

Health Industry Alert

August 4, 2017

Senate Passes Long-Awaited FDA User Fee Package

Following nearly two years of negotiations and hearings examining the Generic Drug User Fee Amendments (GDUFA) and the Biosimilar User Fee Act (BsUFA), the Prescription Drug User Fee Act (PDUFA) and the Medical Device User Fee Amendments (MDUFA), on August 3, 2017, the Senate passed the FDA Reauthorization Act (FDARA). FDARA reauthorizes the user fee programs, which fund much of the operations of the Food and Drug Administration (FDA), for the five-year period beginning October 1, 2017. President Trump is expected to sign FDARA into law.

In addition to setting fees relating to innovator and generic drugs, biologics and biosimilars, and medical devices, and reauthorizing several related programs, FDARA also contains numerous riders of note, summarized briefly below:

Drug Provisions

- **Protecting and strengthening the drug supply chain.** This provision clarifies that prescription drugs that are both manufactured and labeled for marketing outside the United States cannot be diverted into the United States, except as authorized by the Secretary of Health and Human Services (the Secretary) for drugs on the shortage list. The provision also imposes additional criminal penalties with respect to counterfeit drugs (including knowingly making, selling or dispensing, or holding for sale or dispensing, a counterfeit drug).
- **Lowering the cost of prescription drugs.** FDARA includes a Sense of Congress provision that the Secretary should commit to engaging with Congress to enact legislative changes that lower the cost of prescription drugs. These changes should balance innovation and affordability, increase competition in the pharmaceutical market, prevent anticompetitive behavior, and promote the timely availability of high-quality and affordable generic drugs and biosimilars.
- **Competitive generic therapies.** This provision provides for expedited development and review of “competitive generic therapies” (drugs with inadequate generic competition, as defined in the provision). Under this new pathway, a generic drug sponsor would request an FDA designation as a competitive generic therapy. The FDA is directed to act on the designation request within 60 calendar days after receiving the request. The FDA is also directed to issue draft guidance within 18 months of FDARA’s enactment to describe the designation process, and finalize the guidance within one year after the close of the draft guidance comment period.

There are several benefits to receiving a competitive generic therapy designation, including increased communication and meetings with the FDA during the drug development process,

and cross-disciplinary review. Perhaps most importantly, drugs designated as competitive generic therapies are eligible for 180-day marketing exclusivity.

- **Generic review transparency.** This provision would direct the FDA to issue status updates on pending generic applications upon request by the applicant.
- **Tropical disease product applications.** This provision is intended to close a loophole and improve program integrity in the Tropical Disease priority review voucher program.
- **Government Accountability Office (GAO) study on first-cycle approvals of generic medicines.** This provision requires a GAO study of issues regarding first cycle approvals of generic medicines. The Comptroller General is directed to complete the study and submit a report to the FDA and Congress within two years of enactment.
- **Pediatric drugs.** These provisions reauthorize funding for the National Institutes of Health (NIH) to conduct pediatric trials that are not being conducted by drug sponsors. Additionally, the NIH is directed to post data when opening a docket for comments on pediatric labeling changes. The FDA is directed to link to that data.
- **Pediatric study plan.** The FDA is directed, upon request from sponsors, to conduct earlier meetings on pediatric study plans for serious or life-threatening diseases.
- **Development of drugs and biological products for pediatric cancers.** The FDA is authorized to require the study in children of adult cancer drugs that share a common target with pediatric cancer to gather dosing, safety and efficacy information. This authorization begins three years after enactment.

Device Provisions

- **Improvements to inspections process and risk-based inspections.** The inspections provisions implement a risk-based inspection schedule for medical device facilities, similar to what has already been established for drug inspections. Additionally, the FDA is required to review and update existing processes and standards for routine inspections of domestic and foreign device establishments to ensure greater transparency, which will include better communication between the inspector and the facility before, during and after the inspection. For example, in certain circumstances, the FDA is required to provide feedback to companies regarding proposed corrective actions to inspectional observations within 45 days after a request from a company. The FDA is also required to issue draft guidance on the process improvements within 18 months after enactment. Final guidance is required within one year after the draft guidance comment period closes.
- **Reauthorization of third-party inspection program.** The third-party inspection program is reauthorized through October 1, 2022. It is a voluntary program that permits eligible manufacturers, on a voluntary basis, to request inspection by accredited third parties.

- **Certificates to foreign governments for devices.** A Certificate to Foreign Government (CFG) issued by the FDA is required to show proof of FDA compliance in many markets worldwide. This provision will ensure greater transparency to the CFG process and will enable companies to receive a CFG from FDA in certain circumstances where it has been difficult in the past.

Specifically, in certain circumstances in which the FDA denies a request for a CFG, the agency is required to provide the basis for denial in writing and provide a process to request a review of a denial. An inspection report is not permitted to be the sole basis for denial, if a corrective action plan is in place. Both domestic and, under certain circumstances, foreign establishments are eligible for CFGs. Finally, the FDA is to issue draft guidance on this process within one year after enactment and final guidance within one year after the draft guidance comment period closes.

- **Postmarket device pilot projects.** The MDUFA Commitment Letter provides user fee funding for the FDA to pilot, through the National Evaluation System for Health Technology (NEST), potential premarket applications for real-world evidence. In an effort to ensure that NEST, and the FDA's efforts more broadly, also identifies postmarket applications for real-world evidence, this provision directs the FDA to initiate or continue one or more device pilot projects relating to providing timely and reliable information on postmarket device safety within one year of enactment. This provision sets forth various requirements for the projects, including that they be designed to generate safety and active surveillance data and that they inform the development of methods, systems and data criteria that could be used to support safety and active surveillance activities. Certain device types are prioritized, and the agency is required to establish conditions and processes for participation. Finally, FDA is required to report to Congress on the pilot projects being conducted within 18 months after enactment and to conduct a review through an independent third party to evaluate the pilot projects by January 31, 2021.
- **Diagnostic imaging devices** intended for use with contrast agents. These provisions provide clarity with respect to FDA regulation of diagnostic imaging devices that involve the use of contrast agents.
- **Classification of device accessories.** These provisions expand on the provision in the 21st Century Cures Act that directs the FDA to evaluate accessory devices based on their own risk, instead of the risk of their parent devices. They provide a process for the FDA to undertake classifications of accessories.

These provisions enable a sponsor to request that the FDA independently classify an accessory as part of a 510(k) or pre-market approval (PMA) submission for the parent device. In addition, for accessories that have already been granted marketing authorization as part of a submission for its parent device, (i) the FDA will propose a list every five years in the Federal Register of accessories that are suitable for a Class I classification, and (ii) there is a new

process for sponsors to submit a written request to FDA for appropriate classification of an accessory.

- **Pediatric devices.** The FDA is directed to hold a public meeting and aid device manufacturers in facilitating the development, approval or clearance, and labeling of pediatric medical devices.
- **Report on servicing devices.** This amendment directs the FDA to publish on the FDA website a report that presents information related to the regulation of servicing of devices, and how the FDA's regulation and actions relating to servicing could be improved to ensure the quality, safety and effectiveness of devices with respect to servicing. The term "servicing" includes, with respect to a device, refurbishing, reconditioning, rebuilding, remarketing, repairing, remanufacturing or other servicing of the device.
- **Facilitating international harmonization.** Congress authorizes the FDA to recognize auditing organizations that are recognized by government-established organizations to facilitate international harmonization of inspections.
- **Regulation of over-the-counter hearing aids.** These provisions direct the FDA to develop a regulatory category of over-the-counter hearing aids.

In addition to the user fee legislative package, the FDA issues a Commitment Letter for each user fee program to capture the agency's recommendations for the reauthorizations, and performance goals for fiscal years 2018–2022. Several commitments in both the PDUFA VI and MDUFA IV Commitment Letters relate to, or otherwise complement, the user fee legislation riders and are described below.

PDUFA Commitment Letter

- **Enhanced communication during drug development.** The FDA will conduct an independent assessment of current practices of the agency and sponsors in communicating during drug development, host a public workshop on the topic and update guidance based on third-party recommendations, as appropriate.
- **Advance development of combination product review.** To streamline review of combination products, the FDA will establish policies and procedures and train staff on combination product review. The agency will publish guidance describing considerations related to drug-device and biologic-device combination products.
- **Real-World Evidence (RWE).** FDA will gather input via public workshops on issues related to RWE use in regulatory decision-making, and ultimately publish draft guidance on how RWE can contribute to the assessment of safety and effectiveness in regulatory decision-making.
- **Advance postmarketing drug safety evaluation.** The FDA will expand the Sentinel System and integrate its use into the agency's pharmacovigilance activities through staff development and updating of policies and procedures. Additionally, the FDA will update policies and

procedures regarding tracking postmarketing safety signals to include consistent and timely communication with the sponsor about serious safety signals before posting safety notices.

MDUFA Commitment Letter

- **Interactive review.** The FDA will continue to incorporate an interactive review process to encourage informal communication between the FDA and applicants to facilitate timely completion of the review process based on accurate and complete information.
- **Device accessories.** The FDA and industry will explore additional mechanisms for a streamlined, resource-minimal pathway to reclassify accessories previously classified as Class III devices as a part of a PMA review if they meet the requirements of a low or moderate risk device.
- **Third-party review.** The FDA will establish a plan for eliminating routing rereview, strengthen the process for accreditation of third parties and audit reviews conducted by third parties, and publish eligibility and performance information on its website. The FDA intends to expand the scope of the program to some product codes that require clinical data and, as resources permit, pilot certain device areas.
- **Real World Evidence (RWE).** The FDA will use user fee revenues to support NEST. The NEST Coordinating Center will facilitate the use of RWE to support premarket activities, such as expanded indications for use, new clearances/approvals and improved malfunction reporting. The FDA will not require postmarket surveillance studies for devices for which registries and/or other real world data sources exist if it has access to the data and has determined that it is sufficient.
- **Streamlined malfunction reporting.** For most device procodes, the FDA will permit the manufacturers of such devices in those procodes to report malfunctions on a quarterly basis and in a summary MDR format. The FDA will publish the list of eligible device procodes within 12 months of receiving a proposed list from industry. The agency may determine that devices under a new procode (in existence for less than two years) are not eligible for quarterly summary malfunction reporting. If a new type of malfunction occurs that has not been previously reported to the FDA, an individual report must be submitted. Finally, the FDA will publish and maintain on its website a list of eligible device procodes for quarterly summary malfunction reporting. At the time the list is published, the FDA will establish a mechanism for stakeholders to request procodes to be added to the list.
- **Digital health.** The FDA will establish a central digital health unit within the Center for Devices and Radiological Health to ensure proper coordination and consistency, issue guidance on when to submit a 510(k) premarket notification for software modifications and explore premarket pathways tailored to novel digital health technologies that take into account RWE.

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The provisions in FDARA are intended to foster innovation, improve the FDA's efficiency and advance medical product safety. However, FDARA and the accompanying commitment letters only establish a framework; many of the details will be determined by guidances and informal procedures that the FDA adopts over the coming months and years. It is important that industry and other stakeholders engage with the FDA as the agency implements FDARA to ensure that the legislation achieves its full potential.

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