FACT SHEET 2

REGULATION OF BIOLOGICS

International Alliance of
Patients' Organizations

CAN Mezzanine
49-51 East Road London
N1 6AH
United Kingdom

International Federation of
Pharmaceutical Manufacturers
& Associations

Chemin des Mines 9
P.O. BOX 195
1211 Geneva 20
Switzerland

SOURCES

1. World Health Organization. WHO Technical Report Series, 64th Report (No. 987) - Annex 4. Guidelines on the quality, safety and efficacy of biotherapeutic protein products prepared by recombinant DNA technology (Replacement of Annex 3 of WHO Technical Report Series, No. 814). In: WHO Expert Committee on Biological Standardization, ed. WHO Technical Report Series. Geneva, Switzerland, 2013.

2. World Health Organization. WHO Technical Report Series, 60th Report (No. 977) - Annex 2. Guidelines on evaluation of similar biotherapeutic products (SBPs). In: WHO Expert Committee on Biological Standardization, ed. WHO Technical Report Series. Geneva, Switzerland, 2009.

3. World Health Organization. WHO Technical Report Series, 66th Report (No. 999) - Annex 2. WHO good manufacturing practices for biological products. In: WHO Expert Committee on Biological Standardization, ed. Geneva, Switzerland, 2015.

4. World Health Organization. WHO Technical Report Series, 42nd Report (No. 822) - Annex 2. Guidelines for national authorities on quality assurance for biological products. In: WHO Expert Committee on Biological Standardization, ed. Geneva, Switzerland, 1992.

5. World Health Organization. WHO Technical Report Series, 45th Report (No. 858) - Annex 1. Regulation and licensing of biological products in countries with newly developing regulatory authorities. In: WHO Expert Committee on Biological Standardization, ed. Geneva, Switzerland, 1995.

6. World Health Organization. WHO Technical Report Series, 66th Report (No. 999) - Annex 3. Regulatory assessment of approved rDNA-derived biotherapeutics (Addendum to Annex 4 of WHO Technical Report Series, No. 987). In: WHO Expert Committee on Biological Standardization, ed. Geneva, Switzerland, 2015.

7. Renwick MJ, Smolina K, Gladstone EJ, et al. Postmarket policy considerations for biosimilar oncology drugs. The Lancet Oncology 2016;17(1):e31-e38. doi: http://dx.doi.org/10.1016/S1470-2045(15)00381-2

INTRODUCTION TO REGULATIONS OF BIOLOGICS

A biologic medicine is any medicine made using a living organism. They are larger and more complex molecules and because they are made from living organisms, they are inherently more variable. Biologics have been in existence for several decades. However, modern biotechnology techniques introduced in recent years have greatly enhanced the ability to develop biologics safely and consistently.

Biologics require different guidelines (regulatory frameworks) to control how they are developed, manufactured, used in clinical practice, and approved by regulatory authorities.

INTERNATIONAL STANDARDS FOR REGULATION OF BIOLOGICS

Biologic medicines are a relatively new and evolving category of medicines, and many regulatory authorities are gaining experience on the approval process. If regulations are too onerous, innovation and access are stifled. By drawing upon the accumulated collective experience with biologics, the WHO has established global regulatory standards that define minimum requirements for the approval of all biologic medicines.[1][2][3][4][5][6]

By adhering to these standards, all regulators can contribute to assuring that the biologics available to patients are as safe and effective as possible, regardless of where they reside.

Moreover, WHO guidelines should be applied not just to new biologics but also to those approved before the development of WHO[2] and other national guidelines. Some of these products approved through a regulatory pathway for small-molecule medicines may not meet up-to-date standards in terms of consistent quality, clinical trial evidence, and plans for post-market scrutiny WHO defends that these products "need to be reassessed to ensure that they meet the new requirements."[6] As an example, FDA in the US has set up an approval pathway specifically for biosimilars, even though in the past some products called "follow-on biologics" have been approved through a process reserved for products closely related to the originators that don't fit in the category of generics (Figure 1).

Key components are:

Ensuring consistent quality by controlling the manufacturing process: This requires systematically controlling the genetic consistency[2] and minimising the level of genetic impurities[6] of the cells reprogrammed to produce biologics; and systematically preventing or minimising the occurrence of biotoxins or viral contamination.[1] Proper monitoring and removal procedures are therefore needed throughout the manufacturing and development process.[1]

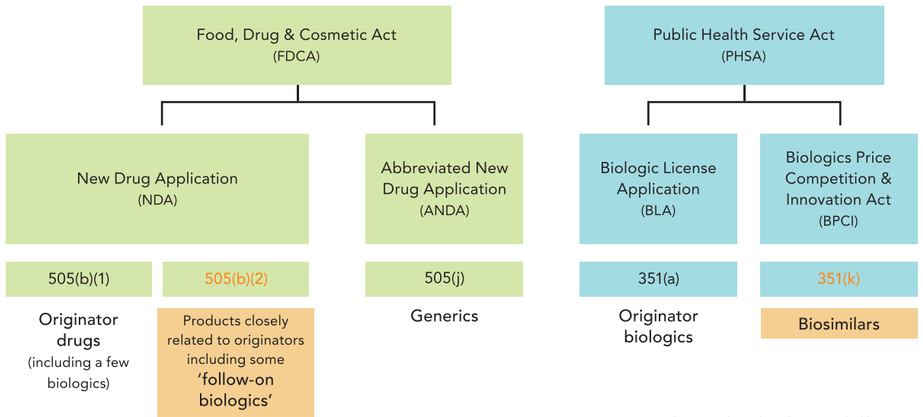
Rigorous clinical studies in patients to demonstrate safety and efficacy: Beyond pre-clinical trials in cell cultures (in vitro studies) and animals (in vivo studies) and clinical trials with healthy volunteers, all biologics must undergo clinical trials with patients who have the targeted disease or condition.[1]

Post-approval monitoring of safety and efficacy of all biologics prescribed to patients in "real-world" clinical practice, also known as pharmacovigilance (For more information, read **Fact Sheet #5** on **Pharmacovigilance: Monitoring and Traceability across the System**). Processes and systems for routinely collecting and analysing the use of biologics, beneficial outcomes, and adverse effects (defined as a response which is noxious and unintended, including lack of efficacy) are essential to ensuring the safe and effective use of biologics.

As displayed in this diagram, biosimilars have now their own approval pathway, under the Biologics Price Competition and Innovation Act.

FDA APPROVAL PATHWAYS

Figure 1.



Adaptation based on data provided by IQVIA.