FDA'S ORPHAN DRUG MODERNIZATION PLAN

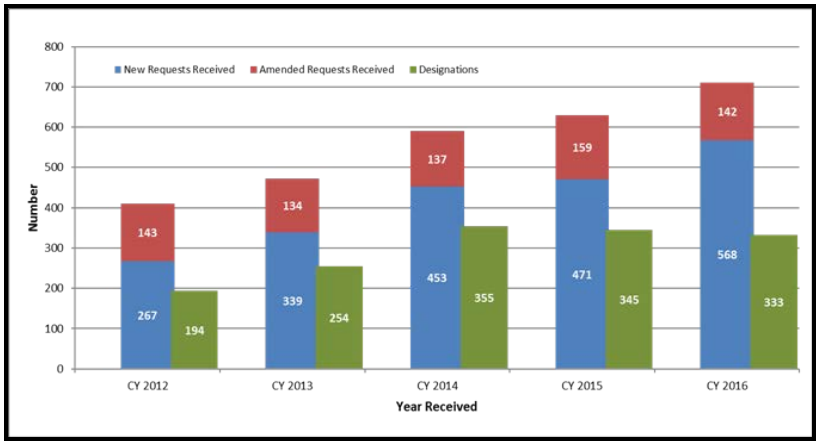
June 29, 2017

SUMMARY

At FDA, the number of orphan drug designation requests has steadily increased over the past five years. In 2016, the Office of Orphan Products Development (OOPD) received 568 new requests for designation – more than double the number of requests received in 2012 (See Figure A). The uptick in designation requests reflects, among other factors, advances in science that allow researchers to target rare diseases that were previously not readily amenable to therapy. This is good news. It is a reflection of substantial medical progress that's allowing us to effectively target many vexing diseases. It is also a reflection of our better understanding of the genetic basis of diseases, which unlocks our ability to define and target rare disorders.

These scientific advances and new opportunities also create additional opportunities for FDA, as well as new challenges. The agency needs to make sure it is able to respond to these requests in a timely fashion, and efficiently grant new designations where it is supported by the underlying data. To ensure timely review of orphan drug designation requests, FDA is undertaking a broad modernization of its approach to its orphan drug designation program. This is being done to both eliminate a backlog of existing designation requests, and to make sure that the agency can respond in a timely fashion to new applications, even as we anticipate that the demands on the orphan drug program will continue to grow as a consequence of commercial opportunities as well as the promises of scientific progress.

Figure A



Note: Designations granted in a given year may include requests received from that year as well as previous years.

BACKGROUND

The orphan drug designation trends of the past five years is an illustration of modern science and the remarkable progress American medicine has made in 34 years since the 1983 Orphan Drug Act was first enacted. Today, drug development and medical care is more personalized, genetically targeted, and more likely to address rare diseases. This is a reflection, in part, of the success of the Orphan Drug Act, and represents a promising advance in medical care for the nearly 30 million[1] Americans that have a rare disease[2] -- defined by the Orphan Drug Act as a disease that affects fewer than 200,000 people in the United States.[3] There are thousands of rare diseases. It is estimated that 85-90 percent are serious or life threatening. But only a few hundred of these rare diseases currently have FDA approved treatments.[4]

To recognize the progress made in the pursuit of treatments for rare diseases, one can compare the number of orphan drugs developed in the past decade to the decade before Congress enacted the 1983 law, when there were only ten FDA approved treatments for orphan diseases.[5] Since the law's passage, there have been more than 600 orphan drug indications approved. This represents remarkable scientific and clinical progress for the millions of patients who are affected by one of these disorders. Yet despite the success, at FDA we remain cognizant that developing rare disease treatments remains enormously challenging and can be costly.[6] Moreover, many rare conditions still lack a clear scientific understanding of the mechanistic basis of the diseases. Or they are so rare that studying them can be challenging. [7]

To address these challenges, and help enable continued progress toward more treatments and even potential cures for rare diseases, FDA is undertaking a new effort to examine where it can help create a more efficient, scientifically advanced, predictable, and modern approach to the approval of safe and effective treatments for rare diseases. This is beginning with a modernization of the process for granting Orphan Drug Designations by our Office of Orphan Products Development. With their leadership and hard work, we will be modernizing the processes in OOPD to make sure we continue to provide timely review of orphan drug designation requests. This will provide more certainty to sponsors, and simplify and ultimately reduce some of the time and costs associated with orphan drug development.

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[1] Haffner, ME, Whitley, J and Moses, M. Two decades of orphan product development *Nature Reviews Drug Discovery* **1**, 821-825 (October 2002) http://www.nature.com/nrd/journal/v1/n10/full/nrd919.html

[2] Rao, Gayatri. The Rise in Orphan Drug Designations: Meeting the Growing Demand. *FDA Voice*. July 18, 2016. https://blogs.fda.gov/fdavoice/index.php/2016/07/the-rise-in-orphan-drug-designations-meeting-the-growing-demand/# Accessed June 23, 2017.

[3] Boat TF, Adamson PC, Asbury C, et al. Rare Diseases and Orphan Products, Accelerating Research and Development Institute of Medicine (US) Committee on Accelerating Rare Disease Research and Orphan Product Development. Washington DC: National Academies Press; 2010.

[4] Id. P. 16

[5] Haffner, ME, Adopting Orphan Drugs — Two Dozen Years of Treating Rare Diseases, N Engl J Med 2006; 354:445-447February 2, 2006DOI: 10.1056/NEJMp058317 http://www.nejm.org/doi/full/10.1056/NEJMp058317

[6] Boat TF, Adamson PC. Pg. 16

[7] Boat TF, et al. P. 20

As part of this new plan, by September 21, 2017, FDA will complete reviews of all orphan drug designations that are older than 120 days. Following that 90 days period, the agency is committing to respond to 100 percent of all new orphan drug designation requests within 90 days of their receipt by FDA. Program improvements and a renewed commitment to timely review to these critical products will ensure we do not build a backlog of designations again.

To achieve these goals, among other steps, the agency will create a SWAT Team of senior, experienced, and proficient OOPD reviewers to focus on designation requests in the order that the agency receives these requests. To reduce administrative burden on the agency's experts, FDA will create and implement a new streamlined "Designation Review Template." The goal of this new template is to facilitate consistent and efficient reviews of new designation requests. CDER and CBER will engage in this cross cutting strategy that will also include the participation of the Offices of Pediatric Therapeutics to jointly review Rare Pediatric Disease Designation requests, in order to review orphan drug designation requests in a timely manner. These are just a few of our programmatic improvements that are further described below in our Orphan Drug Designation Plan.

SUMMARY OF KEY GOALS: FDA'S 90 IN 90 PLAN

1. In 90 days, FDA will complete reviews of all orphan drug designation requests that are older than 120 days (the backlog) while maintaining consistent, scientifically rigorous reviews; and
2. After 90 days, 100 percent of all new orphan drug designation requests will receive a response by the agency within 90 days of receipt. FDA will adhere to this 90-day timeline going forward.

PLAN

Goal #1 – In 90 days (by September 21, 2017) complete reviews of all requests older than 120 days

1. Created a Backlog SWAT Team of senior, experienced, proficient OOPD reviewers to focus solely on reviewing orphan drug designation requests, starting with the oldest ones first
2. Create and implement a new streamlined Designation Review Template to increase consistency, efficiency, and predictability of orphan designation reviews
3. Minimize discretionary work – i.e., FDA will reduce non-designation and non-grant-specific duties and assignments – for all other reviewers to enable the review teams to focus on core activities
4. OOPD will collaborate with FDA's Medical Product Centers to complete a CDER-CBER Orphan Designation Pilot Project – CDER and CBER reviewers will conduct preliminary primary reviews of a subset of drug designation requests, with OOPD conducting secondary reviews
5. OOPD will collaborate with the Office of Pediatric Therapeutics (OPT) to jointly review rare pediatric disease (RPD) designation requests. In these cases, OPT will conduct the pediatric review and OOPD will conduct the rare disease review. This policy began as of May 15, 2017.
6. OOPD transitioned secondary review of FOIA requests to the FOIA office, as of May 18, 2017
7. Continue to track weekly progress, adjust as necessary, and report on progress to the public

Goal #2 – After 90 days, 100 percent of all new orphan drug designation requests made to FDA will receive a response from the agency within 90 days of receipt and consistently thereafter

1. FDA will establish an "FDA Orphan Products Council" to address scientific and regulatory issues related to orphan products to ensure a consistent approach to regulating these products
2. FDA will work to establish and implement a future state including the below changes. We will report on a full timeline of the progress on these activities within the next two months.
3. Organizational re-structuring to maximize expertise and improve workload efficiencies
4. Leverage the inter-center consult process, involving the medical product centers, that was developed for combination products to develop a streamlined process for consistent and timely orphan consults
5. Designation and Exclusivity Programs (Orphan Drug, RPD, Humanitarian Use Device (HUD))
    - Centralize orphan exclusivity review and determinations
    - Continue to enhance the information technology infrastructure, e.g., automating more of the administrative processes for designation reviews
    - Improve and implement streamlined "Designation Review Template" across all designation programs to bring more efficiency, consistency, and predictability to these activities
    - Complete development of web-based training for sponsors to enhance quality of submissions
6. Grant Programs: With respect to the Orphan Products (OPD) Grant Program (Clinical Trials + Natural History) and Pediatric Device Consortia (PDC) Grant Program; FDA will:
    - Revise grant monitoring processes by increasing utilization of desk-top and virtual tools and by implementing a new risk-based approach for conducting in-person site visits to grant recipients
    - Modify and modernize reporting requirements so that FDA can continue to give a high assurance related to appropriate monitoring of federal funds and efficiently measures program success
    - Continue to enhance IT infrastructure for continued efficiency and better monitoring
7. Reduce OOPD office-wide workload
    - Modify Orphan Cluster meetings with EMA from monthly to quarterly
        - The impact of the reduction in frequency of meetings with EMA is mitigated by our well-established and long-standing relationship with our EMA counterparts, which will allow us to have ad hoc meetings should they become necessary in the intervening months.
    - Modify FDA Rare Disease Council meetings from monthly to quarterly
        - The RDC was established in 2012 to serve as a forum to communicate and collaborate across the agency on rare disease issues. It is chaired by OOPD and includes representatives CDER, CBER, CDRH, OHCA, OL, and OOPD. Quarterly meetings would ensure continuity of cross-agency communication but would help reduce workload in administering monthly meetings. The implementation of more joint reviews and closer regular, ongoing collaboration should reduce the need for the larger, RDC meetings.
    - Minimize outreach activities and discretionary projects to only those deemed most meaningful
8. OOPD will create a new "Tracking Dashboard" to monitor and facilitate its efforts to meet the new designation goals and FDA will report on overall workload and progress more regularly