ROPES & GRAY

ALERT

FDA Regulatory

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FDA User Fee Reauthorization Legislation Enacted by Congress

On July 12, 2017, the House of Representatives passed H.R. 2430, the FDA Reauthorization Act of 2017 (FDARA), and on August 3, 2017, the Senate followed suit by passing FDARA without amendment by a vote of 94-1. The President is expected to sign the bill into law within days. This bipartisan legislation reauthorizes the various user fees that help fund the Food and Drug Administration's (FDA) review and oversight of prescription drugs, generic drugs, medical devices, and biosimilars. FDARA includes numerous policy riders that will impact a wide range of issues within FDA's jurisdiction. The riders are not as extensive as in years past, however, due to the recent passage of the 21st Century Cures Act. This Alert briefly summarizes the key provisions from FDARA, as well as other significant legislative proposals that failed to make the cut but are still being considered by Congress outside of the user fee reauthorization process.

Pediatric Product Development Reforms

- ***Pediatric Cancer Drug Development***: FDARA amends the Pediatric Research Equity Act (PREA) to give FDA the authority (beginning with applications submitted three years after enactment) to require that certain developers of new drugs intended to treat adult cancers conduct pediatric studies if the drug is directed at a molecular target that is substantially relevant to the growth or progression of a pediatric cancer. The new study requirements may be applied to developers of orphan drugs, which are ordinarily exempt from PREA study requirements. FDA will be required to publish and regularly update a list of molecular targets that may trigger the new study requirements, as well as a list of targets for which the study requirements will be automatically waived.

- ***Pediatric Devices***: FDARA reauthorizes until 2022 a statutory provision allowing manufacturers of pediatric devices approved through the humanitarian device exemption (HDE) pathway to sell such devices at prices that exceed their direct costs. Normally, manufacturers of HDE devices are limited to recovering the costs or research and development, manufacturing, and distribution of the device. FDARA also provides greater flexibility for HDE devices in general by allowing either an institutional review board or an "appropriate local committee" to review and approve the use of such devices. The bill also requires FDA to hold a public hearing on various issues related to pediatric device development, including the use of extrapolated data from clinical studies of adult patients, as well as the use of pediatric postmarketing registries, to enhance pediatric device labeling.

- ***Pediatric Study Plans***: FDARA requires FDA to meet early in the development process to discuss pediatric study plans with sponsors of drugs and biologics. For sponsors of drugs to treat serious or life-threatening diseases, such meetings will be required to be held no later than the end-of-phase 1 meeting. For other drugs, a meeting to discuss the sponsor's initial pediatric study plan must be held not later than 90 days after FDA's receipt of the plan.

Prescription Drug Reforms

- ***Exclusivity for Single Enantiomers***: FDARA extends through 2022 FDA's authority to grant five years of new chemical entity exclusivity to qualifying drugs containing single enantiomers.

- ***Pediatric Labeling Carve-Outs***: FDARA clarifies and expands the circumstances when pediatric labeling can be "carved out" to permit the approval of a generic drug for adult use. Currently, ANDA applicants can omit pediatric information from generic drug labeling when that information is protected by a patent or 3-year ("new clinical investigations") exclusivity. The labeling of the generic drug is required to include a disclaimer with respect to the omitted information. FDARA expands the provision to apply to 505(b)(2) drug applications as well as ANDAs, and expands the applicable categories of exclusivity to include orphan drug exclusivity, pediatric exclusivity, and qualified infectious disease product exclusivity.

- ***Orphan Drugs***: FDARA codifies FDA's existing regulatory interpretation that a sponsor must demonstrate the clinical superiority of an orphan drug that is otherwise the "same" as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity, despite a court ruling to the contrary. In *Depomed, Inc. v. HHS*, 66 F. Supp. 3d 217 (D.D.C. 2014), the court held that the Orphan Drug Act "unambiguously requires" FDA to recognize an exclusivity period for any orphan-designated drug that is approved for marketing for the orphan disease, even if it is not shown to be clinically superior to a drug that is otherwise the same. FDARA clearly establishes FDA's clinical superiority interpretation as the law. Clinical superiority will be defined as having "a significant therapeutic advantage" with respect to efficacy or safety or by providing a "major contribution to patient care."

- ***Expanded Access***: As an alternative to "right to try" legislation, FDARA includes a number of provisions related to expanded access. First, it will require FDA to convene a public meeting within 270 days to discuss clinical trial inclusion and exclusion criteria and barriers to participation, as well as how changes to clinical trial designs and criteria could affect specific populations, enrollment, or the complexity and length of trials. Within a year of FDA releasing a report on the meeting, the Comptroller General shall assess the expanded access program and the extent to which FDA has expanded individual access to investigational drugs. In addition, FDARA requires FDA to issue guidance regarding steps sponsors can take to broaden eligibility criteria for clinical trials, as well as draft guidance or new regulations to streamline institutional review board review for individual expanded access protocols.

- ***Tropical Disease Priority Review Voucher***: FDARA will reform the tropical disease priority review voucher program by requiring applicants to demonstrate they conducted or sponsored at least one clinical investigation essential to the application and that such investigation was not used as part of an application for approval in various other countries prior to September 27, 2007.

- ***Importation and Counterfeiting***: FDARA clarifies that prescription drugs, except for those on FDA's shortage list or properly imported by individuals, may not be imported for commercial use if they were manufactured in a foreign country, unless they have been approved or are otherwise authorized to be marketed in the United States and are labeled accordingly. FDARA also increases the penalties for knowingly making, selling, or dispensing a counterfeit drug.

Medical Device Reforms

- ***Over-the-Counter (OTC) Hearing Aids***: FDARA establishes a category of OTC hearing aid devices intended for adult patients with mild to moderate hearing impairment. It requires FDA to issue regulations that would, among other things, provide reasonable assurances of the safety and effectiveness of OTC hearing aid devices and describe labeling requirements. FDARA also requires FDA to determine whether such products require a 510(k) and preempts any state or local laws that restrict access to OTC hearing aids.

- ***Risk-Based Inspection Schedule***: FDARA replaces the existing biennial inspection requirement for device establishments and establishes a risk-based schedule that mirrors the schedule for drug establishments. Risk

factors that FDA will take into consideration include, among others, compliance history, prior recalls, inherent risk of the device, inspection history of the establishment, and inspections by foreign governments.

- ***Other Inspection Improvements***: FDARA requires FDA to adopt uniform processes and standards applicable to scheduled inspections of domestic and foreign device establishments that address, among other things, pre-inspection announcements and inspection-related communications with the establishment. The bill also reauthorizes the FDA's authority to conduct inspections via accredited organizations through October 1, 2022, and permits FDA to recognize auditing organizations used by foreign governmental organizations established to facilitate international harmonization.

- ***Foreign Export Certificates***: FDARA clarifies the process by which FDA issues foreign export certificates for domestic and foreign device establishments and provides a process for a manufacturer to appeal a denial and work with the agency to address any outstanding issues.

- ***Risk-Based Classification of Accessories***: Building on a device accessory provision included in last year's 21st Century Cures Act, FDARA establishes a process for classifying (or reclassifying) device accessories based on the risks associated with their intended use.

Generic Drug Access Reforms

- ***"Sense of Congress" Regarding Drug Prices***: A nonbinding "Sense of Congress" provision urges the administration to work with Congress on lowering prescription drug costs, while fostering innovation. This provision reflects widespread congressional interest in the topic of rising drug prices, a concern that likely motivated many of FDARA's provisions to expedite review of generic drug applications and expand competition.

- ***Priority Review for Certain Generic Drugs***: FDARA establishes a priority review track for certain generic drugs, requiring FDA to review within eight months any ANDA for a drug that either (1) has three or fewer approved drug products listed in the Orange Book and is no longer protected by any patent or regulatory exclusivity period, or (2) is on FDA's drug shortage list. To take advantage of this priority review provision, generic drug manufacturers will need to submit manufacturing facility information to FDA at least sixty days prior to submission of an ANDA.

- ***Competitive Generic Therapies***: FDARA authorizes FDA to expedite review of "competitive generic therapies," which refers to drugs with "inadequate generic competition" (i.e., no generic options are available or one generic drug has been approved, but the reference listed drug has been discontinued). The bill lists some of the actions FDA may take to expedite review, including holding meetings with or providing advice to the sponsor prior to submission of the application, involving senior managers and experienced review staff in cross-disciplinary review, or assigning a project lead for the FDA review team to facilitate an efficient review and serve as a liaison between the agency and the sponsor. Drugs that qualify as "competitive generic therapies" and for which there are no unexpired patents or exclusivities will also be eligible for a 180-day exclusivity period, subject to forfeiture if the applicant fails to market the drug within 75 days of approval.

- ***Inspections***: FDARA requires FDA to accelerate review of facility inspection responses and re-inspections in cases where facility issues pose the only remaining barrier to approval.

- ***Enhanced Transparency to Facilitate Generic Drug Competition***: Several FDARA provisions will enhance FDA transparency with respect to generic drugs. The bill requires the agency to update a public list of drugs with limited generic competition at least every six months, provide status updates upon request to ANDA applicants, and post quarterly reports regarding pending generic drug applications, the number of

applications that are eligible for priority or expedited review pursuant to FDARA, and the average time frame for approval.

- ***Manufacturer Reporting Regarding Marketing Status***: Within 180 days of FDARA's enactment, all holders of approved drug applications will need to review the FDA list of approved drugs and file a one-time report noting whether any of the holder's drugs in the active section of the list have been withdrawn from sale or have never been available for sale. Going forward, manufacturers will have to notify the agency 180 days prior to withdrawing an approved drug from the market. For newly approved applications, manufacturers will have to notify FDA if the drug will not be available for sale within 180 days after approval.

Other Legislative Proposals Not in FDARA

FDARA omitted several significant legislative proposals that were discussed during committee markup hearings and that have previously been introduced in Congress via separate bills. In conjunction with the passage of FDARA on August 3, the Senate passed the following bills by unanimous consent, and they will now move to the House for consideration:

- ***Right To Try***: The Senate passed the Trickett Wendler Right to Try Act of 2017 (S. 204). The bill would establish exemptions from relevant provisions of the Food, Drug, and Cosmetic Act to permit an "eligible investigational drug" to be made available to a patient who has been diagnosed with a life-threatening disease or condition, has exhausted approved treatment options, and is unable to participate in a clinical trial of the drug. An eligible investigational drug would have to have been through a Phase 1 trial. Manufacturers providing eligible investigational drugs would be required to comply with certain labeling, promotion, and pricing requirements contained in existing FDA regulations. Despite the "Right to Try" title, the legislation expressly states that a sponsor or other entity cannot be held liable for failing to provide access to an eligible investigational drug.

- ***Patient-Focused Drug Development Data***: The Senate passed the BENEFIT Act of 2017 (S. 1052), which would require FDA to consider relevant patient-focused drug development data, such as data from patient preference studies, patient-reported outcome data, or patient experience data developed by the sponsor or a third party as part of the risk-benefit assessment framework in the new drug approval process.

- ***Opioid Addiction***: The Senate passed Jessie's Law (S. 581), which requires HHS to develop standards for hospitals and physicians to display a patient's history of opioid use disorder in medical records.

Other significant legislative proposals that may still be addressed outside the reauthorization process include:

- ***OTC Drug Monograph Reform***: For more than a year, FDA and OTC industry stakeholders have been discussing a potential user fee program for OTC monograph drugs that would be intended to expedite and reform the existing OTC monograph process. Legislative proposals also contemplate exclusivity incentives for drug developers that submit original clinical data in support of the safety and effectiveness of an OTC drug. On August 23, 2017, FDA will conduct a webinar to provide a status update on the process of FDA and industry discussions regarding the potential OTC user fee program, and according to news reports, the House Energy & Commerce Committee is expected to hold a hearing in September regarding potential legislation.

- ***Manufacturer Communications***: Provisions from the Medical Product Communications Act of 2017 (H.R. 1703) and the Pharmaceutical Information Exchange Act (H.R. 2026) previously introduced in the House were discussed during committee meetings but ultimately not included in FDARA. The Medical Product Communications Act would clarify the definition of "intended use," formally define "scientific exchange,"

and confirm that FDA does not have authority to regulate scientific exchange communications, while the Pharmaceutical Information Exchange Act would expand the scope of permissible communications of health care economic information and scientific information to payors, formulary committees, and similar entities. On July 12, 2017, the Health Subcommittee of the House Energy and Commerce Committee held a hearing to discuss both of these legislative proposals and manufacturer communications issues more generally, which suggests that Congress may still pursue communications reforms independent of FDARA.

- ***Access to Branded Drugs for Generic Drug Developers***: Legislation has been proposed in both the House (Fast Generics Act of 2017, H.R. 2051) and Senate (CREATES Act of 2017, S. 974) that would ensure generic drug developers have access to branded drug products for development purposes. The generics industry has previously expressed concern that branded drug manufacturers have inappropriately withheld access to drugs that are covered by restricted distribution programs as part of their FDA-approved risk evaluation and mitigation strategies (REMS).

Next Steps

As the House and Senate take their August recesses, President Trump is expected to sign FDARA, even though his administration's budget proposal had asked Congress to reopen user fee negotiations and fund FDA entirely through user fees. Ropes & Gray will continue to monitor legislative developments in this area. If you have any questions, please contact any member of Ropes & Gray's FDA regulatory practice or your usual Ropes & Gray advisor.