China Solicits Comments on Biosimilars Guideline

The Center for Drug Evaluation ("the CDE") of the China Food and Drug Administration ("CFDA") recently published a long-awaited guidance document for companies seeking to develop biosimilars. This document, titled *Draft Technical Guideline for the Research, Development and Evaluation of Biosimilars* ("the Draft Guideline"), is open for public comment through November 29, 2014. The Chinese news media has reported that the CFDA had been drafting this guideline since 2012. This first-ever biosimilars guideline issued by the CDE sets forth requirements for research, development and evaluation of biosimilars, covering such areas as pharmacological assessment, preclinical studies, and clinical studies of biosimilars.

Under the Draft Guideline, a biosimilar is defined as a therapeutic biologic that is similar to an approved innovator biologic in quality, safety and efficacy, and that has the same amino acid sequence. Notably, the reference product (including active ingredients used for production or extracted from finished products) to which a biosimilar product is compared must be approved in China. Approved biosimilars cannot themselves act as reference products. The Draft Guideline generally applies to therapeutic recombinant proteins with structures and functions that are distinct enough to permit comparison of the biosimilar and reference products.

The Draft Guideline further sets forth the following basic principles for the technical review of biosimilars: (i) the comparison principle: comparative safety, effectiveness and quality data will be necessary to support the similarity to the reference product; (ii) the stepwise approach principle: biosimilarity must be demonstrated in a stepwise approach to justify exemption or simplification of a comprehensive comparative study; (iii) the consistency principle: consistency is required for samples used in and methodology applied to a comparative study; and (iv) the biosimilarity evaluation principle: biosimilarity will be evaluated based on comparison of pharmacology, pre-clinical and clinical data.

Biosimilarity is proven through (a) analytical studies that demonstrate similarity in features such as physical and chemical properties, bioactivity, and purity as compared to the reference product, (b) animal studies, including PK/PD (pharmacokinetic/pharmacodynamic) studies and toxicological assessment, and (c) clinical studies in human subjects.

Under certain circumstances, extrapolation to approved indications of the innovator reference product may be possible even where the biosimilar has not been tested for that particular indication. Extrapolated indications and the indications under development must address identical disease mechanisms or receptors and have the same mechanism of action for both the biosimilar and reference products. The safety and immunogenicity of the biosimilar product for extrapolated indications must also be sufficiently assessed during research and development.

Currently, all biologics in China are subject to the new drug approval pathway. The time for approval of new drug applications can be as long as 5-6 years. The CDE's issuance of the Draft Guideline suggests that the CFDA may be considering creating a separate pathway for biosimilars in the Drug Registration Rules and the Drug Administration Law.

If you would like to discuss the foregoing or any other related matter, please contact Katherine Wang or your usual Ropes & Gray advisor.