President Signs Law Reauthorizing Drug and Device User Fees: Legislation Contains Several Important FDA Reforms

On Monday, July 9, 2012, President Obama signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA). This statute reauthorizes the Prescription Drug User Fee Act (PDUFA) and the Medical Device User Fee and Modernization Act (MDUFMA), which provide a significant portion of FDA's funding for new product application review. In addition to reauthorizing these user fees, FDASIA includes a number of provisions affecting FDA regulation of drugs and medical devices. Several of the most controversial proposals ultimately were not included in the legislation, including a provision that would have established a national "track and trace" program for drugs and a provision that could have delayed FDA's ability to regulate mobile medical devices. This alert briefly summarizes the law's most important provisions.

Key Provisions in FDASIA

- ***User Fees***: In addition to reauthorizing prescription drug and medical device user fees, FDASIA introduces new user fees for generic drugs and biosimilar product applications.
    - *Generic drug fees*: FDA will establish user fees for generic drug applications for the first time, based on the total amount of such fees authorized by Congress ($299 million for FY 2013, with $50 million designated for a one-time backlog fee);
    - *Biosimilar biologic fees*: FDA will establish several new user fees for biosimilar biologic products. These include: an initial development fee, to be assessed for the submission of a request for a biosimilar biologic product development meeting, or the submission of a clinical protocol for an IND; an annual development fee, due each year following the initial development fee until a marketing application is accepted for filing by FDA, or program participation has discontinued; and, an application fee.
        - *Product application fee*: If clinical safety or efficacy data is required for approval, the fee will be equal to the amount determined by the Secretary minus the cumulative amount of fees paid for that product (i.e., development fees). If safety or efficacy clinical data is not required, the fee will be equal to half the Secretary-established amount, minus cumulative fees paid to date.
        - *Transition rule*: an initial product development fee will be assessed for IND applications submitted prior to the bill's enactment, due at the earlier of 60 days after the bill's enactment, or five days after the Secretary grants a meeting request.
- ***Medical Device Regulatory Improvements***: FDASIA includes a number of important provisions regarding medical devices.
    - *Least Burdensome Standard*: For both PMAs and 510(k)s, FDASIA clarifies that FDA can mandate only the "minimum required" clinical information to support approval or clearance. For 510(k)s, FDASIA further clarifies that the clinical information must support a determination of substantial equivalence between a new device and a predicate device; this provision appears intended in part to constrain 510(k) reviewers from requesting data not directly relevant to a substantial equivalence determination.
    - *Device Modifications*: FDASIA requires FDA to withdraw its draft guidance published in July 2011 on modifications to 510(k)-cleared devices, which industry feared would increase the number of 510(k) submissions required for minor device modifications, and requires FDA to submit a report to Congress within 18 months on the subject of device modifications.

- *Postmarket surveillance*: Under existing authority, FDA can require manufacturers of certain class II or III devices to conduct postmarket surveillance activities. FDASIA clarifies that FDA may require such surveillance at the time of PMA approval or 510(k) clearance as well as any time thereafter, and requires that the surveillance begin within 15 months of the order.
- *Device recalls*: FDASIA requires FDA to establish a program to assess information regarding device recalls, with the purpose of proactively mitigating device risks. It also requires FDA to clarify standards for conducting checks on recall effectiveness, to establish detailed criteria for determining the effectiveness of correction active plans for recalls, and to document the basis for terminating a device recall.

- ***Regulatory Improvements for Drugs***: FDASIA's provisions on drug regulation include the following.
  - *Expedited Drug Review of Breakthrough Therapies*: Under current law, a drug is eligible for expedited review as a "fast track product" if it is intended to treat a serious or life threatening disease or condition and demonstrates a potential to meet an unmet need. FDASIA establishes a new category of drugs—"breakthrough therapies"—that will also be eligible for expedited review. Breakthrough therapies are drugs designed to treat, alone or in combination with another drug or drugs, a serious or life-threatening disease or condition *and for which preliminary clinical evidence suggests substantial improvement over existing therapies*. Such drugs need not necessarily address an "unmet need," but will nevertheless be eligible for expedited review if they offer the potential for substantially improving treatments for patients with serious diseases.
  - *Rare Pediatric Disease Priority Review Voucher*: FDASIA establishes a demonstration project allowing a sponsor that develops a rare pediatric disease product to obtain a priority review voucher for a subsequent application. The priority review voucher entitles the holder to priority review of one human or biological application after the date of the approval of the rare pediatric disease product. The priority review voucher is transferrable, including by sale, from the recipient to another sponsor. The availability of new priority review vouchers will terminate one year after the Secretary awards the third voucher.
  - *Drug Supply Chain Reforms*: FDASIA gives FDA 18 months to draft regulations on the standards for admission of imported drugs, requires the Secretary to carry out drug facility inspections according to a risk-based schedule, and allows the Secretary to accept inspections performed by trusted foreign governments when establishing such schedule. It also expressly grants FDA extraterritorial federal jurisdiction for violations of the Federal Food, Drug and Cosmetic Act.
  - *Drug Shortage Reporting Requirements*: FDASIA requires the manufacturer of a drug that is life-supporting, life-sustaining, or intended for use in a debilitating disease to notify FDA of a permanent discontinuance or meaningful interruption in the drug supply at least six months prior to the date of disruption, or as soon as practicable. These new provisions broaden requirements previously established under FDA regulations.
  - *Incentives for Development of Antibiotics*: To incentivize the development of antibacterial and antifungal drugs, FDASIA establishes a new category of products known as qualified infectious disease products (QIDPs), which are eligible for five years of regulatory exclusivity. FDASIA makes clear that the new five-year exclusivity period would be in addition to any other periods of exclusivity and makes QIDPs eligible for priority review. QIDPs are antibacterial or antifungal drugs intended to treat serious or life threatening infections, including those caused by qualifying pathogens (QPs).

- *Exclusivity for a Single Enantiomer*: FDASIA reauthorizes the statutory provision that provides an exclusivity period for a drug containing a single enantiomer of a previously approved drug, under certain circumstances. The new provision clarifies that, in order for the enantiomer to be considered a different drug from the previously approved product, its approval could not rely on clinical investigations that were part of the approval for the racemic mixture.

- ***Internet Promotion***: FDASIA requires the Secretary, within two years of enactment, to issue guidance outlining FDA policy on promotion of FDA-regulated medical products on the internet, including through social media.

- ***Optimizing Global Clinical Trials***: FDASIA allows FDA to accept data from clinical trials for drugs and devices conducted outside of the United States in well-regulated countries. If FDA does not accept data from one of these jurisdictions, it will need to explain the inadequacy of the data to the drug or device sponsor. Current law allows FDA to accept foreign data under certain circumstances, but the new provision makes this the default.

If you would like to discuss the foregoing or any other related matter, please contact any member of Ropes & Gray's FDA regulatory practice or your usual Ropes & Gray advisor.