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# Congress Passes FDA User Fee Legislation

## Bill Expands User Fee Program to Include Generic Drugs and Biosimilars and Addresses Hot Button Issues Affecting Drug and Device Companies

On July 9, 2012, President Barack Obama signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA). FDASIA enjoyed swift passage through Congress with broad bipartisan support. It includes cornerstone provisions reauthorizing the FDA user fee programs for prescription drugs and medical devices and creating new user fee programs for generic drugs and biosimilars. In addition, however, FDASIA includes a number of significant changes in the areas of medical device approval and regulation, measures to improve pharmaceutical supply chain integrity and avoid drug shortages, and new incentives for developing drugs in certain underserved markets. These new provisions may help smooth the device approval process, as well as create new drug development opportunities, but may also involve additional costs for both the drug and device industry.

### Top-Line Summary

- FDASIA reauthorizes the prescription drug and medical device user fee programs and authorizes new user fee programs for generic drugs and biosimilars. These fees will be in place until October 1, 2017.
- FDASIA modifies the *de novo* device application process, permitting more flexible device reclassification and requiring clarification of certain regulatory standards and guidance.
- FDASIA includes several measures designed to address pharmaceutical supply chain integrity and drug shortage concerns.

## Background on User Fees

The user fee program represents a bargain struck between FDA and regulated industry. Industry pays a fee, used to fund FDA employee salaries, when submitting product applications for review. In exchange, FDA commits to reviewing product applications more quickly and to providing greater transparency regarding review timelines. The first user fee program was enacted in 1992, through the Prescription Drug User Fee Act (PDUFA), in response to mounting dissatisfaction regarding the time it took the agency to review and approve drug applications. User fees for medical devices followed a decade later, with the passage of the Medical Device User Fee and Modernization Act (MDUFMA) of 2002. User fees are subject to congressional reauthorization every five years, and the resulting user fee reauthorization statutes have become the primary vehicle for amending the Federal Food, Drug & Cosmetic Act.

## FDASIA User Fee Provisions

### Drug and Device User Fees

FDASIA reauthorizes the prescription drug and medical device user fee programs through October 1, 2017 (via PDUFA V and MDUFA III). FDA is authorized to collect $693 million in prescription drug and biologic user fees in FY2013. While these fees

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are certainly significant, they represent a 1.3 percent decrease from the $702 million in equivalent fee revenue included in the FY2012 budget. FDA is authorized to collect a much smaller amount in fees from the medical device industry: $595 million over the five-year period from FY2013 through FY2017. However, FDASIA also expands the types of establishments required to pay an FDA registration fee to include all establishments "engaged in the manufacture, preparation, propagation, compounding, or processing of a device."

### New User Fees for the Generic Drug Industry and Additional Fees for Foreign Manufacturers

FDASIA creates a new user fee program for generic drugs through the Generic Drug User Fee Act (GDUFA). FDA is authorized to collect $299 million each year in user fees from the human generic drug industry to support generic approval activity. $50 million of the first year's user fees will come from a one-time fee levied on sponsors of currently pending applications. Going forward, fees will apply to active pharmaceutical ingredient (API) drug master files referenced in a generic drug submission, abbreviated new drug applications, prior approval supplements, and generic drug and API facilities.

GDUFA also includes a number of measures apparently intended to address the significant disparity between FDA's inspection rates for foreign and domestic manufacturing facilities. It is widely believed that this disparity creates incentives for companies to locate their manufacturing operations abroad. The legislation imposes a $15,000 to $30,000 higher inspection fee for foreign facilities to reflect FDA's additional costs in conducting foreign inspections. Additionally, it requires that FDA achieve parity between domestic and foreign inspection schedules by FY2017. If achieved, this goal would go a long way towards leveling the playing field for generic drug manufacturers.

### Biosimilar User Fees

Among other things, the 2010 Patient Protection and Affordable Care Act created an abbreviated approval pathway for biological products that are demonstrated to be "biosimilar" to, or interchangeable with, an FDA-licensed biological product. Through the Biosimilars User Fee Act (BsUFA), FDASIA now authorizes the collection of user fees for biosimilar applications, products, establishments and certain biosimilar product development activities. These fees are set by reference to the fees applicable to prescription drug products, equalizing the expected costs to the innovator biologics and the biosimilars industry.

## Summary of Key FDASIA Provisions and Potential Impact on Industry

### Medical Device Regulation

Recent years have seen increasingly vocal criticism of FDA's medical device approval process including, in particular, the 510(k) clearance program for moderate-risk Class II devices. Industry as well as members of Congress have raised concerns that a lack of transparency in the device clearance process is stifling innovation, delaying clearance of promising medical technologies (often long beyond when those technologies are available abroad) and imposing excessive burdens. FDASIA appears to react to such criticism through a variety of measures aimed at streamlining the device approval and regulation process. These include, among others:

- ***De Novo* Pathway:** Allowing applicants to request that FDA classify certain low-risk and moderate-risk new devices for which no substantially equivalent predicate device exists into Class I or Class II without first issuing a determination that the device is not substantially equivalent (NSE) to a predicate device. This measure should substantially speed overall review times for manufacturers of such devices.

- **Device Reclassification:** Permitting FDA, based on new information, to reclassify a medical device by administrative order (published in the Federal Register and with an opportunity for public comment) instead of by regulation. This reclassification procedure likewise should streamline the device review and approval process by ensuring that devices are subject to the appropriate premarket notification or approval requirement.
- **Explanation of Significant Decisions:** Mandating that FDA provide a summary of the scientific and regulatory rationale behind an agency decision to deny clearance of a 510(k) submission, approval of a premarket approval (PMA) application or approval of an Investigational Device Exemption application, which the recipient then may use to request supervisory review. These summaries may shed some light on what historically has been viewed as an opaque review and approval process.
- **510(k) Modification Guidance:** Requiring FDA to withdraw its July 27, 2011 guidance document regarding when modifications to 510(k) devices require new 510(k) submissions, and report to Congress on the topic within 18 months. FDA may not issue new guidance on the subject until it reports to Congress and, until new guidance is issued, FDA's 1997 guidance on the topic remains the applicable standard. FDA's July 2011 guidance has garnered significant criticism for failing to clarify a confusing regulatory standard and potentially requiring the submission of more 510(k)s; the guidance FDA eventually issues hopefully will shed much-needed light in this area.
- **"Least Burdensome" Standard:** Clarifying FDA's standard for considering the clinical data required to support a premarket approval or notification submission. FDASIA explains that, for purposes of a PMA application, "necessary" data is the minimum required to demonstrate the effectiveness of a device for the conditions of use. For a 510(k) notification, "necessary" data is the minimum required to support a determination of substantial equivalence between a new and predicate device. While uncertainty remains as to the circumstances in which FDA will require clinical data to support a 510(k) submission, FDASIA suggests that FDA may only request clinical data relevant to determining substantial equivalence.

## Drug Supply Chain and Drug Shortages

Recent years have also seen increased concern regarding FDA's ability to safeguard drug products as they move through the supply chain and prevent or quickly respond to shortages of critical drugs. In the former area, concerns abound regarding drug products entering the United States from abroad, such as those stemming from the high-profile recall of heparin in 2008 due to contamination of API manufactured in China. In response, FDASIA includes a number of measures designed to ensure the integrity of the United States drug supply chain and improve communication regarding drug shortages. Significantly, FDASIA does not include controversial proposed requirements to create a national "track and trace" system for drugs. FDASIA's included measures, which are likely to lead to increased operating costs for both manufacturers and drug importers, include:

- **Drug Establishments:** Requiring the creation of a unique facility identifier, which must be included in both foreign and domestic drug establishment registrations, as well as an electronic registration and listing database for drug establishments.
- **Facility Inspections:** Mandating that drug facility inspections be carried out according to a risk-based schedule, which may take into account inspections conducted by trusted foreign governments; authorizing FDA to require a manufacturer to submit records for inspection upon request, in advance or in lieu of an inspection, at the manu-

facturer's expense; and barring the entry of imported drugs from an establishment that has delayed, limited or denied an FDA inspection.

- **Enforcement Authority:** Giving FDA greater enforcement authority with respect to counterfeit, adulterated and misbranded drug products, including increased penalties for knowing and intentional adulteration of drugs and for forging and counterfeiting drugs, and making extraterritorial violations of the FDCA subject to enforcement in the United States.
- **Drug Shortages:** Requiring manufacturers of drugs that are life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition to notify FDA of a permanent discontinuance in manufacturing or a likely meaningful supply disruption at least six months prior to the disruption, or as soon as practicable.

### Development and Approval of Certain Categories of Drugs

FDASIA includes a number of provisions designed to encourage development and production of certain currently underdeveloped categories of drugs. These provisions include:

- **Antibiotics:** Incentives for the development of new qualified infectious disease products (QDIPs) — antibacterial or antifungal drugs intended to treat serious or life-threatening infections — in the form of an additional five years of market exclusivity. QDIPs are also eligible for FDA's current priority review and fast-track review pathways.
- **Accelerated Approvals:** Requiring FDA to facilitate the development and expedite the review of fast-track products (those intended to treat a serious or life threatening disease or condition that demonstrate a potential to meet an unmet need), as well as create a new designation for "breakthrough therapies," which are intended to treat a serious or life-threatening disease or condition and supported by preliminary clinical evidence indicating that the therapy may demonstrate substantial improvement over existing therapies. Unlike products eligible for fast-track status, breakthrough therapies need not show potential to meet an unmet need.
- **Rare Pediatric Diseases:** A demonstration project that provides priority review vouchers to companies that develop products for rare pediatric diseases. The vouchers may be redeemed after the approval of the rare product application for a subsequent application or transferred to another company.

### Other Key Provisions

In addition to reauthorizing and authorizing FDA's user fee programs and significantly modifying FDA's authority to approve and regulate drugs and medical devices, FDASIA contains a number of more generalized amendments to the FDCA. Key among these are:

- **Internet Promotion:** Requiring FDA to issue a guidance document regarding the promotion of FDA-regulated medical products using the Internet, including through social media, within two years. FDA has been promising to issue social media guidance for more than three years, and it appears that Congress — like industry — has grown tired of waiting.
- **Global Clinical Trials:** Mandating that FDA (1) work with peer regulatory agencies to reduce duplication of studies necessary for premarket approval, and (2) in considering drug and device applications, either accept foreign clinical data or explain to the sponsor why it deems the foreign data inadequate. The latter provision may lead to significantly reduced development costs, but also may encourage manufacturers to conduct even more clinical trials abroad.