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FDA User Fees: Highlights from FDARA & Our Forecast for the Next Round

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As discussed in an **earlier blog post**, the process for reauthorizing human medical product user fee programs at the Food and Drug Administration (FDA) for another 5-year period is getting started this year. Below we highlight some changes made to the programs when they were last reauthorized through the 2017 Food and Drug Administration Reauthorization Act (FDARA) (P.L. 115-52) and consider what could be included in the upcoming user fee reauthorization package.

PDUFA

The Prescription Drug User Fee Act (PDUFA) was first enacted in 1992 and authorizes FDA to collect fees from companies that manufacture certain human drugs and biological products in exchange for FDA improving the review process for new drug applications (NDAs) and biologics license applications (BLAs). With the most recent reauthorization, known as PDUFA VI, Congress and FDA created two new fee types: an application fee and an annual prescription drug program fee, which replaced the previously authorized supplemental application fee and annual establishment fee. The new fee types are assessed based on each "prescription drug product," which is defined as an approved drug with a specific strength or potency in its final dosage form that is dispensed only with a valid prescription. Because a single NDA or BLA can cover dozens of prescription drug products, PDUFA VI also limits prescription drug program fees to five fees (*i.e.*, five prescription drug products) per NDA or BLA.

Additionally, FDA committed in PDUFA VI, under the Breakthrough Therapy Program that had been created as part of the 2012 PDUFA cycle, to expedite the development and review of drug and biological products for serious or life-threatening diseases or conditions when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies. PDUFA VI provides funding and resources to this program to enable FDA to continue to work closely with sponsors throughout the designation, development, and review process for breakthrough therapies, which has been considered wildly successful. (It was so successful that Congress codified a similar program into law for medical devices in the 2016 21st Century Cures Act.)

At the same time, however, PDUFA VI has some shortcomings that we expect to be addressed by FDA and Congress as part of the next reauthorization. FDA has said that it requires additional funding to better regulate regenerative medicine products and manufacturing facilities. That industry has grown significantly in just the last few years and may seek, in exchange for fees to support a more predictable premarket review process, clarification from FDA on manufacturing standards and marketing exclusivity for non-traditional product types.

GDUFA

The Generic Drug User Fee Act (GDUFA) was originally enacted in 2012 following negotiations between FDA and the generic drug industry to improve access to generic drugs, making it a very young program in comparison to PDUFA. The first iteration of GDUFA provided FDA with resources to expedite the review of abbreviated new drug applications (ANDAs), including significant resources to eliminate a substantial backlog of ANDAs that had built up over several years and were awaiting a final FDA decision of approvability.

GDUFA II, included as part of FDARA in 2017, changed the structure of the generic drug user fee program by adding a program fee for all approved ANDA holders. User fees under GDUFA II include application fees, facility fees, and Drug Master File fees. In addition, ANDA holders will pay a fixed annual ANDA Sponsor Program fee, which depends on the number of ANDAs owned by companies (ANDA fees are divided into three tiers: small, medium, and large). Although the application fees have increased compared to the program's first iteration, the fees associated with ANDA supplements have been removed. GDUFA II also brought relief to small businesses without any approved ANDAs by postponing payment of the sponsor's facility fee until the ANDA is approved. Similarly, GDUFA II brought relief to contract manufacturing organizations (CMOs) that manufacture the product for another ANDA sponsor.

In addition to those specific fee changes, GDUFA II attempts to quicken the time for approval of certain generic product candidates for which the reference product has limited competition. FDARA requires the FDA to prioritize review of ANDAs that rely upon a reference product that has fewer than three approved

generics and ANDAs for products on the drug shortages list. This provision was not part of the GDUFA II agreement negotiated between FDA and the generics industry; rather, it is an example of how Congress can supplement the negotiated agreements with legislative riders that can be quite significant for industry.

Despite those changes, GDUFA II has also faced significant challenges that we expect will be addressed in the next reauthorization cycle as well. According to the FDA, many ANDAs are not lawfully approvable at the time they are submitted because the reference product still has market exclusivity. Therefore, the ANDA has to undergo several review cycles before it achieves final agency approval. FDA, industry, and Congress may have to think creatively to come up with potential solutions to address this particular challenge.

BsUFA

Like GDUFA, the Biosimilar User Fee Act (BsUFA) was first enacted in 2012 to enable FDA to collect fees from biosimilar companies to aid in the assessment of development programs and applications for marketing approval. A biosimilar is to a reference biological product what a generic is to a brand drug, often referred to as the reference listed drug.

BsUFA II aims to improve the predictability of funding levels and management of resources allocated to the agency's biosimilars program. BsUFA II copies several elements from PDUFA from a financial and programmatic standpoint. Additionally, as part of BSUFA II, FDA committed to devoting more user fee resources to educating health care professionals and patients about the benefits of biosimilars. In particular, FDA is establishing dedicated staff capacity for key functions such as internal training and educational outreach and communication in order to deliver information to the public and to improve public understanding of biosimilarity and interchangeability.

However, BsUFA II has also run into challenges. For instance, "Type 2" meetings between sponsors and the agency – which are meetings designed to discuss a specific issue or question in which FDA can provide targeted advice regarding the Biosimilar Product Development program – continue to suffer from timely scheduling. BsUFA I required the scheduling of Type 2 meetings to occur within 75 days of the request, which was modified in BsUFA II to be within 90 days of the request. Despite the change, however, FDA is still not meeting that performance goal. The agency also has not provided existing staff with enough resources to research and review biosimilar applications for approval. Further, FDA has struggled to hire highly educated, experienced, and talented employees, which is a problem that is unfortunately not unique to the biosimilars program.

MDUFA

The medical device user fee program, known as MDUFA, was enacted in 2002 and is on deck to be reauthorized for the fourth time, bringing us to MDUFA V. The 2017-enacted MDUFA IV created new goals for pre-submissions and introduced performance goals and a fee for De Novo device classification requests. MDUFA IV also included funding for the nascent digital health, patient input, and quality management programs housed within the Center for Devices and Radiological Health, as well as funding for the National Evaluation System for health Technology (NEST), a public-private partnership whose goals include improving the quality and quantity of real world evidence available for regulatory uses.

Because of the novelty of the NEST and sensitivity about industry funding a postmarket surveillance tool (due, in part, to the way the user fee law is written), industry limited its investment and the scope of related activities. For example, the MDUFA IV Commitment Letter requires that NEST investigate using real world evidence to support expanding the indications for use for existing devices and clearances and approvals of new devices, but it said nothing about improving postmarket surveillance (despite FDA touting such functionality as a key benefit of NEST). Further, the Commitment Letter states that NEST management will seek to make the enterprise financially self-sustaining, signaling industry's reluctance to provide funding for the program in perpetuity.

Congress, unsatisfied with the MDUFA IV agreement's limitations on the use of NEST for premarket-focused activities, included a rider in FDARA mandating that NEST be used to conduct one or more postmarket surveillance studies. Like the GDUFA legislative rider mentioned earlier, this is a good example of how Congress can supplement the user fee agreement between industry and FDA with a separate mandate. Unfortunately, however, as was the case for the mandatory NEST postmarket studies, Congress does not always provide additional funding to fulfill its mandates.

We expect to see NEST as a subject of continued discussion in the MDUFA V negotiations. Further, we expect the agency's De Novo and pre-submission performance goals will be refined based on experience and data gathered during the MDUFA IV period. We also anticipate a rider about an issue that has remained unresolved despite Congressional interest during the last user fee reauthorization cycle: medical device servicing. We have **covered** this **topic** extensively over the past several years; in short, there continues to be concerns about the safety of devices serviced without appropriate regulatory oversight, but defining and getting servicers and original equipment manufacturers (OEMs) to agree on what level of regulatory oversight is appropriate remains a challenge.

New and Emerging User Fee Programs

OTC Drug Monographs

We're optimistic that over-the-counter (OTC) drug monograph reform legislation will be enacted soon thanks to the Senate's passage in late 2019 of a bill that aligns with legislation passed by the House earlier in 2019. A key provision in both the House and Senate OTC monograph reform bills is a user fee program for FDA that, like the other human medical product user fee programs, would provide for funding from industry in exchange for improvements to the review of the safety and efficacy of ingredients included or proposed to be included in a monograph. (FDA **describes** an OTC monograph as like a "'recipe book' covering acceptable ingredients, doses, formulations, and labeling" and that "once a final monograph is implemented, companies can make and market an OTC product without the need for FDA pre-approval.") As we wrote in **2017**, both FDA and the OTC drug industry are ready to implement such a program. The parties went as far as holding a series of public meetings in 2016 and 2017 and drafting a Commitment Letter for the would-be OTC Monograph User Fee program that the agency has been referring to as OMUFA.

Laboratory Developed Tests

Additionally, we are eager to see whether and how Congress will resolve the years-long discussion about how best to assure the safety and effectiveness of laboratory developed tests (LDTs), which—with in vitro diagnostic (IVD) devices—have been proposed to be renamed In Vitro Clinical Tests (IVCTs). These IVCTs would become subject to a new regulatory model outlined in discussion drafts of the Verifying Accurate and Leading-Edge IVCT Development (VALID) Act. Although the VALID Act was expected to be formally introduced in Congress in late 2019, it has yet to make an official debut. Notably, however, the discussion drafts provide for a user fee program that would need to be negotiated between FDA, clinical labs, and IVD manufacturers. That means 2020 would be a good year to enact such a significant change to current law because it would give FDA and those stakeholders time to negotiate the structure and goals for this new user fee program in advance of the 2022 reauthorization deadline for the other human medical product user fee programs. (IVDs, which today are approved or cleared under FDA's device authorities, are currently subject to the review timelines and fees under MDUFA.)

Digital Health

Lastly, we believe that FDA's move toward a new regulatory paradigm for digital health products (*i.e.*, software, including mobile apps) creates an opportunity for a new user fee model for such products. FDA has touted more streamlined premarket review (in some cases, no premarket review) for software that is eligible to participate in its **Pre-Cert program** (currently being **piloted**). How will the user fee program for medical devices adapt if the traditional PMA, De Novo, and 510(k) review timelines no longer apply to digital health products? With increasing Congressional interest in the FDA's oversight of software, we anticipate this will be a hot topic during the upcoming user fee reauthorization cycle.

We will continue to monitor and report on agency, Congressional, industry, and other stakeholder activity as the user fee reauthorization process gets underway this year. If any of our readers are interested in hearing more or learning about how to get involved in these deliberative processes, please reach out to **Aaron Josephson** at ML Strategies or your regular Mintz professional who can put you in touch with the **Mintz & ML Strategies FDA team**.

Authors