4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-N-0007]

Fee for Using a Rare Pediatric Disease Priority Review Voucher in Fiscal Year 2017

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing the fee rate for using a rare pediatric disease priority review voucher for fiscal year (FY) 2017. The Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Food and Drug Administration Safety and Innovation Act (FDASIA), authorizes FDA to determine and collect rare pediatric disease priority review user fees for certain applications for review of human drug or biological products when those applications use a rare pediatric disease priority review voucher. These vouchers are awarded to the sponsors of rare pediatric disease product applications that meet all of the requirements of this program, are submitted 90 days or more after July 9, 2012, and upon FDA approval of such applications. The amount of the fee for using a rare pediatric disease priority review voucher is determined each FY based on the difference between the average cost incurred by FDA in the review of a human drug application subject to priority review in the previous FY, and the average cost incurred in the review of an application that is not subject to priority review in the previous FY. This notice establishes the rare pediatric disease priority review fee rate for FY 2017 and outlines the payment procedures for such fees.

FOR FURTHER INFORMATION CONTACT: Robert J. Marcarelli, Office of Financial Management, Food and Drug Administration, 8455 Colesville Rd., COLE-14202F, Silver Spring, MD 20993-0002, 301-796-7223.

SUPPLEMENTARY INFORMATION:

I. Background

Section 908 of FDASIA (Pub. L. 112-144) added section 529 to the FD&C Act (21 U.S.C. 360ff). In section 529 of the FD&C Act, Congress encouraged development of new human drugs and biological products for prevention and treatment of certain rare pediatric diseases by offering additional incentives for obtaining FDA approval of such products. Under section 529 of the FD&C Act, the sponsor of an eligible human drug application submitted 90 days or more after July 9, 2012, for a rare pediatric disease (as defined in section 529(a)(3)) shall receive a priority review voucher upon approval of the rare pediatric disease product application. The recipient of a rare pediatric disease priority review voucher may either use the voucher for a future human drug application submitted to FDA under section 505(b)(1) of the FD&C Act (21 U.S.C. 355(b)(1)) or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)), or transfer (including by sale) the voucher to another party. The voucher may be transferred (including by sale) repeatedly until it ultimately is used for a human drug application submitted to FDA under section 505(b)(1) of the FD&C Act or section 351(a) of the Public Health Service Act. A priority review is a review conducted with a Prescription Drug User Fee Act (PDUFA) goal date of 6 months after the receipt or filing date, depending on the type of application. Information regarding PDUFA goals is available at http://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf.

The applicant that uses a rare pediatric disease priority review voucher is entitled to a priority review of its eligible human drug application, but must pay FDA a rare pediatric disease priority review user fee in addition to any user fee required by PDUFA for the application. Information regarding the rare pediatric disease priority review voucher program is available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm375479.htm.

This notice establishes the rare pediatric disease priority review fee rate for FY 2017 at $2,706,000 and outlines FDA's procedures for payment of rare pediatric disease priority review user fees. This rate is effective on October 1, 2016, and will remain in effect through September 30, 2017.

II. Rare Pediatric Priority Review User Fee for FY 2017

Under section 529(c)(2) of the FD&C Act, the amount of the rare pediatric disease priority review user fee is determined each fiscal year based on the difference between the average cost incurred by FDA in the review of a human drug application subject to priority review in the previous fiscal year, and the average cost incurred by FDA in the review of a human drug application that is not subject to priority review in the previous fiscal year.

A priority review is a review conducted with a PDUFA goal date of 6 months after the receipt or filing date, depending on the type of application. Under the PDUFA goals letter, FDA has committed to reviewing and acting on 90 percent of the applications granted priority review status within this expedited timeframe. Normally, an application for a human drug or biological product will qualify for priority review if the product is intended to treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. An application that does not receive a priority designation will receive a standard review. Under the PDUFA

goals letter, FDA has committed to reviewing and acting on 90 percent of standard applications within 10 months of the receipt or filing date depending on the type of application. A priority review involves a more intensive level of effort and a higher level of resources than a standard review.

Section 529 of the FD&C Act specifies that the rare pediatric disease priority review voucher fee amount must be based on the difference between the average cost incurred by the Agency in the review of a human drug application subject to a priority review in the previous fiscal year, and the average cost incurred by the Agency in the review of a human drug application not subject to a priority review in the previous fiscal year. FDA is setting a fee for FY 2017, which is to be based on standard cost data from the previous fiscal year, FY 2016. However, the FY 2016 submission cohort has not been closed out yet, thus the cost data for FY 2016 are not complete. The latest year for which FDA has complete cost data is FY 2015. Furthermore, because FDA has never tracked the cost of reviewing applications that get priority review as a separate cost subset, FDA estimated this cost based on other data that the Agency has tracked. FDA uses data that the Agency estimates and publishes on its Web site each year--standard costs for review. FDA does not publish a standard cost for "the review of a human drug application subject to priority review in the previous fiscal year." However, we expect all such applications would contain clinical data. The standard cost application categories with clinical data that FDA publishes each year are: (1) New drug applications (NDAs) for a new molecular entity (NME) with clinical data and (2) biologics license applications (BLAs) with clinical data.

The standard cost worksheets for FY 2015 show standard costs (rounded to the nearest thousand dollars) of $5,251,000 for an NME NDA, and $5,055,000 for a BLA. Based on these standard costs, the total cost to review the 56 applications in these two categories in FY 2015 (32

NME NDAs and 24 BLAs with clinical data) was $289,352,000. (Note: These numbers exclude the President's Emergency Plan for AIDS Relief NDAs; no investigational new drug (IND) review costs are included in this amount.) Twenty-five of these applications (18 NDAs and 7 BLAs) received priority review, which would mean that the remaining 31 received standard reviews. Because a priority review compresses a review schedule that ordinarily takes 10 months into 6 months, FDA estimates that a multiplier of 1.67 (10 months divided by 6 months) should be applied to non-priority review costs in estimating the effort and cost of a priority review as compared to a standard review. This multiplier is consistent with published research on this subject which supports a priority review multiplier in the range of 1.48 to 2.35 (Ref. 1). Using FY 2015 figures, the costs of a priority and standard review are estimated using the following formula:

$$(25\ \alpha \times 1.67) + (31\ \alpha) = \$289{,}352{,}000$$

Where "α" is the cost of a standard review and "α times 1.67" is the cost of a priority review. Using this formula, the cost of a standard review for NME NDAs and BLAs is calculated to be $3,977,000 (rounded to the nearest thousand dollars) and the cost of a priority review for NME NDAs and BLAs is 1.67 times that amount, or $6,642,000 (rounded to the nearest thousand dollars). The difference between these two cost estimates, or $2,665,000, represents the incremental cost of conducting a priority review rather than a standard review.

For the FY 2017 fee, FDA will need to adjust the FY 2015 incremental cost by the average amount by which FDA's average costs increased in the 3 years prior to FY 2016, to adjust the FY 2015 amount for cost increases in FY 2016. That adjustment, published in the Federal Register on July 28, 2016 (see 81 FR 49674 at 49676), setting the FY 2017 PDUFA fee, is 1.5468 percent for the most recent year, not compounded. Increasing the FY 2015 incremental

priority review cost of $2,665,000 by 1.5468 percent results in an estimated cost of $2,706,000 (rounded to the nearest thousand dollars). This is the rare pediatric disease priority review user fee amount for FY 2017 that must be submitted with a priority review voucher for a human drug application in FY 2017, in addition to any PDUFA fee that is required for such an application.

III. Fee Schedule for FY 2017

The fee rate for FY 2017 is set out in table 1:

Table 1.--Rare Pediatric Disease Priority Review Schedule for FY 2017

Fee Category	Fee Rate for FY 2017
Application submitted with a rare pediatric disease priority review voucher in addition to the normal PDUFA fee	$2,706,000

IV. Implementation of Rare Pediatric Disease Priority Review User Fee

Under section 529(c)(4)(A) of the FD&C Act, the priority review user fee is due (i.e. the obligation to pay the fee is incurred) when a sponsor notifies FDA of its intent to use the voucher. Section 529(c)(4)(B) of the FD&C Act specifies that the application will be considered incomplete if the priority review user fee and all other applicable user fees are not paid in accordance with FDA payment procedures. In addition, section 529(c)(4)(C) specifies that FDA may not grant a waiver, exemption, reduction, or refund of any fees due and payable under this section of the FD&C Act. Beginning with FDA's appropriation for FY 2015, the annual appropriation language states specifically that "priority review user fees authorized by 21 U.S.C. 360n and 360ff (section 529 of the FD&C Act) shall be credited to this account, to remain available until expended." (Pub. L. 113-235, Section 5, Division A, Title VI).

The rare pediatric disease priority review fee established in the new fee schedule must be paid for any application that is received on or after October 1, 2016. In order to comply with this requirement, the sponsor must notify FDA 90 days prior to submission of the human drug application that is the subject of a priority review voucher of an intent to submit the human drug

application, including the date on which the sponsor intends to submit the application.

Upon receipt of this notification, FDA will issue an invoice to the sponsor who has incurred a rare pediatric disease priority review voucher fee. The invoice will include instructions on how to pay the fee via wire transfer or check.

As noted in section II, if a sponsor uses a rare pediatric disease priority review voucher for a human drug application, the sponsor would incur the rare pediatric disease priority review voucher fee in addition to any PDUFA fee that is required for the application. The sponsor would need to follow FDA's normal procedures for timely payment of the PDUFA fee for the human drug application.

V. Reference

The following reference is on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and is available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Ridley, D. B., H. G. Grabowski, and J. L. Moe, "Developing Drugs for Developing Countries," Health Affairs, vol. 25, no. 2, pp. 313-324, 2006.

Dated: September 26, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016-23624 Filed: 9/29/2016 8:45 am; Publication Date: 9/30/2016]