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FDA Adjustment to Orphan Drug Review May Indicate Increased Scrutiny of Designations

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In recent years, applications for orphan drug designations have flooded into FDA at a rapid pace, and this year appears to be no exception. Orphan drug applications received by FDA rose by approximately 30% over the previous year in 2009, 2010, 2013, *and* 2014, with 467 applications submitted in 2014. FDA reports that the number of orphan drug applications received so far in 2016 indicate that the total number will represent another 30% increase over the 472 applications received in 2015. These robust numbers show that pharmaceutical companies are treating orphan drugs – or drugs and biologics used to treat rare diseases – as a significant part of their pipelines, which makes sense given the lower cost of development due to the incentives offered by the Orphan Drug Act and implemented in **FDA's Orphan Drug Program**.

In fact, FDA is so inundated with applications for orphan drug status that the Office of Orphan Products Development ("OOPD") finally cried uncle in an **FDAVoice blog post** on July 18, 2016 written by OOPD Director Dr. Gayatri Rao. Dr. Rao stated that OOPD will be changing its internal timeframe for reviewing orphan drug applications. Although there is no statutory standard for the timing of orphan drug review, Dr. Rao set a goal of reviewing 75% of applications within 120 days of receipt, an increase of 30 days over the original goal of 75% within 90 days.

Possible Increased Scrutiny of Orphan Drug Designations

Although Dr. Rao strikes a positive tone in her post – emphasizing the benefits orphan products offer to patients and the importance of issuing timely designations so that companies can continue research development – the news comes at the same time as FDA is apparently increasing its scrutiny of orphan products. Recently, FDA revoked orphan designations for four products:

1. Valsartan Oral Solution (Carmel Biosciences) – Received orphan drug designation 10/28/2015 for "treatment of hypertension in pediatric patients 0 through 16 years of age"
2. Lisinopril Oral Solution (BioRamo, LLC) – Received orphan drug designation 1/27/2015 for "treatment of primary hypertension with complications and secondary hypertension in pediatric patients"
3. Lisinopril Oral Solution (Silvergate Pharmaceuticals, Inc.) – Received orphan drug designation 10/14/2015 for "treatment of hypertension in pediatric patients 0 through 16 years of age"
4. Enalapril Maleate Powder for Oral Solution (Silvergate Pharmaceuticals, Inc.) – Received orphan drug designation 1/30/2013 for "treatment of hypertension in pediatric patients)

Per the Orphan Drug Regulations (21 C.F.R. § 316.29(a)), the Agency can revoke an orphan drug designation for three reasons:

1. The request for designation contained an untrue statement of material fact;
2. The request for designation omitted material information required by the Orphan Drug Regulations]; or

3. FDA subsequently finds that the drug in fact had not been eligible for orphan drug designation at the time request was submitted .

FDA revocation of an orphan drug designation is not unheard of, but it doesn't happen that often. So it is significant that the Agency recently reviewed and decided to revoke four individual designations. These revocations, plus the recently announced extended timeline for application review by OOPD could signal increased FDA scrutiny of orphan product designations. The Agency may be attempting to weed out designations that may have been inappropriately granted and, possibly, applications that use carefully crafted information about the patient population in order to claim eligibility as a treatment for a rare disease.

To avoid possible adverse action by FDA, companies should take care to provide sufficient information in orphan product applications to accurately characterize the target population and potential market.

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