

## 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?<sup>1,2</sup>

# 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**

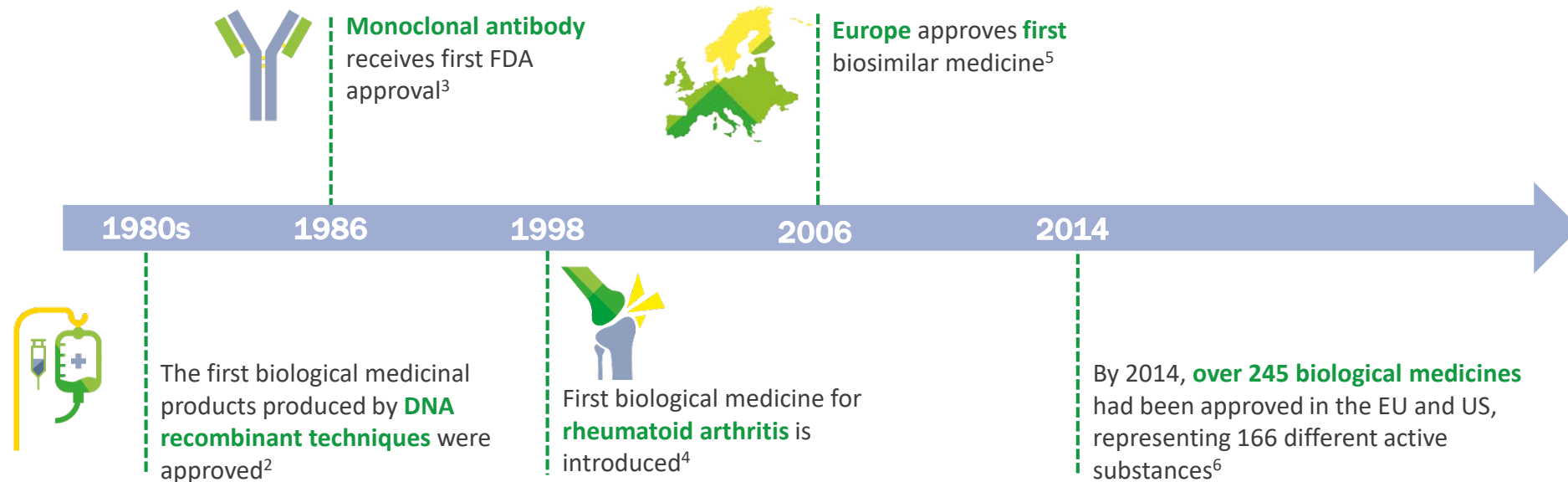


**Diabetes**

Biological medicines 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 source<sup>1</sup>

- Since their first use in the 1980s, biological medicines have grown to become an indispensable tool in modern medicine<sup>2</sup>



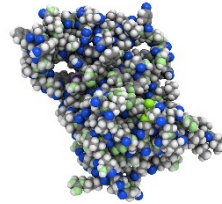
Biological medicines are an integral and indispensable part of modern medicine<sup>6</sup>

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



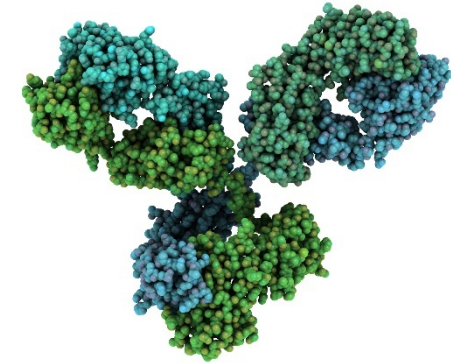
## Chemically synthesized medicine

<b>Type of molecule</b>	Small molecule
<b>Synthesis</b>	Chemical
<b>Uniformity</b>	Single substance
<b>Size</b>	21 atoms (aspirin)



## Growth hormone

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



## Antibody

<b>Type of molecule</b>	Glycoprotein (variable sugars)
<b>Synthesis</b>	Mammalian
<b>Uniformity</b>	Mixture of variants
<b>Size</b>	>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. Available at: <http://bit.ly/2qZm7N1>. Accessed July 2017.

# Producing biological medicines tends to be more complex than producing chemically derived medicines<sup>1,2</sup>

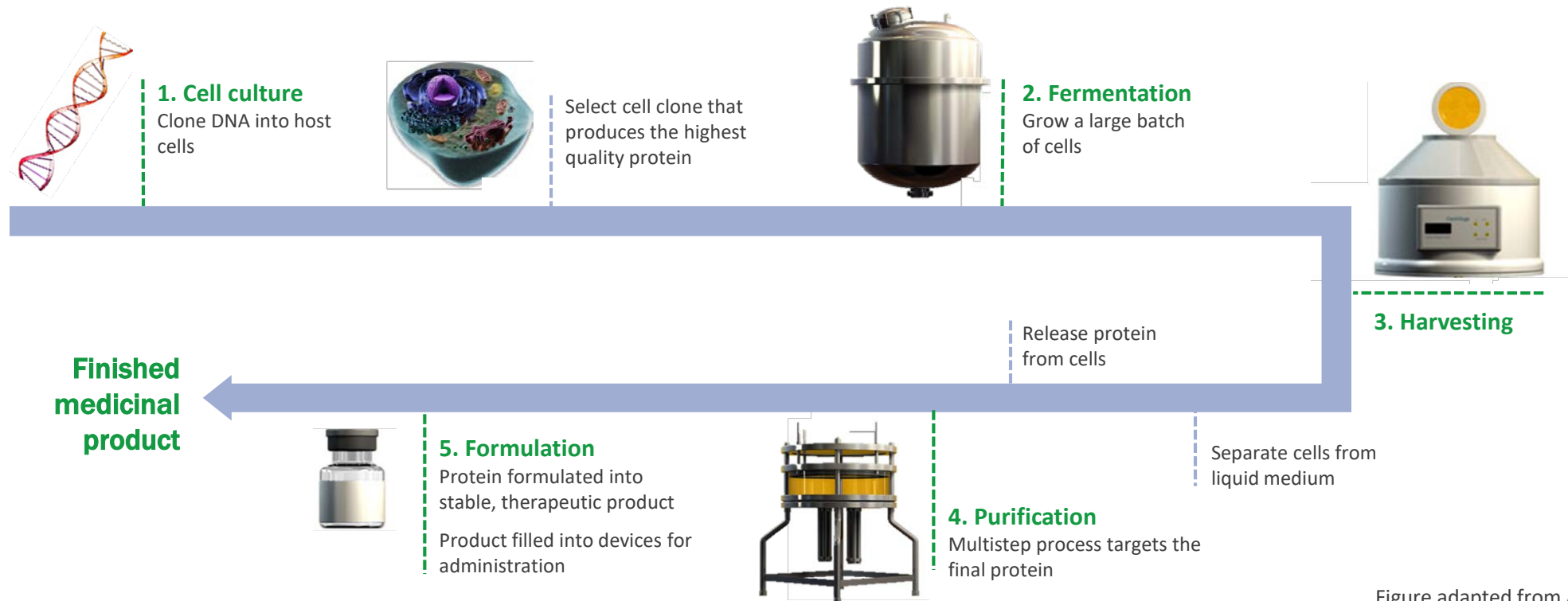


Figure adapted from Apobiologix<sup>3</sup>

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

**References:** **1.** WHO. Annex 3: Guidelines for assuring quality of pharmaceutical and biological products prepared by recombinant DNA technology. 1991. Available at: <http://bit.ly/2pSf1tC>. Accessed July 2017; **2.** EC/EMA. Biosimilars in the EU – Information guide for Healthcare Professionals 2017. Available at: <http://bit.ly/2qXnNpl>. Accessed July 2017; **3.** Apobiologix. Manufacturing. Available at: <http://bit.ly/2ryyAUW>. Accessed July 2017.

# A biological medicine is a mixture of closely related variants of the same protein<sup>1</sup>

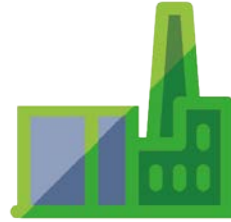
- The living organisms used to make biological medicines are **naturally variable**<sup>2</sup>
- An inherent degree of minor variability ('**microheterogeneity**') is thus normally present in biological medicines<sup>2</sup>
- Microheterogeneity is also present **within and/or between batches** of the same biological medicine<sup>2</sup>
- The degree of variability **must fall within a range** agreed upon by the health authority to ensure consistent safety and efficacy<sup>2</sup>
- **Strict controls** are always in place during manufacturing to ensure batch-to-batch consistency, and that the differences do not affect safety or efficacy<sup>1</sup>

Strict controls ensure safe and efficacious biological medicines<sup>1</sup>

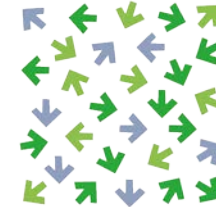
# Summary: The era of biological medicines



Biological medicines contain one or more active substances **made by or derived from a biological** source<sup>1</sup>



The complexity of biological medicines is such that they **cannot usually be synthesized** by conventional methods<sup>2</sup>



The **variability** of the living organisms contributes to **microheterogeneity**<sup>3</sup>



Microheterogeneity is normal, and seen **within or between different batches** of the same biological product<sup>4</sup>



**Strict controls** during manufacturing **ensures safe and effective** biological medicines<sup>4</sup>



Biological medicines have grown to become an **indispensable tool** in modern medicine<sup>5</sup>