FACT SHEET 2

REGULATION OF BIOLOGICS
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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 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."\(^6\)

Post-approval monitoring of safety and efficacy of all biologics prescribed to patients in "real-world" clinical practice, also known as pharmacovigilance, is essential to ensuring the safe and effective use of biologics.

Key components are:

- **Ensuring consistent quality by controlling the manufacturing process:** This requires systematically controlling the genetic consistency\(^7\) and minimizing the level of genetic impurities\(^6\) of the cells reprogrammed to produce biologics; and systematically preventing or minimizing the occurrence of biotoxins or viral contamination.\(^7\) 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. Properly monitoring and removing procedures are therefore needed throughout the manufacturing and development process.\(^1\)

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

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**FDA APPROVAL PATHWAYS**

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**Figure 1.**

- **Food, Drug & Cosmetic Act (FDCA)**
- **Public Health Service Act (PHSA)**
- **Biologic License Application (BLA)**
- **Biologics Price Competition & Innovation Act (BPCI)**
- **Originate biologics**
- **Biosimilars**
- **New Drug Application (NDA)**
- **Abbreviated New Drug Application (ANDA)**
- **Generics**

Adaptation based on data provided by IQVIA.