What Determines the Duration of BLA Approvals

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Abstract

The Biologics License Application (BLA) approvals differ significantly from NDA by nature, and progressed in a surprising speed. To better understand this quickly emerging field of compounds, the effect of firm size and lobbying behaviors on the approval speed merits investigation. Overall, I investigate the role that different factors play in affecting the approval speed for BLAs, and find that (1) priority review status help reduce the waiting period; (2) firm size does not reveal statistically significant effects in the approval process; (3) lobbying strategies do not have significant effects; (4) past experience with does help reducing the approval duration when firms apply for BLA approvals.

Introduction

To legally market a new drug in the United States, the applicant will need to receive approval from FDA under either the New Drug Application (NDA) or Biological License Application (BLA). Even though NDA approval have long been regarded as the major indicator of success among pharmaceutical companies, the fast-growing market of biological products also draws attention from both the drug developers and the regulators.

It is FDA's goal to improve communication between applicants and FDA review teams, to improve transparency of reviews, and improve efficiency and effectiveness of reviews. Thus, the duration of review cycles become a very important metric to assess the overall smoothness among NDA and BLA applications. Both FDA and the Government Accountability Office [1] have provided PDUFA performance reports as program assessment, among which they find some factors to be related to shorter approval time while others are correlated with longer time period to approval.

Beginning with the implementation of Prescription Drug User Fee Amendment V (PDUFA V), fiscal year 2013, NMEs and Original BLAs were reviewed under the Program for Enhanced Review Transparency and Communication, which provided additional review clock time for the agency, as the PDUFA clock begins after conclusion of the 60-day filing period [2]. The most recently PDUFA VI reauthorized the program from fiscal year 2018 through fiscal year 2022.

The empirical evidence present in this paper seeks to explore the impacts of different characteristics on FDA approval speed, and hope to shed light upon the importance of some specific attributes and contribute to the knowledge of future decision makers both in the pharmaceutical industry and the regulatory institutions.

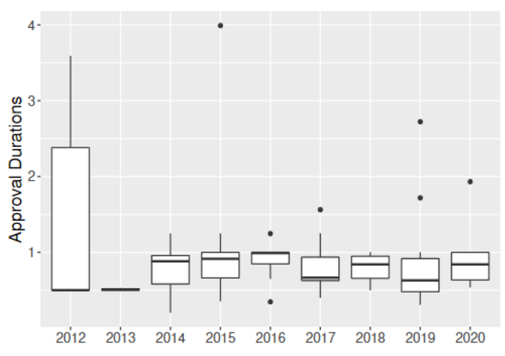

Figure 1. BLA Approval Duration by Year.

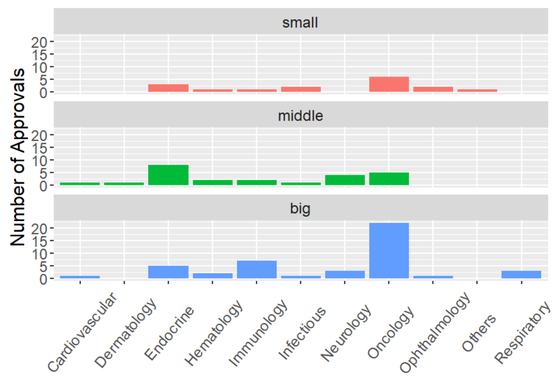

Figure 2. Number of Approvals by Therapeutic Class across Different Size of Firms

Methods and Materials

This paper focuses on the BLA approvals ranging from year 2013 to 2020. The BLA duration data is obtained from CDER NME drug and original BLA calendar year approval reports by FDA, cross validated from Purple Book [3], and compilation dataset [4] of NME and BLA approvals. The firm level information is obtained from COMPUSTAT database. The annual lobbying information on the firm level is obtained from the Center for Responsive Politics (CRP).

To estimate the effect of each variable on BLA approval duration, I utilized maximum likelihood duration model, and Cox Proportional Hazard model. The baseline of the maximum likelihood duration model assumes normal distribution, and other parametric models involve different assumptions, including log-normal and exponential distributions. Cox proportional hazard models assume no specific distribution for the data.

Results

Regression results show that priority review status always plays a significant and positive effect in accelerating the speed of approval. Firms with better regulatory familiarity observe shorter duration. There is no evidence on the impact of firm's lobbying behavior, nor is there evidence of scale advantage from the regression results. The results are quite consistent with the literature. The findings suggest that FDA decision-makings may not be influenced by firm lobbying or size, but that past approval experience works better in securing a faster review process for the new BLA applications.

	Dependent variable:			
	GLM	Log-Normal	Exponential	CoxPH
	(1)	(2)	(3)	(4)
Employee_N	−0.0002	−0.002	0.0001	0.001
	(0.001)	(0.002)	(0.001)	(0.004)
Lob_int	268.374	260.429	67.993	816.545
	(516.504)	(644.996)	(403.023)	(1,200.615)
BLA_CUM	−0.005	0.007	−0.017	0.090**
	(0.017)	(0.017)	(0.014)	(0.043)
Priority	−0.669***	−0.711***	−0.667***	5.264***
	(0.147)	(0.158)	(0.115)	(1.109)
Orphan.Drug	−0.190	−0.247*	−0.101	0.383
	(0.130)	(0.133)	(0.102)	(0.342)
Therapeutic.Class	YES	YES	YES	YES
Constant	YES	YES	YES	YES
Observations	79	79	79	79
R^2				0.791
Log Likelihood	−39.558	−37.093	3.113	−207.384
Note:				*p<0.1; **p<0.05; ***p<0.01

Discussion

Firm size may have a confounding effect on other factors, for instance, the deep-pocket advantage in rent-seeking; also, potentially easier enrollment of priority programs due to agency familiarity. Figure 3 shows that the proportion of special designations are not significantly different by firm size. In addition, Figure 4 demonstrates that, although larger firms spend greater amount in lobbying compared to smaller competitors, the relative ratios of lobbying over scale (lobbying intensity) tend to share similar fashion across all sizes. Further, despite that larger firms have wider coverage of various therapeutic classes, no evidence suggest a significant approval speed benefit from a specific therapeutic class.

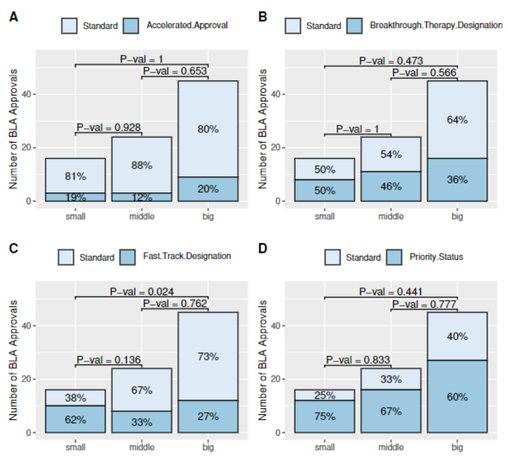

Figure 3. Types of Designation by Firm Size

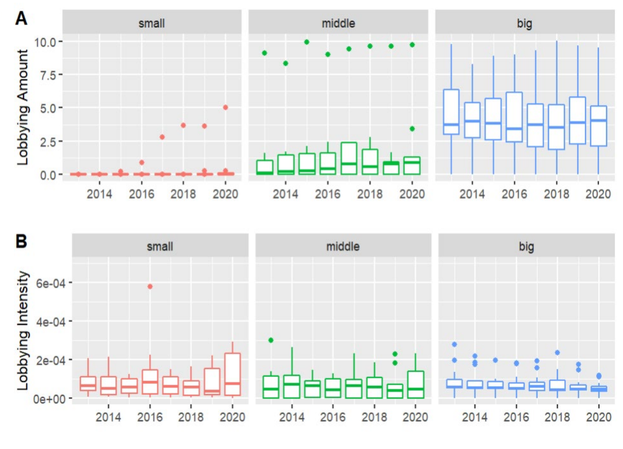

Figure 4. Lobbying Amount and Intensity by Firm Size

Conclusions

Regression results show that priority review status always plays a significant and positive effect in accelerating the speed of approval. Firms with better regulatory familiarity observe shorter duration. There is no evidence on the impact of firm's lobbying behavior, nor is there evidence of scale advantage from the regression results. The results are quite consistent with the literature. The findings suggest that FDA decision-makings may not be influenced by firm lobbying or size, but that past approval experience works better in securing a smooth review process for the new BLA applications.

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References

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