Some May Come and Some May Go: FDARA Brings Changes to User Fees and Other FDA Programs

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On August 18, 2017, the President signed the FDA Reauthorization Act of 2017 (FDARA), which revises and extends several of FDA's user fee programs.[1] The user fee programs establish filing fees for various application types and other fees, and FDA's review performance goals. FDARA reauthorizes the following user programs:

- Prescription Drug User Fee Amendments (PDUFA)
- Medical Device User Fee Amendments (MDUFA)
- Generic Drug User Fee Amendments (GDUFA)
- Biosimilar User Fee Act (BsUFA)

The changes to the user fee programs will take effect at the beginning of the 2018 fiscal year (FY), October 1, 2017, and will need to be reauthorized for FY 2023. FDARA also includes additional changes to the Federal Food, Drug, and Cosmetic Act (FDCA) affecting orphan drugs and pediatric drugs and devices. In this bulletin, we provide an overview of major changes to PDUFA, MDUFA, and GDUFA, as well as some changes affecting pediatric products and the orphan drug program.

PDUFA

FDARA reauthorizes PDUFA for the fifth time (PDUFA VI). The most significant changes in PDUFA VI are the elimination of two types of user fees.[2] The first is the elimination of a user fee for a supplement application. Supplement applications are used when there is a change to a drug with an approved New Drug Application (NDA) or Abbreviated New Drug Application (ANDA). Changes that have "substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency" are considered "major changes" and may require clinical data.[3] The user fee for a supplement with clinical data (other than bioavailability or bioequivalence studies) was one half of the full NDA fee; in FY 2017 the user fee for a supplement with clinical data was $1,019,050.[4] FDARA eliminates all user fees for supplements.

The other major fee for drug manufacturers that has been eliminated by FDARA is the establishment registration fee. The establishment registration fee was assessed annually for each party named as the applicant in a human drug application, with some limited exceptions, and for each listed establishment that manufacturers a prescription drug.[5] In FY 2017, the annual establishment registration fee was $512,000.[6] Although the establishment fee has been eliminated, the establishment registration and drug listing requirements are still in effect. The PDUFA VI user fees will be $2,410,495 for an NDA with clinical data and $1,210.748 for an application not requiring clinical data.[7]

1 https://www.congress.gov/bill/115th-congress/house-bill/2430/text
2 21 U.S.C. § 379h(a)(1)
3 21 C.F.R. 314.70(b)
4 https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/
5 21 U.S.C. § 379h(a)(2)
6 https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/
7 https://www.federalregister.gov/documents/2017/09/14/2017-19494/prescription-drug-user-fee-rates-for-fiscal-year-2018

MDUFA

The second reauthorization of MDUFA, MDUFA III, creates a new user fee for medical device *de novo* classification requests.[8] Medical devices that have no legally marketed predicate device are automatically classified as Class III devices. However, the *de novo* process allows applicants to seek classification as a Class I or II device without a predicate device under certain circumstances.[9] Prior to FDARA, there was no fee associated with these applications. Now, the user fee for a *do novo* request will be 30% that of a PMA; in FY 2018 the *de novo* fee will be $93,229 for the standard fee and $23,307 for a qualifying small business fee.[10]

GDUFA

In the first reauthorization of GDUFA, GDUFA II, FDARA creates a new annual program user fee, which is based on the number of approved ANDAs the applicant holds. There will be three tiers of program fees: small, medium, and large. In GDUFA II, 35% of the user fee revenue will come from the new program fees.[11] The number of approved ANDAs that define each tier, the annual program fee, and the total number of applicants in each tier as of April 30, 3017 are as follows:[12]

Tier	Number of Approved ANDAs	FY 2018 Program Fee	Total Applicants
Small	1-5	$159,079	339
Medium	6-19	$636,317	74
Large	20+	$1,590,792	65

Additionally, under GDUFA II, there is also a significant increase in the ANDA application fee. In FY 2017, the ANDA fee was $70,480; in FY 2018 it will jump to $171,823.[13]

GDUFA II also includes, for the first time, a facility fee for contract manufacturers, which is one-third the fee assessed to noncontract manufacturers.[14] Foreign contract manufacturers will also pay an additional $15,000. In FY 2018, the facility fee for a domestic contract manufacturer will be $70,362 and $85,362 for foreign contract manufacturers.

Orphan Drugs

FDARA codifies FDA's longstanding practice regarding clinical superiority of orphan drugs in the FDCA.[15] In order to grant orphan exclusivity to a drug that is the same as a drug already approved for the same orphan indication, the sponsor must show that its new product is "clinically" superior to the existing product.[16] Clinical superiority is established by showing that the new product has a therapeutic advantage in safety or efficacy, or by providing a major contribution to patient care.[17] In effect, this standard means that a drug that has orphan designation will be granted orphan exclusivity even if it is the same as an already approved drug for the same orphan indication, if the sponsor can show clinical superiority.

8 21 U.S.C. 379j(a)
9 21 U.S.C. 360c(f)
10 https://www.fda.gov/ForIndustry/UserFees/MedicalDeviceUserFee/ucm573383.htm
11 21 U.S.C. § 379j-42(b)(2)(E)
12 https://www.federalregister.gov/documents/2017/08/29/2017-18377/generic-drug-user-fee-rates-for-fiscal-year-2018
13 https://www.federalregister.gov/documents/2017/08/29/2017-18377/generic-drug-user-fee-rates-for-fiscal-year-2018
14 21 U.S.C. § 379j-42(b)(2)(C)
15 21 CFR 316.3(b)(13)
16 21 U.S.C. § 360cc(c)
17 *Id.*

Pediatric drugs and devices

FDARA also corrects a discrepancy regarding labeling carve-outs of pediatric information in drug applications. Applicants are permitted to "carve out" information that is protected by a patent or exclusivity in their proposed labeling, as long as the product as labeled would still be safe and effective. The FDCA expressly permits such labeling carve-outs of protected pediatric information for ANDAs submitted under section 505(j).[18] FDARA expands this provision to also include NDAs submitted under section 505(b)(2).

There are a few FDARA provisions that affect several different pediatric programs for both drugs and devices. FDARA reauthorizes through 2022 the provision in the FDCA allowing manufacturers of pediatric devices that were approved through the humanitarian use exemption to sell their devices for an amount greater than their direct cost.[19] Humanitarian use devices (HUD) are intended to benefit patients in the treatment or diagnosis of a disease that affects fewer than 8,000 people per year in the United States. There are only two narrow exceptions that allow a HUD to be sold for a profit, one of which applies to devices for pediatric patient populations or subpopulations.

AGG Observations

1. The codification of FDA's clinical superiority in the FCDA essentially nullifies the precedent set by *Depomed, Inc. v. HHS*.[20] In that case, the court found that under that Orphan Drug Act a drug that was granted orphan designation is automatically entitled to orphan exclusivity upon approval, even it is not clinically superior to an already approved product for the same condition with the same active ingredient. After the decision, FDA issued a policy clarification on orphan drug exclusivity saying it interpreted the court's decision in *Depomed* to apply only to the drug at issue in that case and that it would continue to apply its clinical superiority framework.[21] By amending the FDCA to add the clinical superiority requirement, the inconsistency between case law and FDA policy is eliminated.
2. The GDUFA II user fee framework has changed significantly. Under GDUFA I, 56% of user fees came from facility fees, which has now been reduced to 20% under GDUFA II. As noted above, there is also a new annual program fee based on the number of approved ANDAs an applicant holds. ANDA holders should review the changes closely as they will be subject to different fees beginning October 1.

18 21 U.S.C. § 355a(o)
19 21 U.S.C. § 360e-1(a)(3)
20 66 F.Supp. 3d 217 (D.D.C. 2014)
21 https://www.gpo.gov/fdsys/pkg/FR-2014-12-23/pdf/2014-29920.pdf

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