

Public Policy Statement: Biosimilars and Originator Biologics

Biologics have revolutionized the treatment of patients suffering from some of the most debilitating and life-threatening diseases, and the potential for discovering novel biological therapies remains high. Biologics are complex proteins derived from living sources and are generally more complex than small-molecule drugs, which are usually produced through a chemical process.

Over the last decade, regulatory authorities around the world have been establishing formal regulatory pathways for approval of biosimilars, sometimes referred to as "follow-on biologics" (FOBs), "subsequent entry biologics" (SEBs), and "similar biotherapeutic products" (SPBs). Biosimilars are new versions of approved originator biological products. Due to the complex development and manufacturing process for biological products, a biosimilar is not required to be "identical" to its reference product, as is the case for small-molecule generics. Instead, a biosimilar is "highly similar" to the reference biological product, notwithstanding minor differences in clinically inactive components. Further, to achieve regulatory approval, there can be no clinically meaningful differences between the biosimilar product and the reference biological product in terms of safety, purity, and potency.

In addition to Merck's robust and expanding pipeline of originator biological products to address unmet medical needs, we believe high quality biosimilars can improve patient accessibility to these lifesaving biological medicines across the globe, while respecting the intellectual property rights of the originator.

Merck's Position on Biologics: Originators and Biosimilars

- Merck supports legislation and administrative rulemaking that enables national or regional health agencies to develop regulatory frameworks, scientific standards, and administrative processes for the review and approval of all biosimilars. Further, we support efforts by regional health authorities to harmonize such standards to ensure consistency on a global level.
- We believe that all biosimilar applicants should be required to conduct comparative (i.e., head-to-head) analytical and clinical trials with an approved originator reference product. These trials should be designed to demonstrate safety (including immunogenicity), efficacy, purity, and potency profiles that are highly similar to that of the reference biologic.
- The prescribing physician should have the option to designate exactly which biological product should be dispensed to the patient. In such cases, substitution should not be permitted. Pharmacies and alternative drug dispensers should be allowed to substitute between reference biological products and biosimilars, as long as the prescribing physician has not designated the biological product to be dispensed, and provided that:
 - the biosimilar is designated as 'interchangeable' (or the equivalent national regulatory standard) by the relevant National Regulatory Authority (NRA);
 - **and** adequate pharmacovigilance systems are in place to facilitate product tracking and the rapid and accurate identification of the dispensed product;
 - **and** the substitution is accompanied by the timely communication to the prescribing physician, as well as the patient or patient's representative.

- To maintain consistency across all product platforms, national and regional health agencies should ensure that the standards used to determine post-marketing studies for drug and biological products are applied to biosimilars. We believe that post-marketing commitments should be based upon what is known about the product class and about any specific safety concerns with a given product.
- We believe that nonproprietary naming conventions should allow for the ability to distinguish between each biological product, while conveying the relationship to the reference product. This could be achieved by requiring distinguishable-but-related International Nonproprietary Names (INNs), a process that is governed by the World Health Organization (WHO). International harmonization of nonproprietary naming conventions for biologics, preferably through the WHO/INN system, should therefore be supported. However, if a country diverges from the international convention, naming policies should be applied consistently at the national level to all biological products marketed within that country.
- While patents and data protection are both necessary incentives for biological innovation, patent protection alone is not sufficient. In the case of biologics, a product patent may provide insufficient protection because a biosimilar competitor can circumvent the patent under the similarity standard for approval of the biosimilar. Merck believes it is essential for biologics to be granted a substantial period of market and data exclusivity to preserve an environment that promotes the discovery of innovative therapies. Furthermore, legislation should establish a fair, transparent, and workable system for all parties to promptly resolve any patent disputes.
- The potential for significant savings to national health care systems clearly exists if high quality originator and biosimilar biological products can be brought efficiently to the marketplace to offer patients, physicians, and payors added choices through class competition and affordability. Merck believes that the market for originator and biosimilar medicines should be based on sustainable competition that reflects patients' safety and health outcomes, access to a variety of medicines, the need for continued investment to discover and develop innovative biological products, and savings for healthcare systems.

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