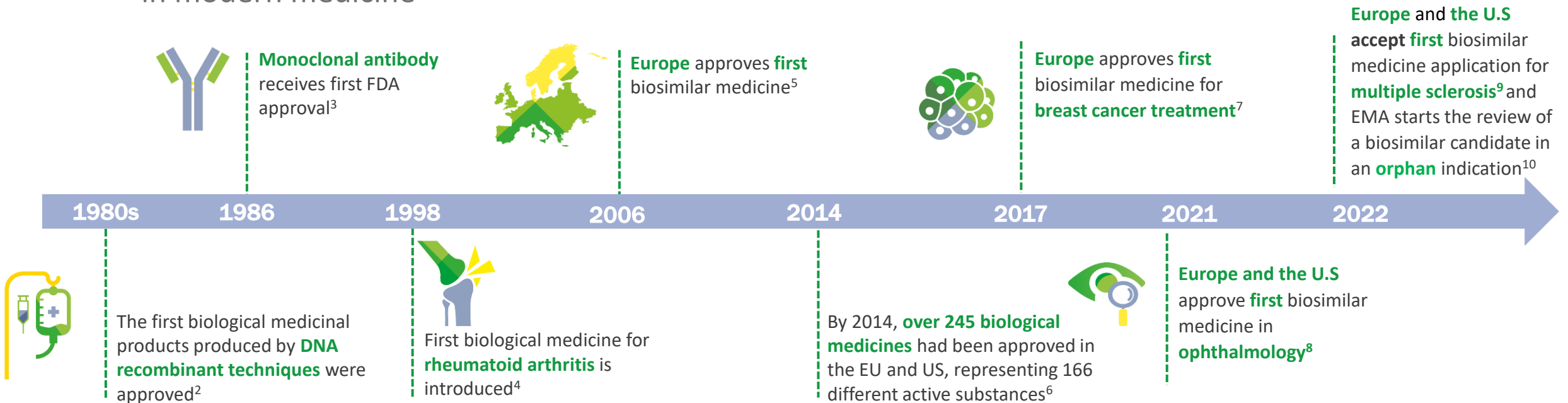


Ophthalmology

Biological medicines are developed based on a deep understanding of the disease biology

Biological medicines contain one or more active substances made by or derived from a biological source¹

- Since their first use in the 1980s, biological medicines have grown to become an indispensable tool in modern medicine²



Biological medicines are an integral and indispensable part of modern medicine⁶

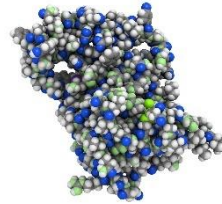
References: 1. EMA. [Biosimilar medicines](#). Accessed March 2020; 2. Kinch MS. *Drug Discov Today* 2015;20:393–8; 3. Liu JKH. *Ann Med Surg (Lond)* 2014;3:113–6; 4. De Keyser F. *Curr Rheumatol Rev* 2011;7:77–87; 5. Medicines for Europe. [Factsheet on Biosimilar Medicines 2016](#). Accessed February 2020; 6. Walsh, G. *Nat Biotechnol* 2014;32: 992–1000; 7. EMA rituximab biosimilar EPAR Truxima | European Medicines Agency (europa.eu); 8. Byooviz (ranibizumab): EU approval - Byooviz (ranibizumab-nuna) FDA approval. Accessed October 2021; 9. <https://www.biopharma-reporter.com/Article/2022/07/20/EMA-accepts-application-for-Polpharma-Biologics-MS-biosimilar-natalizumab>. Accessed July 2022; 10. Applications for new human medicines under evaluation. [link](#) Accessed July 2022

Biological medicines are predominantly larger and more complex than chemically synthesized medicines



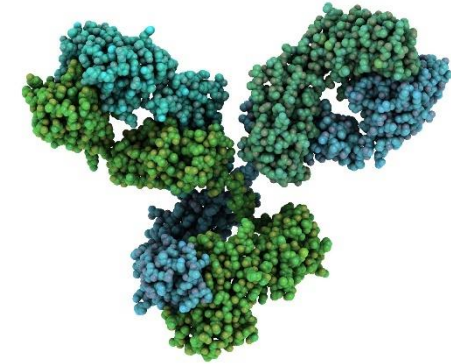
Chemically synthesized medicine

Type of molecule	Small molecule
Synthesis	Chemical
Uniformity	Single substance
Size	21 atoms (aspirin)



Growth hormone

Type of molecule	Protein (without sugars)
Synthesis	Bacterial
Uniformity	Single main substance
Size	3000 atoms (HGH)



Antibody

Type of molecule	Glycoprotein (variable sugars)
Synthesis	Mammalian
Uniformity	Mixture of variants
Size	>20,000 atoms (mAb)

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

Abbreviations: HGH, human growth hormone; mAb, monoclonal antibody.

References: International Alliance of Patients' Organizations. [Briefing paper on Biological and Biosimilar Medicines 2013](#). Accessed February 2020.

Producing biological medicines tends to be more complex than producing chemically derived medicines^{1,2}

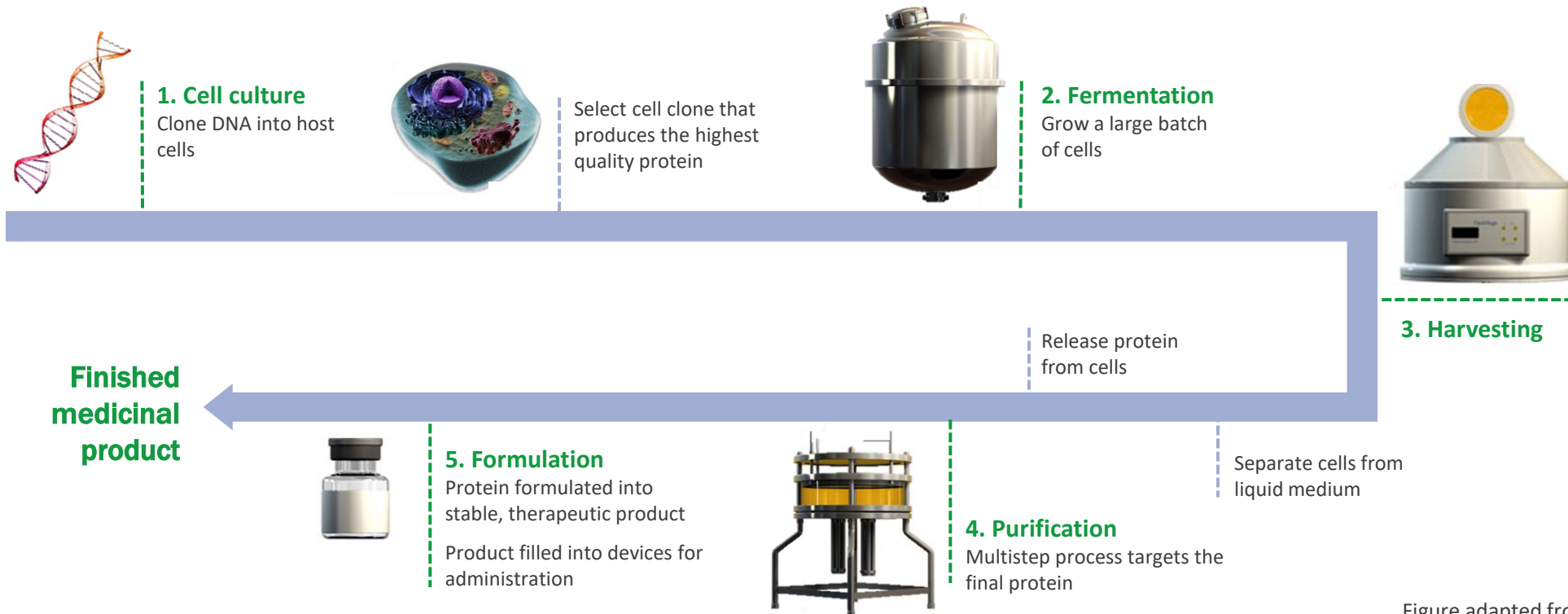


Figure adapted from Apobiologix³

The inherent variability of living organisms and the manufacturing process result in the biological medicine displaying a certain degree of variability ('microheterogeneity')¹

A biological medicine is a mixture of closely related variants of the same protein¹

- The living organisms used to make biological medicines are **naturally variable**²
- An inherent degree of minor variability (‘**microheterogeneity**’) is thus normally present in biological medicines²
- Microheterogeneity is also present **within and/or between batches** of the same biological medicine²
- The degree of variability **must fall within a range** agreed upon by the health authority to ensure consistent safety and efficacy²
- **Strict controls** are always in place during manufacturing to ensure batch-to-batch consistency, and that the differences do not affect safety or efficacy¹



Strict controls ensure safe and efficacious biological medicines¹

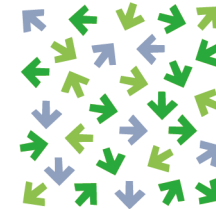
Summary: The era of biological medicines



Biological medicines contain one or more active substances **made by or derived from a biological** source¹



The complexity of biological medicines is such that they **cannot usually be synthesized** by conventional methods²



The **variability** of living organisms contributes to **microheterogeneity**³



Microheterogeneity is normal, and seen **within or between different batches** of the same biological product⁴



Strict controls during manufacturing consistently **ensures safe and effective** biological medicines⁴



Biological medicines have grown to become an **indispensable therapeutic tool** in modern medicine⁵