An application for a biosimilar cannot be approved in the first 12 years after the initial licensure of a reference product; an application cannot be filed with the FDA during the first 4 years after the first licensure of the reference product.* Roughly comparable with 180-day exclusivity for generic drug products approved under an ANDA, the first interchangeable biosimilar receives a period during which other interchangeable biosimilars cannot be approved.†

In February 2012, a draft guidance on biosimilars was issued.‡ Early approvals for biosimilars are likely to consist of therapeutic protein products, typically produced through biotechnology. On the grand scale of all biologics, these products are "simple" biologics. At this time, "traditional" biologics, such as blood and blood products and vaccines, are far too complex to be candidates for the biosimilar approval mechanism. Likewise, so-called "frontier" biologics, such as cell-based treatments and gene therapy, are unlikely candidates.

At the time of this writing, user fee legislation for biosimilars is likely to be enacted; the user fee program would start with fiscal year 2013 (beginning October 1, 2012).

## MISCELLANEOUS

### Withdrawal of Approval of Innovator Drug

The Hatch–Waxman Amendments provide that an ANDA may be based on an innovator drug that is no longer marketed, provided the innovator drug was not withdrawn from sale for safety or effectiveness reasons.§ An ANDA sponsor that wants to base its product on a discontinued innovator drug must petition the FDA to make a determination that the product was not discontinued for safety or effectiveness reasons.¶ In addition, an ANDA may not be based on an innovator product for which the FDA has begun the formal administrative process to withdraw NDA approval for safety or effectiveness reasons.**

The withdrawal of approval of the innovator product upon which an ANDA is based can present special obstacles. In one case, the approved innovator product was in tablet form. Less than 1 month before the expiration of nonpatent exclusivity on the innovator product, the innovator firm obtained FDA approval for a capsule form of its drug product. It then discontinued the tablet form and attempted to attribute a safety reason for this decision: prevention of counterfeit versions of its tablet product and the elimination of mix-ups of the tablet product with similar appearing drug products. Thereafter, the FDA determined that the innovator tablet product had not been withdrawn for safety or effectiveness reasons. This determination

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* 42 USC § 262(k)(7).

† 42 USC § 262(k)(6).

‡ *Draft Guidance for Industry, Biosimilars: Questions and Answers Regarding Implementation of the Biosimilars Price Competition and Innovation Act of 2009*, February 2012. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM273001.pdf. Accessed June 13, 2013.

§ 21 USC § 355(j)(4)(I).

¶ 21 CFR § 314.122.

** 21 USC § 355(j)(4)(I).