CORRESPONDENCE

Regulatory Review of New Therapeutic Agents — FDA versus EMA, 2011–2015

TO THE EDITOR: The Food and Drug Administration (FDA) faces continual pressure to accelerate the regulatory review and approval of new medicines. Although the 21st Century Cures Act, which was signed into law in December 2016, includes several reforms that are intended to further streamline FDA evaluations,[1] the speed of the regulatory review process is directed by the Prescription Drug User Fee Act (PDUFA).[2] With Congress poised to consider the reauthorization of the PDUFA before it expires in October 2017, the speed of the FDA regulatory review process will come under renewed scrutiny. To inform these discussions, we compared review times for new therapeutic agents that were approved by the FDA or the European Medicines Agency (EMA), the primary drug regulator in Europe, between 2011 and 2015.

Using methods similar to our previously published comparison of agency review times,[3] we identified all the new therapeutic agents that had been approved by the FDA or the EMA between 2011 and 2015, classifying them according to therapeutic area and orphan status. Next, we abstracted key regulatory dates and compared the median total review times (i.e., the total number of days of regulatory review before approval) between the two agencies using Wilcoxon tests. A P value of 0.0125 was used to adjust for multiple comparisons.

The FDA approved 170 new therapeutic agents between 2011 and 2015, and the EMA approved 144. The therapeutic areas of the approvals were similar in the two agencies, although more therapeutic agents that were designated as orphan drugs were approved by the FDA than by the EMA (43.5% vs. 25.0% of the approved agents, P<0.001). The median total review time was 306 days (interquartile range, 239 to 371) at the FDA, as compared with 383 days (interquartile range, 327 to 446) at the EMA (P<0.001) (Fig. 1). The total review times were shorter at the FDA than at the EMA for therapeutic agents that are used for the treatment of cancer and hematologic disease, but not for other therapeutic areas, and for therapeutic agents that were designated as orphan drugs. Among the 142 therapeutic agents that were approved by both the FDA and the EMA (with approval by at least one regulator occurring during the sample period), the median total review time was 303 days (interquartile range, 202 to 365) at the FDA, as compared with 369 days (interquartile range, 322 to 420) at the EMA (P<0.001).

For new therapeutic agents that were approved between 2011 and 2015, the regulatory reviews by the FDA were, on average, 60 days shorter than those by the EMA. The magnitude of the difference in the total review times between the two

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Subgroup	New Therapeutic Agents Approved *no. (%)*	Median Total Review Time (Interquartile Range) *days*	P Value
Overall			<0.001
FDA	170 (100)	306	
EMA	144 (100)	383	
Therapeutic area			<0.001
Cancer and hematologic disease			
FDA	53 (31.2)	206	
EMA	50 (34.7)	379	
Cardiovascular disease, diabetes mellitus, and hyperlipidemia			0.79
FDA	25 (14.7)	364	
EMA	22 (15.3)	372	
Infectious disease			0.10
FDA	25 (14.7)	245	
EMA	20 (13.9)	358	
All other			0.05
FDA	67 (39.4)	365	
EMA	52 (36.1)	395	
Orphan status			
Yes			<0.001
FDA	74 (43.5)	294	
EMA	36 (25.0)	403	
No			0.04
FDA	96 (56.5)	355	
EMA	108 (75.0)	380	

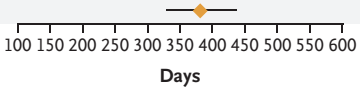

Figure 1. Median Total Review Time in Days for New Therapeutic Agents Approved by the Food and Drug Administration (FDA) or the European Medicines Agency (EMA) between 2011 and 2015.

agencies is similar to, or perhaps even greater than, that observed in our previous analysis of new therapeutic agents that were approved between 2001 and 2010.[3] Our analysis provides reassurance that the FDA continues to complete regulatory reviews more quickly than the EMA and has the potential to inform discussions regarding the reauthorization of the PDUFA.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. H.R.34 — 21st Century Cures Act, 114th Congress (2015-2016). December 13, 2016 (https://www.congress.gov/bill/114th-congress/house-bill/34).
2. Avorn J. Paying for drug approvals — who's using whom? N Engl J Med 2007;356:1697-700.
3. Downing NS, Aminawung JA, Shah ND, Braunstein JB, Krumholz HM, Ross JS. Regulatory review of novel therapeutics — comparison of three regulatory agencies. N Engl J Med 2012;366:2284-93.

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Treatment of Pediatric Migraine

TO THE EDITOR: Powers and colleagues (Jan. 12 issue)[1] report the results of a randomized, double-blind, placebo-controlled trial investigating the efficacy of amitriptyline and topiramate versus placebo as potential preventive treatments in children and adolescents with migraine. Placebo