

Biosimilars Public Policy Statement

Background

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. However, based on the demonstrated efficacy and safety of currently marketed biologics (originator biologics), companies are developing biosimilars, also referred to as "follow-on biologics" (FOBs) and "subsequent entry biologics" (SEBs), of these originator molecules. Biosimilars are not generic medicines. The complexity of development and manufacture of biosimilars results in a product which is similar to the originator product, but not identical.

Merck's Position on Biosimilars

- Merck supports the establishment of a regulatory pathway for approval of biosimilars that assures patient safety and preserves incentives that encourage continued biologics innovation.
- Merck supports legislation or 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 clinical trials that demonstrate safety, efficacy, and lack of deleterious immunogenicity for biosimilar products. Immunogenicity testing is a critical component of product development. Without evaluation in human subjects, we do not believe it is possible to predict either the degree of an immune response or its consequences.
- Merck does not support the interchangeability between an original biological product and a biosimilar product. The impact of interchanging products on the safety, efficacy, or immunogenicity of a product cannot be adequately predicted by analytical characterization, structure-function relationships or animal studies. It may be possible to evaluate the impact of interchangeability on safety, efficacy, and immunogenicity in human clinical studies; however, the size and duration of such studies to rule out differences (i.e., demonstrate non-inferiority) in the rates of rare but potentially clinically important events may make such an approach unfeasible.
- 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

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known about the product class and about any specific safety concerns with a given product.

- Because biosimilars are similar to an approved product (rather than the same), we believe that all biotechnology derived therapeutic proteins should have unique names so that they may be distinguished in prescribing, in dispensing, and for pharmacovigilance purposes. This could be achieved by requiring unique International Non-Proprietary Names (INNs), a process that is governed by the World Health Organization (WHO).
- Patents and data protection are both necessary incentives for biological innovation. Patent protection is necessary but not alone sufficient to provide adequate incentives for biological innovation. In the case of biologics, a product patent may provide insufficient protection if a biosimilar competitor can circumvent the patent under the similarity standard for approval of the biosimilar.
- Recognizing that biologics typically have longer development periods and higher research, development and manufacturing costs than most small molecule drugs, 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 resolve promptly any patent disputes.
- The potential for significant savings to national health care systems clearly exists if high quality biological products can be brought efficiently to the marketplace to offer patients, physicians, and payors added choices through class competition and affordability. Estimates of savings are very sensitive not only to the specific legislation or regulation enacted, but also to a range of critical assumptions about scientific, regulatory, and clinical issues, the nature of competition in markets for specific biologics, as well as future intellectual property protection, and related litigation and the development of case law. All of these factors are highly uncertain, and any one of them could have a substantial impact on the magnitude of potential savings and the speed with which they are realized.

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Merck and Schering-Plough are now one company. We are working to update our public policy position statements to reflect our new global organization.