small clinical trial is used to assess bioequivalency. If these issues cannot be resolved within the Office of Generic Drugs, a "consult" opinion from the corresponding new drug review division is necessary. These "consults" are typically assigned a low priority by the new drug review division because they do not count against FDA's user fee deadlines and quotas. Waiting for a "consult" opinion can result in a delay in ANDA review and approval. Thus, in appropriate situations, a 505(b)(2) NDA may be preferable to an ANDA, as the 505(b)(2) application will get the benefit of the user fee time commitments.

Therapeutic Equivalence

Senior FDA officials have long been on record as stating that there is no evidence that an FDA-approved generic product cannot be safely and effectively substituted for its brand-name counterpart. Nevertheless, concerns have arisen at different times and in different contexts. Recently, publicized concerns have been raised by clinicians regarding apparent clinical differences between some FDA-approved generic products and their brand-name counterparts, particularly in the area of mental health and antiseizure drugs.

Under state pharmacy laws, a pharmacist may (or must) substitute a generic version of an innovator product when the physician prescribes the innovator product by brand name, unless the physician or patient objects to substitution. The substitution provisions of most state pharmacy laws cover all ANDA products that have been approved by the FDA as therapeutically equivalent to their brand-name counterparts. However, in a small number of states, state formulary boards may conduct their own review of the information and data submitted to the FDA to support an ANDA approval and may make their own decisions on product substitutability within that state. These states that engage in making their own drug substitution decisions provide another opportunity for innovator drug sponsors to block substitution. Most recently, these efforts have focused on mental health drugs. Prior efforts focused on so-called "narrow therapeutic index" drugs.

Risk Evaluation and Mitigation Strategies

The FDAAA codified a number of existing FDA practices, and granted FDA new authorities, in the areas of postapproval safety and surveillance, a major component of which is known as REMS.* In general, REMS may include labeling, communication strategies with healthcare providers, and limited distribution systems such as limiting distribution to specially certified pharmacies and practitioners.

In general, an ANDA that is approved for an innovator drug subject to REMS will have to mimic the innovator's REMS. Special challenges are presented if certain aspects of the innovator's REMS plan, such as a patient registry and a limited distribution systems, are trade secrets or are patented. If possible, all generic firms are to use a "single, shared system" with the innovator firm. However, the FDA may waive the requirement for a single, shared system if a generic firm is unable to obtain

* 21 USC § 355-1 (as added by FDAAA).