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.

A biosimilar is a biological product that is highly similar to and has no clinically meaningful differences from an existing approved reference biologic product. 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.

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 payers added choices through class competition and affordability, while respecting the intellectual property rights of the originator. 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.

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 product applicants should be required to demonstrate equivalence (i.e., biosimilarity) in safety (including immunogenicity) and efficacy, and no differences in purity and potency profiles between the originator reference product and the biosimilar candidate. We believe the FDA has instituted such a standard with its Totality of the Evidence approach, "including structural and functional characterization, nonclinical evaluation, human PK and PD data, clinical immunogenicity data, and comparative clinical study(ies) data."

Interchangeability

- We believe it is important to distinguish between the regulatory concept of interchangeability (unique to FDA, and pursuant to U.S. statute) and a physician's ability to exercise sound clinical judgement regarding product substitution. Recognizing that physicians and patients are in the best position to determine appropriate therapies on a case-by-case basis, the physician must always have the authority to decide which version of a biologic product is dispensed to the patient.

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- However, there is currently significant misunderstanding about the definitions and implications of the regulatory concept of interchangeability, particularly among prescribers. Merck believes that providing additional clarification of existing FDA interchangeability guidance, or new FDA guidance to facilitate regulatory claims of interchangeability, would be a critical step toward incentivizing more effective biosimilar competition with the reference biologic.

- We recommend that the FDA address interchangeability through a risk-based approach, rather than a one-size-fits-all approach for all biosimilars, regardless of risk. A one-size-fits-all approach may create unnecessary barriers (e.g., scientific analysis, time, and money), given the diversity of candidate products and evolving science. For example, a switching study may be necessary for products with a narrow benefit-risk margin, while they may not be required for products with a wide benefit-risk margin.

Intellectual Property, Naming Conventions, and Post-Marketing Commitments

- 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.

- 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 all biologics (not limited to just biosimilars), 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.

- 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.

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