# Important Changes under the FDA Safety & Innovation Act: New User Fees for Generic Drugs and Biosimilars, Global Supply Regulations, and New Criminal Acts and Penalties

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On July 9, 2012, President Obama signed the Food and Drug Administration Safety and Innovation Act ("the Act"), which includes the fifth reauthorization of prescription drug fees under the Prescription Drug User Fee Act ("PDUFA V") and the third reauthorization of medical device fees under the Medical Device User Fee Act ("MDUFA III") and newly provides for similar user fees for generic drugs and biosimilars.[1] In addition to user fee authorizations, the Act follows the trend set by the Food Safety Modernization Act ("FSMA") by expanding FDA's authority to regulate global supply chains, including by expressly authorizing FDA to exercise its jurisdiction extraterritorially and strengthening FDA authority to conduct global inspections and oversee drug importation.

This client advisory proceeds by analyzing the following aspects of the Act:

- the reauthorization of existing user fees for prescription drugs and medical devices;
- the creation of new user fees for generic drugs and biosimilars;
- the expanded regulation of the global supply chain;
- the addition of newly prohibited acts and increased criminal penalties; and
- miscellaneous provisions affecting various FDA-regulated products.

## Reauthorization of User Fees for Drugs and Medical Devices

The Act provides the fifth reauthorization of PDUFA and the third reauthorization of MDUFA, both of which were set to expire on September 30, 2012. Initially enacted in 1992, PDUFA authorizes three types of fees for prescription drugs: application fees, establishment fees and product fees. For FY 2010, FDA estimates that PDUFA fees funded 62 percent of the total $931,845,581 obligated in support of the process for the review of human drug applications.[2]

The medical device user fees were initially authorized in 2002 and provide for user fees for the review of premarket applications, reports, supplements and premarket notification submissions for medical devices. FDA estimates that MDUFA fees funded approximately twenty percent of the $292,707,540 obligated in support of the process for the review of medical device submissions in FY 2010.[3]

## New Authorization of Fees for Generic Drugs and Biosimilar Biologics

As part of the Act, the Generic Drug User Fee Amendments of 2012 ("GDUFA") newly authorize four user fees for generic drugs, which are estimated to generate $299 million in revenue annually, including $50 million to be generated immediately based on a onetime backlog fee for generic drug applications pending on October 1, 2012.[4] As of July 17, 2012, FDA estimated a backlog of more than 2,500 applications for new generic drugs seeking approval.[5]

Similarly, the Biosimilar User Fee Act of 2012 ("BsUFA") newly authorizes FDA to assess six fees to support the review of marketing applications for biosimilar biological products. Biosimilar biological products are modeled after already approved biological products and the approval process is similar to the process for generic drugs modeled after already approved drugs.

## Expanded FDA Authority over Global Supply Chain

While the passage of the Act was driven primarily by the need to reauthorize user fees, it also served as a legislative vehicle to enact important changes to FDA oversight of the global supply chain. These changes were largely modeled after those enacted by FSMA, which similarly expanded FDA authority to regulate the global food supply chain. The most notable changes include:

**Extraterritorial jurisdiction.** The Act amends the Federal Food, Drug and Cosmetic Act ("FDCA")

by expressly extending FDA jurisdiction to "any article regulated under this Act if such article was intended for import into the United States or if any act in furtherance of the violation was committed in the United States."[6] Prior to the Act, there was no express authorization of extraterritorial jurisdiction, thus allowing foreign businesses to deny FDA access to their facilities without adverse consequences even if those facilities were manufacturing articles intended for import into the United States.[7] The new provision allows FDA to exercise its inspection and any other of its regulatory powers extraterritorially in regards to any FDCA-regulated product so long as the product was intended for import into the United States or if any act in furtherance of an FDCA violation occurred in the United States.

**Current good manufacturing practice (cGMP) requirements.** The Act expands on the existing requirement that facilities and methods used in the manufacture, processing, packing, or holding of drugs conform to current good manufacturing practice by adding that current good manufacturing practice "includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products."[8] The failure to do so renders the drug adulterated under FDCA section 501. As the new standard does not reference a particular jurisdiction and FDA may now exercise its authority extraterritorially, manufacturers must employ these practices across the global supply chain.

**Registration of commercial drug importers.** The Act requires commercial importers of drugs to register with FDA and instructs FDA, in consultation with the Secretary of Homeland Security, to promulgate regulations governing such registration and also establishing "good importer practices that specify the measures an importer shall take to ensure imported drugs are in compliance with the requirements of this Act and the Public Health Service Act."[9] The Act requires FDA to discontinue registration for any commercial importer that fails to follow good importer practices and makes the failure to register a prohibited act under FDCA section 301. Additionally, the Act provides that a drug that was imported or offered for import by an unregistered commercial importer will be considered misbranded under FDCA section 502.

**New standard for admission of imported drugs.** The Act authorizes FDA to require drug importers to provide information that demonstrates that the drug complies with all applicable requirements, including information demonstrating the regulatory status of the drug (e.g., the relevant drug application or drug master file number), facility information (e.g., proof of registration and the unique facility identifier), and information demonstrating compliance with good manufacturing practice (e.g., testing results and certifications).[10]

**Administrative detention authority.** The Act amends FDCA section 304(g) to extend FDA's administrative detention authority to include drugs, if during an inspection it is found that there is reason to believe a drug is adulterated or misbranded.[11] FDA administrative detention authority permits an officer or employee to order a drug detained for a reasonable period not to exceed twenty or thirty days, depending on whether FDA plans to initiate condemnation proceedings under FDCA section 304(a). Previously, FDA only had the authority to administratively detain a device or tobacco product under FDCA section 304(g) or a food product under 304(h).

**Risk-based inspections.** While maintaining the requirement of biennial inspections for medical device establishments, the Act amends FDCA section 510(h) to provide for risk-based inspections of establishments engaged in the manufacture, preparation, propagation, compounding, or processing of a drug. Under the amendments, inspection of drug manufacturing facilities, domestically and abroad, must be based on risk assessment factors, including its compliance history, its history and nature of recalls, the inherent risk of the drug being manufactured, and whether the establishment has been inspected by a foreign government.[12]

**Prohibition against delaying, denying, limiting or refusing inspection.** The Act amends FDCA section 501 to provide that a drug will be considered adulterated if it is manufactured at a facility that delays, denies, limits or refuses inspection.[13] The Act requires FDA to issue guidance that defines the circumstances that would constitute delaying, denying or limiting inspection for the purposes of amended FDCA section 501.

**Electronic databases for medical device and drug establishments.** The Act requires FDA to maintain electronic databases containing unique identifiers for any establishment engaged in the manufacture, preparation or processing of a drug or medical device.[14] The Act further requires FDA to ensure the accuracy of each database and coordinate between databases to identify and inform risk-based inspections of drug establishments.

**Acceptance of globally conducted clinical trials.** In reviewing a new drug or device for approval, FDA is expressly authorized by the Act to accept data from clinical investigations conducted outside of the United States, including the European Union, if the applicant demonstrates that such data are adequate under applicable standards to support approval, licensure, or clearance of the drug or device in the United States.[15] FDA is also directed to further harmonize global clinical trial standards.

## New Criminal Acts and Increased Penalties

In addition to expanding FDA authority to regulate the global supply chain, the Act seeks to promote drug safety by adding new criminal provisions under FDCA sections 301 and 303. Specifically, the

Act provides new prohibited acts under FDCA section 301, which are thus subject to criminal penalties provided for in FDCA section 303:

**Failure to register as a commercial importer.** The Act amends FDCA section 301 to include as a prohibited act the "failure to register in accordance with [new FDCA] section 801(s)," which requires registration of commercial importers of drugs and the discontinuance of registration of any commercial importer that fails to comply with good importer practice regulations to be established by FDA.[16]

**Failure to notify of drug-related danger, theft or counterfeiting.** The Act amends FDCA section 301 to include as a prohibited act the "failure to notify the Secretary in violation of [new FDCA] section 568," which requires a "regulated person" to notify the Secretary if the person knows (1) that the use of a drug may result in serious injury or death, (2) of a significant loss or known theft of a drug intended for use in the United States, or (3) that a drug is being counterfeited.[17] The Act defines regulated person to be a drug or device facility required to register under FDCA section 510, a commercial importer required to register under section 801(s), a wholesale distributor of a drug product, or any other person that distributes drugs except a person that distributes drugs exclusively for retail sale.

**Increased penalties for intentional adulteration.** The Act amends FDCA section 303(b) to increase penalties for any person that knowingly and intentionally adulterates a drug to allow up to 20 years imprisonment and a fine of up to $1,000,000.[18]

**Increased penalties for trafficking in counterfeit drugs.** The Act amends the federal criminal code to provide for enhanced penalties for trafficking in counterfeit drugs, permitting sentences up to 20 years imprisonment and fines up to $5 million for an individual's first offense and fines up to $15 million for the first offense of a corporation or other entity.[19]

## Other Notable Provisions

The Act also includes a number of miscellaneous provisions designed to, amongst other goals, incentivize the development of certain drugs, expedite the approval process for drugs and devices with particular emphasis on drugs for serious or life-threatening conditions, and reduce shortages of already approved drugs. Along these lines, the Act includes the following notable provisions, which affect a wide array of FDA-regulated products.

### Product-Neutral Regulations

**Nanotechnology research.** The Act directs Health and Human Services to intensify and expand activities related to enhancing scientific knowledge regarding nanomaterials included or intended for inclusion in any FDA-regulated product with particular attention directed at the potential toxicology of such nanomaterials, the potential benefit of new therapies derived from nanotechnology, the effects of such nanomaterials on biological systems, and the interaction of such nanomaterials with biological systems.[20]

**Advisory committee recruitment and conflicts of interest.** The Act directs FDA to develop and implement strategies for the recruitment of advisory committee members to ensure FDA receives diverse and disinterested advice, including by requiring FDA to request referrals for members from various stakeholders. The Act also requires FDA to disclose the type, nature and magnitude of the financial interests of any advisory committee member when certain written determinations or certifications are made by the advisory committee.[21]

### Medical Device Regulations

**Premarket approval and notification standards.** The Act provides clarification regarding the "least burdensome standard" for medical device approval and directs FDA to provide guidance on when modification to a legally marketed device requires premarket notification under FDCA section 510(k).[22]

**Recalls.** The Act directs FDA to establish a program to improve the efficiency and effectiveness of device recalls, including by clarifying procedures for conducting recall audit checks, developing detailed criteria for assessing the effectiveness of a recall, and documenting the basis for each FDA termination of a device recall.[23]

### Drug Regulations

**Infectious disease products.** The Act incentivizes the development of new qualified infectious disease products by, among other things, providing for an additional five-year market exclusivity period and eligibility for priority and fast track review for certain antibacterial or antifungal drugs intended to treat serious or life threatening conditions.[24]

**Drug labeling and disclosures.** The Act directs FDA to review and revise its communication plan to inform and educate patients and health care providers regarding the benefits and risks of medical products, with particular focus on ensuring information is provided to underrepresented subpopulations, including racial and ethnic subgroups.[25]

**Drug shortages.** The Act seeks to address shortages of approved drugs by requiring drug manufacturers to notify FDA of any interruption or discontinuance likely to lead to a meaningful disruption in the supply of certain drugs and requiring FDA to maintain a list of drugs determined to

be in shortage.[26]

### Miscellaneous Product Provisions

**Internet advertising.** The Act directs FDA to issue a guidance explaining its policy regarding the promotion of regulated medical products on the internet, including social media, by July 2014.[27]

**Sunscreen products.** The Act provides that sunscreen products subject to the final rule issued on June 17, 2011 must be in compliance by December 17, 2013 for products with annual sales of less than $25,000 or by December 17, 2012 for all other products subject to the rule.[28] The provision codifies a May 2012 rule that delayed the initial compliance dates of June 2012/2013 and means those dates cannot be pushed back any further consistent with the Act.

**Laboratory-developed tests.** The Act requires FDA to notify the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate 60 days in advance of publishing any draft or final guidance concerning the regulation of laboratory-developed tests (LDTs).[29] FDA has historically exercised enforcement discretion with regard to LDTs, but held a July 2010 public meeting suggesting that this approach should be revisited.[30]

The Act's numerous mandates and directives will require FDA to issue a series of rules and guidances to meet its obligations. FDA's ongoing implementation of FSMA may provide insight into how it will implement the Act, particularly those provisions designed to protect the global supply chain.

## Kelley Drye & Warren LLP

Kelley Drye's team of Food and Drug lawyers strives to integrate our clients' business strategies with FDA compliance and to help resolve regulatory enforcement matters when they arise. Working side-by-side with business development and marketing professionals, we provide comprehensive regulatory counseling and assist in developing products, labels, and promotional materials that achieve our clients' goals without running afoul of regulatory requirements. With close knowledge of FDA's enforcement priorities and deep experience with the FTC's regulation of advertising, our team can provide comprehensive legal advice with an eye towards giving clients a competitive edge.

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[1] Generic Drug User Fee Amendments of 2012, Pub. L. No. 112-144 § 301 (2012); Biosimilar User Fee Act of 2012, Pub. L. No. 112-144 § 401 (2012).

[2] Statement of Margaret A. Hamburg, M.D., Commissioner of Food and Drugs, before the Committee on Health, Education, Labor and Pensions, U.S. Senate (July 28, 2011), *available at:* http://www.fda.gov/NewsEvents/Testimony/ucm265170.htm.

[3] *Id.*

[4] Food and Drug Administration Safety and Innovation Act § 302, amending Food, Drug & Cosmetic Act § 744B(b).

[5] Fact Sheet: New User Fees for Generic Drugs Will Enhance Americans' Access to Less Expensive Drugs and Generate Major Cost Savings, *available at*: http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAc

[6] Food and Drug Administration Safety and Innovation Act § 718, adding Food, Drug & Cosmetic Act § 311.

[7] See Statement of Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research before the Subcommittee on Health, Discussion Draft of the "Food and Drug Administration Globalization Act" Legislation: Drug Safety (May 1, 2008), available at: http://www.fda.gov/NewsEvents/Testimony/ucm115241.htm.

[8] Food and Drug Administration Safety and Innovation Act § 711, amending Food, Drug & Cosmetic Act § 501.

[9] Food and Drug Administration Safety and Innovation Act § 714, amending Food, Drug & Cosmetic Act § 801.

[10] Food and Drug Administration Safety and Innovation Act § 713, amending Food, Drug & Cosmetic Act § 801.

[11] Food and Drug Administration Safety and Innovation Act § 709, amending Food, Drug & Cosmetic Act § 304(g).

[12] Food and Drug Administration Safety and Innovation Act § 705, amending Food, Drug & Cosmetic Act § 510(h).

[13] Food and Drug Administration Safety and Innovation Act § 707, amending Food, Drug & Cosmetic Act § 501.

[14] Food and Drug Administration Safety and Innovation Act § 704, amending Food, Drug & Cosmetic Act § 510(p).

[15] Food and Drug Administration Safety and Innovation Act § 1123, amending Food, Drug & Cosmetic Act § 569B.

[16] Food and Drug Administration Safety and Innovation Act § 714(a), adding Food, Drug & Cosmetic Act § 301(aaa).

[17] Food and Drug Administration Safety and Innovation Act § 715, amending Food, Drug & Cosmetic Act §§ 301, 568.

[18] Food and Drug Administration Safety and Innovation Act § 716, amending Food, Drug & Cosmetic Act § 303(b).

[19] Food and Drug Administration Safety and Innovation Act § 717, amending 18 U.S.C. § 2320.

[20] Food and Drug Administration Safety and Innovation Act § 1126.

[21] Food and Drug Administration Safety and Innovation Act § 1142, amending Food, Drug & Cosmetic Act § 712.

[22] Food and Drug Administration Safety and Innovation Act §§ 602, 604, amending Food, Drug & Cosmetic Act §§ 510(n), 513(a)(3)(D).

[23] Food and Drug Administration Safety and Innovation Act § 605, adding Food, Drug & Cosmetic Act § 518A. For more information on how FDA is working to improve recalls of medical devices, see Kelley Drye & Warren Client Advisory, FDA Proposes Rule Mandating Unique Device Identifiers for Medical Devices, *available at*: http://www.kelleydrye.com/publications/client_advisories/0752. [24] Food and Drug Administration Safety and Innovation Act §§ 801-06.

[25] Food and Drug Administration Safety and Innovation Act § 1138.

[26] Food and Drug Administration Safety and Innovation Act Title X, Drug Shortages.

[27] Food and Drug Administration Safety and Innovation Act § 1121.

[28] Food and Drug Administration Safety and Innovation Act § 1130; see Final Rule: Labeling and Effectiveness Testing; Sunscreen Drug Products for Over-the-Counter Human Use, 76 Fed. Reg. 35620 (June 17, 2011).

[29] Food and Drug Administration Safety and Innovation Act § 1143.

[30] Oversight of Laboratory-Developed Tests; Public Meeting; Request for Comments, 75 Fed. Reg. 34463 (June 17, 2010).