In situations where the sponsor of a 505(b)(2) NDA seeks to rely on FDA's finding of finding and effectiveness for a previously approved drug product, the 505(b)(2) NDA sponsor must establish an appropriate scientific basis for that reliance. In many cases, this reliance can be justified based on "bridging" studies, often consisting of bioavailability and/or bioequivalence studies.* In addition, one or more clinical studies may be necessary to demonstrate that the proposed product is safe and effective.

Although, in theory, an ANDA can be based on any innovator product that was approved under an NDA, special hurdles exist for biological-type drug products and recombinant protein products, such as human growth hormone and insulin. These problems stem from the inherently variable nature of these products. The FDA has to date taken the position that it will not approve an ANDA for a generic version of these products because it cannot evaluate these products adequately under the Hatch–Waxman ANDA provisions; however, a 505(b)(2) NDA may be appropriate. A synthetic version of a naturally derived innovator product approved through a 505(b)(2) NDA could be regarded as having a different active ingredient than the innovator product,† meaning it cannot be rated as therapeutically equivalent.

A 505(b)(2) NDA may be appropriate for drug products that present bioequivalence difficulties, where it may be preferable to conduct a clinical trial to assess product comparability rather than a traditional bioequivalence trial. Such a drug product approved through a 505(b)(2) NDA is not automatically rated as therapeutically equivalent to its brand-name counterpart and thus could not be substituted for the innovator product by a pharmacist under typical state pharmacy laws. It may be necessary to "detail" such a product to physicians, thereby creating new marketing hurdles for some generic firms. However, where the innovator and 505(b)(2) NDA products are regarded by the FDA as "pharmaceutically equivalent" (same active ingredient, dosage form, route of administration, and strength/concentration), it may be possible to conduct additional testing to demonstrate bioequivalence and therapeutic equivalence with the innovator product.

PATENT-RELATED ISSUES

Scope of Hatch–Waxman Patent Listing Provisions

The Hatch–Waxman Amendments require each NDA sponsor to submit for Orange Book listing "any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug."‡ If such a patent issues after the NDA is approved, patent information must be submitted to the FDA within 30 days after patent issuance.§

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* FDA August 12, 2005 letter, *supra*, n. *, p. 353.

† *Compare* Premarin® ("conjugated estrogens") *with* Cenestin® ("synthetic conjugated estrogens, A"). See n. §, p. 349, *supra*.

‡ 21 USC § 355(b)(1).

§ 21 USC § 355(c)(2).