The Food and Drug Administration Safety and Innovation Act of 2012: Assessing the Impact on the Medical Device Industry

On July 9, 2012, President Obama signed the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) into law. The legislation, which stemmed from separate bills that made their way through both houses of Congress over the past several months, amends the Federal Food, Drug and Cosmetic Act (FDCA) to reauthorize the Food and Drug Administration (FDA) user fee programs for drugs and medical devices through September 30, 2017. The law also creates new user fee programs for generic drugs and biosimilars, and enacts several Agency reforms, including provisions aimed at improving various FDA regulatory processes and priorities, including the medical device review and approval process. FDASIA was developed through an extensive two-year collaboration between FDA, industry and the public, and the legislation enjoyed support throughout, including bipartisan congressional sponsorship and consistent backing from the White House. This Alert provides an overview of the statute’s medical device provisions and their impact on the regulated industry.

Medical Device User Fees

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA I) was enacted to enable user fee payments by the medical device industry to supplement congressional appropriations to FDA in return for Agency commitments to outlined performance goals. These goals focused on more timely premarket reviews and increased FDA communication and guidance in the regulatory process. The Medical Device User Fee Act (MDUFA II) was enacted in 2007 as a reauthorization of the program along with the prescription drug user fee reauthorization, and the program has, over the last 10 years, allowed FDA to help bring medical devices and diagnostics to market more quickly. However, the medical device premarket review process has faced increasing criticism in recent years for its alleged lack of transparency and consistency, which has resulted in considerable uncertainty for medical device developers and manufacturers. As a result, MDUFA reauthorization, which must occur every five years to avoid the law’s sunset provision, has been the subject of much negotiation between the Agency and regulated industry, producing significant commitments from FDA.
The Medical Device User Fee Amendments of 2012 (MDUFA III) contained in FDASIA, authorizes $595 million in user fees over the next five years in return for significant changes in FDA performance and accountability. The fees are divided into two categories — premarket application fees and establishment registration fees — both of which are nearly doubled by the new legislation from the last reauthorization of MDUFA. Much of the increase in revenue for FDA will be attributable to an expansion of the types of establishments required to pay FDA a registration fee. In return, FDA has agreed to the following:

- Earlier and more transparent and predictable interactions between FDA and applicants, both during the early product development or pre-submission stage as well as during the review process;
- More detailed and objective criteria for determining when a premarket submission is incomplete and should not be accepted for review;
- More streamlined FDA review goals that will provide better overall performance and greater predictability, including a commitment to meet with an applicant if FDA's review of its submission extends beyond the goal date, permitting the parties to discuss how to resolve any outstanding issues;
- Additional resources to support guidance development, reviewer training, and professional development, and an independent assessment of the premarket review process to identify potential enhancements to efficiency and effectiveness;
- More detailed quarterly and annual reporting of program performance; and
- A joint commitment between FDA and industry to accomplish shared outcome goals to reduce the total average calendar time to a decision for premarket applications (PMAs) and 510(k) premarket notifications.

In addition, as with all other user fee programs, FDA will be required to report to Congress on its MDUFA performance. Jeffrey Shuren, the director of FDA's Center for Devices and Radiological Health (CDRH), has reminded Congress and public stakeholders that unlike the prescription drug user fee program, which funds more than 60 percent of drug review costs, MDUFA fees fund only about a third of the total cost of the medical device premarket review process. However, with this nearly doubling of MDUFA fees in the current reauthorization, CDRH will have a harder time in the future arguing that it lacks the funding to effectively administer the medical device review program.

Medical Device Regulatory Improvements

A major industry initiative in the user fee negotiations of the past two years was to obtain certain regulatory improvements to clarify FDA authority, streamline Agency procedures, and pave a transparent path to market for new medical devices. After years of increased scrutiny for CDRH, many of the final legislation's changes have been widely supported by the regulated industry. Others have been praised by consumer safety advocates, though some claim the provisions do not go far enough to ensure device safety. On the whole, the improvements are perceived to represent a successful compromise among stakeholders and include the following provisions:

- **Investigational Device Exemptions.** FDA is required to approve investigational device exemptions (IDEs) based on the standards enumerated in the FDCA and FDA regulations. FDASIA clarifies this requirement by limiting FDA to considering the enumerated IDE standards only, not the standards applicable to potential subsequent approvals. Specifically, as amended by FDASIA, the FDCA now explicitly precludes FDA from denying an IDE on the basis that a proposed investigation may not support a premarket notification or premarket approval
application or that additional or different investigations may be necessary to support clearance or approval.

- **Clarification of the Least Burdensome Standard.** FDA is required to consider, in consultation with applicants, the least burdensome appropriate means of evaluating the data necessary to establish device effectiveness for purposes of approval. FDASIA clarifies this requirement by adding language to define the term “necessary” as “the minimum required information that would support a determination” that a PMA provides a reasonable assurance of effectiveness or that a 510(k) supports a determination of substantial equivalence, thereby reaffirming the least burdensome approach codified in the FDA Amendments Act of 2007.

- **Agency Documentation and Review of Significant Decisions.** CDRH is required, going forward, to provide a substantive summary of the scientific and regulatory rationale for any significant decision regarding an IDE, 510(k), or PMA submission, including documentation of significant controversies or differences of opinion and their resolutions. CDRH must furnish this summary to the submitter upon request, and any person, including submitters and Agency personnel, may request an expedited supervisory review of the significant decision, with an in-person or teleconference meeting if desired.

- **Device Modifications Requiring Premarket Notification Prior to Marketing.** FDASIA requires FDA to withdraw its controversial draft guidance document on when a new 510(k) must be submitted for a change to an existing device. Moreover, within the next 18 months, FDASIA requires FDA to prepare and submit a report to Congress providing FDA's interpretation of several key terms including definitions of “could significantly affect the safety or effectiveness of the device,” “a significant change or modification in design, material, chemical composition, energy source, or manufacturing process,” and “major change or modification in the intended use of the device.” In preparing the report, FDASIA requires FDA to consider the input of industry. FDASIA further restricts FDA from issuing a final guidance or proposed regulation that addresses the topic until one year after the submission of the required report to Congress. In the meantime, FDASIA confirms that the FDA's 1997 guidance document on when to submit a new 510(k) for a modification or change to an existing device will continue in effect.

- **Program to Improve the Device Recall System.** FDA is required to establish a program to routinely and systematically assess information relating to device recalls and use this information to proactively identify strategies for mitigating health risks presented by defective or unsafe devices. FDASIA further requires FDA to clarify device recall audit check procedures, develop detailed criteria for assessing recall corrective action plans, and document the basis for each device recall termination.

- **Clinical Holds on Investigational Device Exemptions.** FDASIA permits FDA to issue a clinical hold prohibiting an IDE sponsor from conducting an investigation if FDA determines that the device involved represents an unreasonable risk to clinical subject safety. FDA may also establish other reasons for issuing a clinical hold by regulation. FDA must respond in writing to a written request to remove a clinical hold within 30 days.

- **Modification of De Novo Application Process.** Under the current de novo classification process, FDA must issue a not-substantially-equivalent (NSE) determination to a premarket notification submission, automatically placing the device in Class III, before the device sponsor can submit a de novo petition to request that the device be down-classified to Class I or II due to its low or moderate risk. FDASIA modifies and therefore streamlines the de novo process.
by permitting low- or moderate-risk device sponsors to submit a de novo classification request to FDA without first submitting a 510(k) and receiving an NSE determination. In order to submit a de novo classification request to FDA under this new process, the applicant must first determine that there is no legally marketed predicate device for purposes of establishing substantial equivalence. FDA may decline the request if the device is not low- or moderate-risk, or if it determines there is a predicate device upon which it can base the review.

- **Reclassification Procedures.** FDASIA permits FDA to change the classification of a device by administrative order instead of by regulation based on new information regarding the device. Before issuing its administrative order, FDA must publish the proposed reclassification in the Federal Register and provide a substantive summary of the valid scientific evidence concerning the proposed reclassification. The amended FDCA enumerates the types of evidence that must be included in the proposed reclassification order. The Director of CDRH, in consultation with the Commissioner of FDA, is required to issue the reclassification order, and the Agency is required to provide an annual reporting of its reclassification orders on its website.

- **Harmonization of Device Premarket Review, Inspection, and Labeling Symbols.** FDA is permitted to enter into arrangements with foreign countries on harmonizing regulatory requirements, including those regarding inspections and common international labeling symbols.

- **Participation in International Fora.** The US Department of Health and Human Services Office of International Relations is currently permitted to participate in meetings with representatives of other foreign governments to work toward harmonized regulatory requirements. This authority is clarified to permit FDA participation in appropriate fora, including the International Medical Device Regulators Forum, and provide transparency on such international activities.

- **Reauthorization of Third-Party Review and Inspection.** FDASIA reauthorizes the third-party review and third-party inspection programs, under which FDA may accredit third parties to perform medical device reviews and establishment inspections, through October 1, 2017.

- **Humanitarian Device Exemptions.** Under current humanitarian device exemption (HDE) requirements, FDA may grant an exemption from the prohibition on profit for HDE devices for devices intended for use in pediatric patients. FDASIA expands this exemption to include HDE devices intended for use in adults if the device is intended to treat a disease or condition that does not occur in pediatric patients, or that occurs in such numbers that the device’s pediatric development is impossible, highly impracticable, or unsafe. Additionally, the annual distribution number for HDE devices permitted to be sold at a profit is set at the amount of devices needed to treat 4,000 individuals in the US during any calendar year unless the FDA grants a request to modify the annual distribution number.

- **Unique Device Identifier.** FDA is required to issue proposed regulations establishing the unique device identification system required under the FDA Amendments Act of 2007 no later than December 31, 2012, finalize the regulation within six months of the comment period closing, and implement the system for implantable, life-saving, and life-sustaining devices within two years after the regulations are finalized, taking into account patient access to medical devices and therapies.

- **Sentinel.** FDA is required to extend its “Sentinel” active post market risk identification and analysis system to medical devices, and to engage outside stakeholders to help ensure effective implementation of the system with respect to devices. Sentinel is a national electronic system under development that will enable FDA to query diverse automated healthcare data holders in order to proactively evaluate and mitigate possible medical product safety issues.
• **Postmarket Surveillance.** FDASIA clarifies that FDA has the authority to order a manufacturer to conduct post market surveillance for any Class II or Class III device either at the time of approval or clearance or at any time thereafter. Manufacturers must also now commence such surveillance no later than 15 months after the date of FDA's order.

• **Custom Devices.** The legal framework for custom devices, which exempts them from all premarket requirements, is restricted to apply only to devices that are created for the purpose of treating a sufficiently rare condition, such that conducting clinical investigations would be impractical. The manufacturer of such a device must now limit production to under five units per year of a particular device type, and must also notify FDA of its custom device manufacturing.

• **Health Information Technology.** FDA is required to work with the National Coordinator for Health Information Technology and the Chairman of the Federal Communications Commission to issue a report on a proposed risk-based regulatory framework pertaining to health information technology, including mobile medical applications.

• **Good Guidance Practices Relating to Devices.** FDASIA amends the FDCA to clarify that a notice to industry guidance letter, a notice to industry advisory letter, and any similar notice that sets forth initial interpretations of a regulation or policy or sets forth changes in interpretation or policy, should be treated as an FDA guidance document. By clarifying that these letters and agency interpretations are guidance documents, FDASIA confirms that these communications are subject to FDA’s good guidance practice rules.

• **Pediatric Device Consortia.** FDASIA reauthorizes the demonstration grant program for nonprofit consortia to promote pediatric device development. However, this reauthorization reduces the amount of the previous authorization level. FDA is also required to issue a regulation implementing the requirement for pediatric use device applications to include a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, and the number of affected pediatric patients.

**Additional Amendments and Provisions Pertinent to the Medical Device Industry**

The final title of FDASIA contains several provisions aimed at miscellaneous Agency reforms. Some of the more significant provisions impacting the medical device industry include the following:

• FDA must issue guidance on its policy regarding Internet and social media promotion of regulated medical products.

• FDA must work with other regulatory authorities and international organizations to foster uniform global clinical trial standards, facilitate the use of foreign data in FDA regulatory submissions and minimize the need for sponsors to conduct duplicative studies.

• FDA must solicit the views of patients during the medical product development process and consider the perspectives of patients during regulatory discussions.

• FDA will have greater flexibility under its conflict of interest rules, allowing it to fill advisory committee vacancies with experts who have a financial interest that could be affected by the advice given to FDA with respect to the matter before the advisory committee, provided FDA adequately discloses the nature of such interest.

• FDA is prohibited from issuing guidance on the regulation of laboratory developed tests, a subset of *in vitro* diagnostic devices, unless it notifies Congress of its intent to take such action 60 days prior to the issuance of the guidance.
Conclusion

Though there were many controversial proposals associated with the FDASIA legislation, most of which did not make it into the final statute, the user fee bills nonetheless enjoyed consistent support from the majority of public stakeholders through the development process, as well as backing from the White House, which lauded the bipartisan effort. FDASIA was considered “must pass” legislation, as PDUFA and MDUFA were set to expire this October without reauthorization. Many of the legislative reforms confirm or clarify the scope of FDA’s authority and require FDA to continue working with industry to successfully implement the medical device provisions. As a result, FDA and industry must now begin the onerous task of understanding, and implementing, those provisions.

Endnotes

3 See, e.g., John R. Manthei, Ben Haas & Rebecca Brandt, Medical Device Reform Is (Almost) Here: FDA Announces Action Items for Improving the Agency’s 510(k) Premarket Clearance Program, BNA MED. DEVICES L. & INDUSTRY REP. (Mar. 9, 2011) (describing the outcomes of two FDA task forces convened to review and propose changes to the 510(k) program to address “critical challenges facing the Center and [its] external constituencies”).
4 See Reauthorization of MDUFA, supra note 2.
5 Id.
8 FDA released a final guidance in March 2012 committing its PMA and de novo petition reviewers to using a benefit-risk determination worksheet in all of their reviews, and making the worksheet part of the administrative record. See FDA, “Guidance for Industry and Food and Drug Administration Staff: Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications” (Mar. 28, 2012), http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM296379.pdf; see also Ben Haas, Elizabeth Richards & Amy Gaither, Client Alert: Medical Device Benefit-Risk Determinations: FDA Releases a Novel Guidance Giving Industry an Inside View of Agency Decision-Making (Apr. 12, 2012). This provision of the FDA Safety and Innovation Act takes the commitment one step further by, among other requirements, mandating a documented rationale for all types of applications and significant decisions within the medical device review cycle.
9 FDA, “Guidance for Industry and FDA Staff: 510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device: Draft Guidance” (July 27, 2011), http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM265349.pdf. See also, Carolyne Hathaway, John Manthei, Rebecca Brandt & Elizabeth Richards, A Guide to FDA’s Draft Guidance on 510(k)s, MASS DEVICE (Oct. 19, 2011) (“Although the FDA has suggested that the new guidance does not change its current policy or practice regarding submission of 510(k)s for modified devices, it is estimated that, if finalized in its current form, the Draft Guidance will increase the number of modified devices requiring 510(k)s.”).


12 FDA issued a guidance document and convened a public meeting on mobile medical applications in 2011, but the Agency’s current stance on the topic, and health information technology in general, remains vague and uncertain. See Ben Haas, FDA Regulation of E-Health Technology and Services, in E-HEALTH, PRIVACY, AND SECURITY LAW (W. Andrew H. Gantt III ed., 2d ed. 2011).

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