Biological and Biosimilar Medicines
Fact Sheet 3: How are biosimilar medicines regulated?

International Alliance of Patients' Organizations
A global voice for patients

This Fact Sheet provides information about how biosimilar medicines are regulated and why they have a different regulatory process from chemical medicines. It also provides information about the regulatory situation worldwide.

All medicines, whether chemical or biological, have to be regulated and approved before being marketed and made available for patients. This is to ensure they are safe and effective.

Chemical and biological medicines have different approval and regulation pathways; they will require different tests and amounts of data – this is due to their different characteristics (see Fact Sheet 2).

It is important to understand that biosimilar medicines are regulated differently to generic medicines (identical copies of branded chemical medicines) and to new biological medicines.

Chemical medicines, e.g. aspirin, are made using chemical ingredients and chemical reactions which can be easily reproduced and well controlled. Their structure and chemical make up can be easily worked out. For these reasons, it is fairly straightforward to produce an identical copy of a branded chemical medicine – a **generic medicine**. Their approval is fairly straightforward and the medicine needs to show bioequivalence with the branded chemical medicine, i.e. that it works in the body in the same way.

Biological medicines, on the other hand, are large, complex molecules which are made using living organisms and therefore have a degree of inherent variability. Furthermore, they are very sensitive to manufacturing processes. For these reasons, it is impossible to produce an exact copy of a biological medicine and, due to batch-to-batch variability, no two biological medicines can be considered the same. For these reasons, their approval is more complex.

Biosimilar comparability exercise

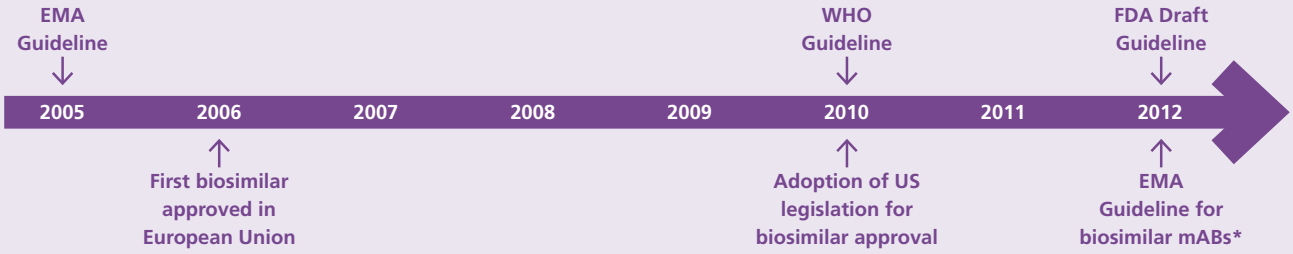
A biosimilar medicine is approved on the basis that any inherent variability or difference seen between the biosimilar medicine and the reference product have no effect on the medicine.

- Biosimilar medicines are approved on the basis that they are **highly similar** to the reference product in terms of **safety**, **quality** and **efficacy**.
- The basic principle underlying the development and approval of a biosimilar medicine is that it is comparable to the reference product in terms of safety, quality and efficacy. This is assessed through a **biosimilar comparability exercise**.
- A biosimilar comparability exercise is composed of three steps: quality comparability, non-clinical comparability and clinical comparability (clinical trials in patients).

The aim of the comparability exercise is not to show the therapeutic benefit of the biosimilar medicine, but to show that any differences between the two have no impact on its safety, quality and efficacy. This is why the approval process is different to that of new biological medicines and the data required for each step in the exercise will often differ between the biosimilar medicine and the reference product. Finally, the approval of chemical, generic, biological and biosimilar medicines requires a **post-approval monitoring** and **risk management plan** including a pharmacovigilance plan (see Fact Sheet 4 for further details).

Key influential regulatory pathways and guidelines for biosimilar medicines

- The first guidelines for biosimilar medicines were developed by the European Medicines Agency (EMA) in 2005.
- This was followed by the World Health Organization (WHO) in 2010.
- The US Food and Drug Agency (FDA) published their draft guidelines in 2012.

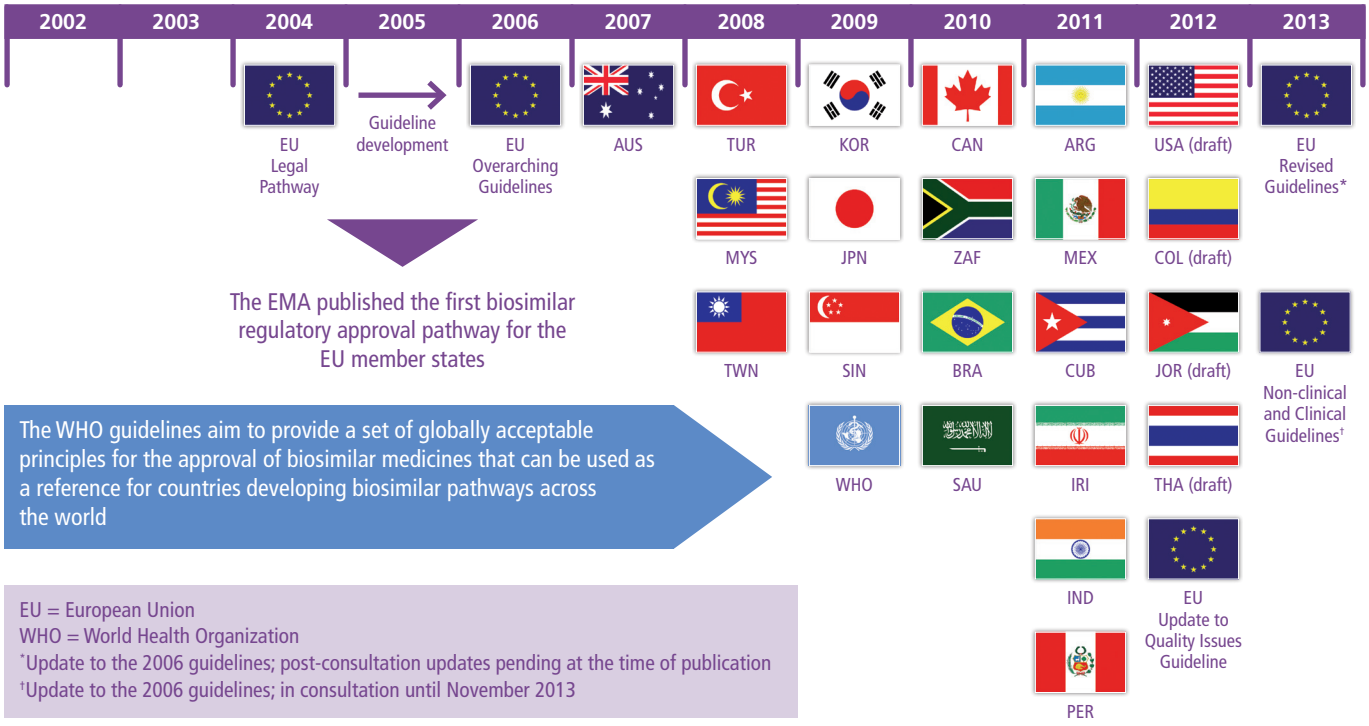


*mAB = monoclonal antibody

Regulatory pathways worldwide

It is widely accepted that the WHO, EMA and FDA guidelines should provide a strong and complete basis for approving biosimilar medicines. Many countries have developed or are in the process of developing frameworks and guidelines for the development and approval of biosimilar medicines. However, not all guidelines across the world meet all of the WHO requirements (such as a full comparability exercise), potentially compromising patient safety. Similarly, there is concern that in some developing countries the approval process and the post-approval quality control need to be improved.

Global biosimilar guideline/regulation development



EU = European Union
WHO = World Health Organization
*Update to the 2006 guidelines; post-consultation updates pending at the time of publication
†Update to the 2006 guidelines; in consultation until November 2013

[Adapted from timeline provided by Amgen. Data source: publically available information from national health authorities and WHO regulatory guidelines]