FDA Draft Guidance Clarifies Criteria and Process for Obtaining Rare Pediatric Disease Priority Review Vouchers

On November 17, 2014, the Food and Drug Administration ("FDA") released a draft guidance entitled *Rare Pediatric Disease Priority Review Vouchers*, which describes an incentive program for the development of drugs intended to treat rare pediatric diseases. Congress established this program more than two years ago when it enacted the Food and Drug Administration Safety and Innovation Act, adding section 529 to the Federal Food, Drug, and Cosmetic Act. Section 529 provides that the sponsor of a "rare pediatric disease product application," upon approval of such application, is eligible for a voucher that can be used to obtain priority review for a subsequent new drug application ("NDA") or biologics license application ("BLA"). Priority review means that an application has an FDA review clock of six months, rather than the standard review clock of ten months.[1]

FDA's draft guidance clarifies key statutory definitions, explains the processes by which sponsors can request a rare pediatric disease designation and a rare pediatric disease priority review voucher, and elaborates on other aspects of the program, including the transferability of vouchers and the relationship between rare pediatric disease designation and orphan drug designation.

Definition of a Rare Pediatric Disease Product Application

Under section 529(a)(4), a rare pediatric disease product application is defined as a human drug application (i.e., an NDA or BLA, with limited exceptions) that meets the following criteria:

- Is for the prevention or treatment of a "rare pediatric disease," meaning a disease that satisfies the definition of "rare disease or condition" under the Orphan Drug Act and that primarily affects individuals from 0-18 years old;
- Is for a drug that contains no active ingredient (including any ester or salt of the active ingredient) previously approved in another application;
- Is deemed by FDA as eligible for priority review;
- Is not an abbreviated new drug application or biosimilar application;
- Relies on clinical data derived from pediatric studies and dosages of the drug intended for the pediatric population;
- Does not seek approval for an adult indication in the original rare pediatric disease product application; and
- Is approved after July 9, 2012.

FDA's draft guidance clarifies key aspects of these criteria. FDA interprets the definition of "rare pediatric disease" to require that greater than 50% of the affected population in the U.S. be aged 0 through 18 years. Additionally, with regard to the criterion that the original application not seek approval for an adult indication, FDA's draft guidance states that, to preserve voucher eligibility, the applicant cannot seek approval for a different adult indication (i.e., for a different disease/condition) in the original rare pediatric disease application. If the applicant is seeking approval in both pediatric and adult populations for the same rare pediatric disease, the applicant is still eligible for a voucher. FDA explains that it is adopting this liberal interpretation to avoid incentivizing sponsors to exclude adults from clinical trials for rare pediatric diseases or to exclude adult data from original applications.

[1] Under FDA's commitments as part of the Prescription Drug User Fee Act V, the FDA review clock begins at the end of a 60-day filing review period following the original submission of an application.

Designation Request and Voucher Request Processes

The draft guidance also outlines procedures for requesting rare pediatric disease designation and rare pediatric disease priority review vouchers, including the information to include in such requests. Under section 529, any request for rare pediatric disease designation must be submitted at the same time as a request for orphan drug designation or fast track designation. The draft guidance provides that FDA will accept designation requests submitted at other times, so long as they are received before FDA has filed the original marketing application for the drug.

FDA emphasizes that the rare pediatric disease designation process is entirely voluntary. Even if a sponsor does not request designation, the sponsor may still request, and is still eligible for, a voucher when submitting the original marketing application. Additionally, although voucher requests by sponsors are not technically required under section 529, FDA notes that the submission of such requests will ensure that FDA has all the necessary information to evaluate voucher eligibility.

Recent Developments Under the Existing Program

Although relatively new, the rare pediatric disease priority review voucher program may prove to be a powerful incentive. In February 2014, FDA awarded the first rare pediatric disease priority review voucher to BioMarin Pharmaceutical Inc. when the company received approval for Vimizim (elosulfase alfa), an enzyme replacement therapy to treat the metabolism disease Morquio A syndrome. Even though FDA's approval of Vimizim covered both pediatric and adult use for Morquio A syndrome, FDA determined BioMarin's application was eligible for a priority review voucher, consistent with the liberal interpretation of section 529 adopted by the draft guidance. In July 2014, Biomarin announced that it had sold the voucher to Regeneron Ireland for $67.5 million.

Ropes & Gray will continue to monitor 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.