- The PK and biodistribution of the product in different patient populations (relevant PD measures also may provide important information on the mechanism of action);
- The immunogenicity of the product in different patient populations;
- Differences in expected toxicities in each condition of use and patient population (including whether expected toxicities are related to the pharmacological activity of the product or to "off-target" activities); and
- Any other factor that may affect the safety or efficacy of the product in each condition of use and patient population for which licensure is sought.

Differences between conditions of use with respect to the factors described above do not necessarily preclude extrapolation. A scientific justification should address these differences in the context of the totality of the evidence supporting a demonstration of biosimilarity.

In choosing which condition of use to study that would permit subsequent extrapolation of clinical data to other conditions of use, the FDA recommends that a sponsor consider choosing a condition of use that would be adequately sensitive to detect clinically meaningful differences between the two products.

The sponsor of a proposed product may obtain licensure only for a condition of use that has been previously licensed as the reference product. If a reference product has a condition of use that was licensed under section 506(c) of the FD&C Act and 21 CFR part 601, subpart E (accelerated approval), and the reference product's clinical benefit in this condition of use has not yet been verified in postmarketing trials, the proposed product sponsor should consider studying another condition of use for which the reference product is licensed to avoid potential complications in the event that postmarketing trials fail to verify the clinical benefit of the reference product for the condition of use.

*Q. I.12:* How can an applicant demonstrate that its proposed injectable biosimilar product has the same "strength" as the reference product?

*A. I.12:* Under section 351(k)(2)(A)(i)(IV) of the PHS Act, an applicant must demonstrate that the "strength" of the proposed biosimilar product is the same as that of the reference product. As a scientific matter, there may be a need to take into account different factors and approaches in determining the "strength" of different types of biological products.