Changing the Landscape for Device Manufacturers: Medical Device User Fee and Modernization Act of 2002

By John R. Manthei, Carolyne R. Hathaway and Marc Leib

Introduction

On October 26, President Bush signed into law H.R. 5651, the Medical Device User Fee and Modernization Act of 2002 (“Act”).¹ The Act reforms the Federal Food, Drug and Cosmetic Act (“FFDCA”)² in several significant respects, and enacts what are arguably the most significant series of reforms to the FFDCA for the device industry since the 1976 Medical Device Amendments.³ In particular, the Act institutes user fees for premarket submissions; allows accredited third parties to conduct Quality System Regulation (“QSR”) inspections on behalf of the FDA; establishes the Office of Combination Products within the FDA Commissioner’s Office to streamline the review of combination products; and imposes stronger premarket and postmarket controls on reprocessed medical devices that are approved or cleared for single-use only.

Title I – User Fees

For the first time, medical device premarket submissions will be subject to user fees.⁴ The fees are based on the Prescription Drug User Fee Act (PDUFA)⁵ model currently in place for the drug and biologic industries. In 2001, the average review-time for premarket approval applications (PMAs) continued to increase to 411 days, over twice as long as the statutory mandate of 180-days. At the same time, FDA has seen its staffing decrease by 10% since 1995. The fees are expected to result in more timely, higher quality reviews.

The actual fee varies depending on the type of submission. PMAs, Pre-Market Reports (newly established submissions for reprocessed versions of Class III devices approved for single use only), Panel Track Supplements, and Efficacy Supplements are all assessed the full fee. 180-day supplements will be assessed 21.5% of the full fee, Real-Time Supplements will be assessed 7.2% of the full fee, and 510(k) notifications will be assessed 1.42% of the full fee.⁶

Applications for humanitarian use, submissions sponsored by a state or the federal government, 510(k)s submitted under the third party review program, and submissions solely for pediatric indications are exempt from user fees. Pediatric use devices will be subject to user fees, however, if the applicant later pursues an adult indication for the device. In addition, reprocessors that submitted a PMA prior to October 1, 2002, and subsequently submit their first Pre-Market Report for the same product and indication are also exempt from user fees.
Rather than dictate the actual fees, the Act sets the total revenues to be generated by the new fees on an annual basis, and permits FDA to make needed adjustments. Under the Act, the user fees must generate the following revenues: $25,125,000 in federal fiscal year ("FY") 2003; $27,255,000 in FY 2004; $29,785,000 in FY 2005; $32,615,000 in FY 2006; and $35,000,000 in FY 2007. These revenue goals are adjusted upward yearly based on several factors, including: 1) inflation; 2) adjustments to reflect changes in the workload of the FDA to review device applications; 3) adjustments to reflect any cumulative surpluses or deficits from prior year fees, and 4) final year adjustments to provide fees during the first three months of FY 2008. The Act sets the initial fee at $154,000 for FY 2003, but future fee levels will partially depend on whether the fees generate the required revenues for the year. FDA will announce the new fees for the next fiscal year in a Federal Register notice by August 1st of each year.

In addition to the exemptions noted above, the Act provides for fee waivers and fee reductions for applicants that meet the definition of a “Small Business.” Under the Act, a Small Business is defined as one that has $30 million or less in gross receipts or sales in its most recent tax return, including returns of all affiliates, partners and parent firms. Fees are waived for Small Businesses submitting their first PMA or Pre-Market Report for review. Small businesses may be assessed fees for subsequent PMAs, Reports or supplements at a reduced rate of 38% of the usual fee; and a reduced rate for 510(k) notifications of 80% of the usual fee. If the $30 million Small Business threshold reduces user fee revenues by more than 16%, FDA has discretion under the Act to adjust the threshold to a lower level.

Based on the initial statutory assignment of $154,000 for the full fee, the following approximate fees will be assessed on large/small businesses for each category in FY 2003:

- PMAs, Premarket Reports, Panel Track PMA Supplements and Efficiency Supplements—$154,000/$58,520.
- 180-day supplements—$33,110/$12,582.
- Real-time supplements—$11,088/$4,213.

Fees are due upon submission of the application, but under some circumstances manufacturers are entitled to refunds of fees paid. Manufacturers whose submissions are refused for filing are entitled to a 75% refund. Manufacturers who withdraw their submissions prior to a filing decision by the FDA are also entitled to a 75% refund and those who withdraw submissions after filing but before a first action by the agency may be entitled to a refund based on the amount of effort that FDA has already expended. FDA's decision of how much, or whether to issue a refund, is not reviewable. If an applicant resubmits an application that FDA refused to file, or that the applicant withdrew, a new fee must be paid, the amount of which is determined by the agency and not subject to review.

Various consumer advocacy groups have raised concerns that user fees and the related performance goals create too close a relationship between FDA and industry, and that FDA may compromise safety standards in response to pressure to approve products quickly. The Act attempts to address these concerns by authorizing additional appropriations for postmarket surveillance—including an additional $3 million for FY 2003, $6 million for FY 2004, and “such sums that may be necessary” in subsequent years. Although authorized by the Act, FDA will not receive the funds unless they are appropriated by Congress each year. The Act also requires FDA to conduct a study, and issue a report to both the House Commerce, and Senate Labor Committees outlining the impact of the user fee program on the Agency’s ability to conduct post-market surveillance on medical devices, identifying programmatic improvements or changes necessary for adequate surveillance, and examining the extent to which user fees should be dedicated to post-market surveillance.
Title II – Device Center Reforms

Title II of the Act contains several provisions reforming the Center for Devices and Radiological Health (“CDRH”) that were advocated by the device industry, and were originally contained in H.R. 3580. These include:

Third-Party Inspections

For the first time, the Act permits FDA to accredit third-parties to inspect qualified manufacturers of Class III and Class II devices. Within 6 months of enactment, FDA is required to publish criteria for accrediting 3rd parties. The Act contains stringent conflict of interest standards to ensure that accredited 3rd parties have no financial interest in the company, the products being inspected, or any other FDA-regulated products. To qualify for accreditation, a person or entity cannot be: 1) an employee of the federal government; 2) owned, operated or controlled by a manufacturer, supplier or vendor of articles regulated under the FFDCA; or 3) engaged in the design, manufacture, promotion or sale of articles regulated under the FFDCA. The FDA must accredit 3rd party inspectors by October 26, 2003 and keep a current list of accredited inspectors on its website. It will also ensure that accredited entities remain qualified to perform their functions and will remove those that are not in compliance with the requirements.

The Act imposes several restrictions on the use of the new third party inspection program. Establishments are eligible for third-party inspections only if: 1) the most recent inspection resulted in “no action indicated” or “voluntary action indicated” reports; 2) the establishment notifies the FDA of its intent to use an accredited entity and identifies the accredited party that it will use for the inspection; 3) at least one device manufactured at the facility is marketed in the U.S. and at least one device is marketed or intended to be marketed in a foreign country that recognizes inspections by the FDA; and 4) the entity conducting the inspection did not conduct the two immediately preceding inspections of that establishment.

The FDA must respond to a request for inspection by an accredited entity within 30 days. No response by FDA within 30 days is deemed to be acceptance of the request. The FDA may, however, request additional information regarding the relationship between the establishment and the accredited entity. If it does request such information, the agency must make its decision within 60 days of its receipt, either approving or denying inspection by the requested entity. If the request is denied, the establishment may either select another accredited entity or request a review of the FDA’s decision.

The entity performing the establishment inspection must record its observations in writing and present the observations to the establishment’s designated representative. Similar to a FDA exit interview following an inspection, the 3rd party inspector must orally describe each observation. These inspection results are then presented to FDA and the establishment in a final report. The report must identify:

1) the persons responsible for good manufacturing practice compliance;
2) the dates of the inspection;
3) the scope of the inspection;
4) each observation in detail;
5) any other matters that relate to compliance; and
6) any recommendations made by the entity as a result of the inspection.

Final report must be sent to both the FDA and the establishment within three weeks after the inspection. If the inspector observes any conditions that could cause an unreasonable risk to the public health it is required to notify the FDA immediately. The Act establishes civil and criminal penalties for inspectors who do not disclose “material facts” to FDA. Compensation for inspections is paid by the establishment directly to the accredited third party performing the inspection. The amount and terms of compensation is negotiated between the manufacturer and the 3rd party.
Third-Party Review of 510(k)s
The Act extends, for five more years, the 3rd party review program established under the FDA Modernization Act of 1997 (“FDAMA”). Significantly, the program remains restricted to 510(k)s that are not supported by clinical data. Efforts by the device industry to extend the program to include all 510(k)s were not successful. The Act also requires FDA to report the results of this program to the House Commerce and Senate Labor Committees by January 10, 2007. FDA’s report must include: 1) the number of devices reviewed; 2) the number of devices approved; 3) the number of devices not approved; 4) the average time for approval by this process as compared to the time for approval by the FDA; 5) the quality of reviews under this program and whether the program has jeopardized the quality of such reviews; 6) whether the program has improved or jeopardized the public health; and 7) any suggestions for continuation, modification or termination of the 3rd party program.

Regulation of Combination Products
The Act requires the Secretary of the Department of Health and Human Services (“Secretary”) to establish a new Office of Combination Products within the FDA’s Commissioner’s Office. Prior to enactment of this provision, combination products (products that combine elements of drugs, devices and biologics) have been subject to lengthy, inconsistent reviews, and often lead FDA to apply an amalgam of sometimes inappropriate post market controls. The Office of Combination Products is tasked with ensuring prompt assignment of combination products to appropriate agency centers; timely and effective pre-market review of such products; and consistent and appropriate post-market regulation of like products. The Office will also be charged with reviewing and implementing new guidance documents governing combination products, which will likely be subject to notice and comment prior to implementation. To monitor the Office’s progress, FDA is required to issue an annual report to Congress regarding, among other things, the number and type of combination products under review, and the timeliness of assignment to agency centers.

Electronic Labeling, and Registration
The Act permits manufacturers of prescription devices intended for use in a health care facility to provide labeling for those devices solely by electronic means. The labeling must still comply with all applicable regulatory requirements. In addition, the manufacturer must provide an opportunity for the facility to request and receive labeling in paper form. The Act also now permits companies to register manufacturing establishments electronically.

PMA Modular Review Program
The Act codifies the FDA’s PMA modular review program. This highly regarded program, which is currently implemented pursuant to CDRH’s 1997 re-engineering initiative, allows PMA applicants to submit portions of a PMA for review prior to the completion of the entire application.

Intended Use Provision Now Permanent
The Act also removes the statutory sunset and codifies the “intended use” provision (Section 513(i)(1)(E) of the FFDCA) established under FDAMA. This provision requires the FDA to consider only the proposed indications for use when reviewing 510(k) notifications, unless off-label use is reasonably likely and could cause harm.

Institute of Medicine Pediatric Safety and Breast Implant Study
The Act requires the FDA to request the Institute of Medicine (“IOM”) to conduct a study to determine whether current FDA systems for post-market surveillance provide adequate safeguards regarding the use of medical devices in pediatric patients. Based on the results of this study, the FDA must issue guidance on the type of information necessary to provide reasonable assurance of safety.
and effectiveness of medical devices intended for use in pediatric patients. The FDA also must establish protections for pediatric subjects in clinical investigations. The FDA is also charged with evaluating the adequacy of information provided to women undergoing breast implant surgery. Pursuant to the directive, FDA must evaluate: 1) the type of information given to women undergoing breast implant surgery; 2) who provides this information; 3) whether the information is in written or verbal form; 4) whether the information as a whole provides a complete and accurate discussion of the risks and benefits of breast implants and the extent to which women understand the information provided; 5) the number of adverse events and whether these events have been adequately investigated; and 6) whether women participating in research studies are given adequate information to give informed consent. The Act authorizes the National Institutes of Health ("NIH") to conduct or support research to examine long-term health implications of both saline and gel filled breast implants and to report on its findings.

Title III – The Reuse Provisions

Perhaps the most controversial provisions of the bill include reforms to FDA’s regulation of the practice of reprocessing medical devices that are approved or cleared by FDA for single use only. The reforms included in Title III of the Act contain several new premarket submission requirements for reprocessed devices and will require the submission of premarket data on the maximum number of times Class III devices can be safely and effectively reprocessed. They also mandate new labeling for reprocessed devices and likely will eliminate several existing exemptions from premarket submission requirements for Class I and Class II reprocessed devices.

Premarket Submissions

Within six months of enactment, FDA must publish in the Federal Register a list of reprocessed devices that will be subjected to enhanced 510(k) requirements to ensure that they remain substantially equivalent to the predicate device after a specified number of uses. The Act provides no further guidance to FDA regarding the standard to be applied in developing its list. In order to receive 510(k) clearance, submissions for these devices must include validation data regarding cleaning, sterilization, and functional performance demonstrating the maximum number of times that the device can be safely and effectively reprocessed. Reprocessors that obtain marketing clearance before the publication of the list will be given nine months to resubmit the enhanced 510(k)s for clearance. The enhanced requirements will apply immediately to 510(k)s filed after the publication of the list.

Premarket submission and review of validation data on the maximum number of uses is a significant new requirement for reprocessed products. The existing 510(k) provisions require reprocessors to demonstrate only that the device is safe and effective for one additional use. Despite this requirement, FDA’s “multiple single use” policy has allowed reprocessors to market a product for several uses, with only self imposed limitations that are regulated by FDA through post market QSR inspections. The new reuse provision will eliminate the “multiple single-use” paradigm for these products. It is also expected to result in an affirmative label statement specifying the maximum number of times the product may legally be reprocessed.

Review of Exemption

Within six months after enactment, FDA must review and determine the viability of the existing premarket exemptions for Class I and Class II reprocessed “critical” single-use devices. FDA has eighteen months to review the viability of the existing exemptions for “semi critical” reprocessed single use devices. If the exemption is removed, reprocessors will be required to submit enhanced 510(k)s that must include validation data demonstrating the number of times the device
can be safely and effectively reprocessed. As above, these additional data will likely result in labeling that specifies the maximum number of times the device can legally be reprocessed and, significantly, will eliminate the "multiple single-use" paradigm for these products. If an exemption is removed, reprocessors will be required to file 510(k) within 15 months.

New Premarket Report Under Section 515 For Class III Devices
The Act will require reprocessors of Class III devices to file Reports under Section 515 of the FFDCA (Premarket Approval Applications) that are essentially identical in scope to the PMA submission required for the original device. The Act excepts from these stringent requirements only certain manufacturing data that is not accessible to reprocessors because it is protected by the original equipment manufacturer as trade secrets. The new amendments to Section 515 of the FFDCA restrict FDA’s ability to require anything less than full PMAs for reprocessed Class III devices. These Reports will have to comply with the same stringent requirements applicable to the submission for the original single-use product. Reports for reprocessed Class III devices will be subject to PMA user fees.

The Act also requires the Report for reprocessed Class III devices to contain validation data demonstrating the maximum number of times the device can be safely reprocessed. This is also expected to result in labeling that will state how many times the product can be legally reprocessed, and eliminate the "multiple single-use" paradigm for reprocessed, single-use Class III devices.

Changes to the Medwatch Form
To facilitate reporting of incidents involving reprocessed devices, the Act requires FDA to modify, within six months, the Medwatch (Medical Device Report) mandatory and voluntary reporting forms that are used to report patient injuries to FDA.25 This change is intended to achieve more accurate reporting of patient injuries that are caused by reprocessing that may currently be attributed to the original equipment manufacturers.

Labeling
Section 301 requires that reprocessors attach directly to the device a label that "prominently and conspicuously" identifies the reprocessor.26 FDA may, waive this requirement if compliance is “not feasible” or “would compromise the provision of reasonable assurance of the safety and effectiveness” of the device. This provision becomes effective eighteen months after enactment, and applies only to devices introduced into commerce after the effective date.

The Act also requires that reprocessed devices introduced into commerce fifteen months after the enactment date be labeled with the following statement:
"Reprocessed device for single use. Reprocessed by _______________."

Conclusion
H.R. 5651, “The Medical Device User Fee and Modernization Act” enacts historic reforms, that are intended to give FDA much needed additional resources to further strengthen CDRH review of medical devices. In addition, the User Fee, Third Party Inspection, and Reuse provisions of the Act present strategic opportunities for medical device manufacturers. Companies need to carefully review the new law to determine its impact on products already on the market as well as on devices in their product pipeline. In particular, companies should:

- Assess budgetary implication of new premarket submission fees and third party inspection provisions and make needed adjustments to ensure the timing of market entry for new products is not impacted;
- Provide the FDA with data (e.g., sterility, performance) regarding reprocessed devices that should be subjected to the FDA’s enhanced 510(k) submissions to ensure patient safety;
For combination products, assess premarket strategy, including impact on potential competitors and future versions of the product that may require premarket submissions, to position the product for assignment to either the Center for Devices, or Center for Drugs and Biologics; and

Identify opportunities to provide data to the FDA and participate in the Agency’s implementation of these requirements.

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Endnotes
1 Pub. L. 107-250.
4 See Act § 102 (adding § 738(a) to the FFDCA).
5 Pub. L. 102-517.
6 See Act § 102 (adding § 738(a) to the FFDCA).
7 See id. (adding § 738(b) to the FFDCA).
8 See id. (adding § 738(c) to the FFDCA).
9 See id. (adding §§ 738(d) and (e) to the FFDCA).
11 See Act § 104.
12 See id. at § 201.
13 See id. at § 202.
15 See Act § 204.
16 See id. at § 206.
17 See id. at § 209.
18 See id. at § 208.
19 See id. at § 212.
20 See id. at § 214.
21 See id. at § 302.
22 See id. A “critical” device is defined as one that is intended to contact normally sterile tissue or body spaces during use. A “semi-critical” device is defined as one that is intended to contact intact mucous membranes and not penetrate normally sterile areas of the body. These statutory definitions were adopted from the criteria established by E. H. Spaulding Proceedings of International Conference on Nosocomial Infections, 1970.
23 See Act § 302.
24 See id. at § 303.
25 See id. at § 301.
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