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Market competition among manufacturers of novel high-risk therapeutic devices receiving FDA premarket approval between 2001 and 2018

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INTRODUCTION

The US Food and Drug Administration (FDA) regulates high-risk medical devices through the premarket approval (PMA) pathway, which requires clinical evidence assuring safety and effectiveness for approval.[1] After approval, manufacturers may face barriers to successful commercialization, such as uncertainties about reimbursement or limited market exclusivity.[2 3] These clinical, financial and operational hurdles may discourage market entry by manufacturers, thereby limiting competitive innovation.[2] We sought to evaluate the extent of market entry by manufacturers of first-in-class devices and subsequent competitors.

METHODS

We conducted a retrospective cross-sectional analysis of novel high-risk therapeutic devices approved via the PMA pathway between 1 January 2001 and 31 December 2018. Using the PMA database and FDA-designated product codes,[4] we identified all first-in-class therapeutic devices approved during this period. To evaluate whether each first-in-class device manufacturer subsequently faced intraclass competition, we determined whether ≥1 other manufacturer received approval for a device with the same product code.

For each device type with intraclass competition, we determined the number of competing manufacturers as of 8 February 2022. We further extracted FDA review type (expedited/non-expedited) and dates for first-in-class/second-in-class/(as applicable) third-in-class devices. We calculated FDA review times (difference between application receipt/approval) for each device and times to competitor device approval (difference between FDA approval dates) for each device type.

We used descriptive statistics to characterize device types, FDA review times and times to competitor device approval. We performed χ^2 and Kruskal-Wallis tests as appropriate to examine for differences in FDA review type and time between first-in-class/second-in-class/third-in-class devices; statistical tests were two tailed with a type 1 error rate of 0.05. All analyses were performed using Microsoft Excel and JMP Pro.

RESULTS

Between 2001 and 2018, FDA approved 97 types of first-in-class high-risk therapeutic devices via the PMA pathway (online supplemental figure 1), including 6 (6.2%) originally approved for use in pediatric patients. As of February 2022, manufacturers faced intraclass competition for 40 (41.2%) device types (table 1), of which FDA designated 20 (50.0%) as cardiovascular, 31 (77.5%) as implantable and 17 (42.5%) as life-sustaining; 2 (5.0%) were originally approved for use in pediatric patients. The median number (IQR) of competing manufacturers was 2.0 (2.0–3.25) per device type.

Among the 40 device types with intraclass competition, the first-in-class device was more likely to undergo expedited FDA review than the second-in-class or third-in-class device (45.0% vs 11.9%; p=0.0002), although there was no difference in median duration of FDA review time (table 1; p=0.20).

The median times after FDA approval of first-in-class devices and competitor device approval were 25.6 months for second-in-class devices (IQR: 5.9–78.6 months) and 56.2 months for third-in-class devices (IQR: 33.1–86.1 months).

Table 1 Characteristics of novel high-risk therapeutic device types receiving initial FDA premarket approval with subsequent intraclass competition, 2001–2021

	No of device types (%)
All	40 (100.0)
Specialty	
Cardiovascular	20 (50.0)
Orthopedic	5 (12.5)
Ophthalmic	4 (10.0)
Genitourinary	3 (7.5)
Neurological	3 (7.5)
All other	5 (12.5)
Implantable	
Yes	31 (77.5)
No	9 (22.5)
Life-sustaining	
Yes	17 (42.5)
No	23 (57.5)
Initial approval year	
2001–2009	25 (62.5)
2010–2018	15 (37.5)
Expedited review*	
First-in-class	18 (45.0)
Second-in-class or third-in-class	7 (11.9)
Approved for pediatric use†	
Yes	2 (5.0)
No	38 (95.0)
	Median (IQR)
No of competing manufacturers	2.0 (2.0–3.25)
FDA review time (months)	
First-in-class	14.2 (9.1–22.1)
Second-in-class	10.6 (7.6–17.1)
Third-in-class‡	13.9 (11.0–16.0)
Time to competitor device FDA approval (months)	
Second-in-class	25.6 (5.9–78.6)
Third-in-class‡	56.2 (33.1–86.1)

*The FDA granted expedited review for medical devices with the potential to significantly improve the prevention, diagnosis or treatment of serious conditions through several pathways during the study period, including the Innovation Pathway (2011–2014), Priority Review Program (2012–2016), Expedited Access Pathway (2015–2016) and Breakthrough Devices Program (2016–present).
†Proportion determined based on original FDA-approved indication; additional indications may be approved via supplemental applications.
‡Among device types with at least 2 approved competitor devices (n=20).
FDA, Food and Drug Administration.

DISCUSSION

Between 2001 and 2018, approximately two-fifths of manufacturers receiving FDA PMA for first-in-class therapeutic devices subsequently faced intraclass competition. When present, intraclass competition was typically limited to few manufacturers, commencing a little more than 2 years after initial device approval on average. These results suggest market dynamics of new product entry and follow-up competition may be similar between pharmaceuticals and devices. Recent analysis indicates that 36% of first-in-class drugs subsequently face intraclass competition with a median time to follow-on drug approval of 40 months.[5]

Our study has limitations. First, our findings may not be generalizable to diagnostic or moderate-risk devices. Second, we did not account for other factors influencing the extent of manufacturer competition, such as market size, device obsolescence/withdrawal or interclass overlap in device indications.

Our findings suggest that policy makers should implement measures to stimulate competition for some device types and reward innovation for others. Increasing federal seed funding for small firms[6] and providing tax credits for development costs of competitor devices could spur manufacturer entry. Complementary policies granting value-based market exclusivity[7] could simultaneously incentivize manufacturers to generate robust evidence supporting device safety and effectiveness. Manufacturers may otherwise limit investment in the development of novel technologies and potential therapeutic alternatives that may improve patient care.

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Contributors VKR was responsible for the conception and design of this work and manuscript drafting. VKR and JLJ were responsible for statistical analysis. All authors participated in the analysis and interpretation of the data and critically revised the manuscript for important intellectual content. VKR is the guarantor.

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Competing interests VKR reports prior employment by F-Prime Capital to identify and qualify investment opportunities in early stage life-sciences companies.

Patient consent for publication Not applicable.

Ethics approval This study analysed publicly available information and, therefore, did not require institutional review board exemption or approval.

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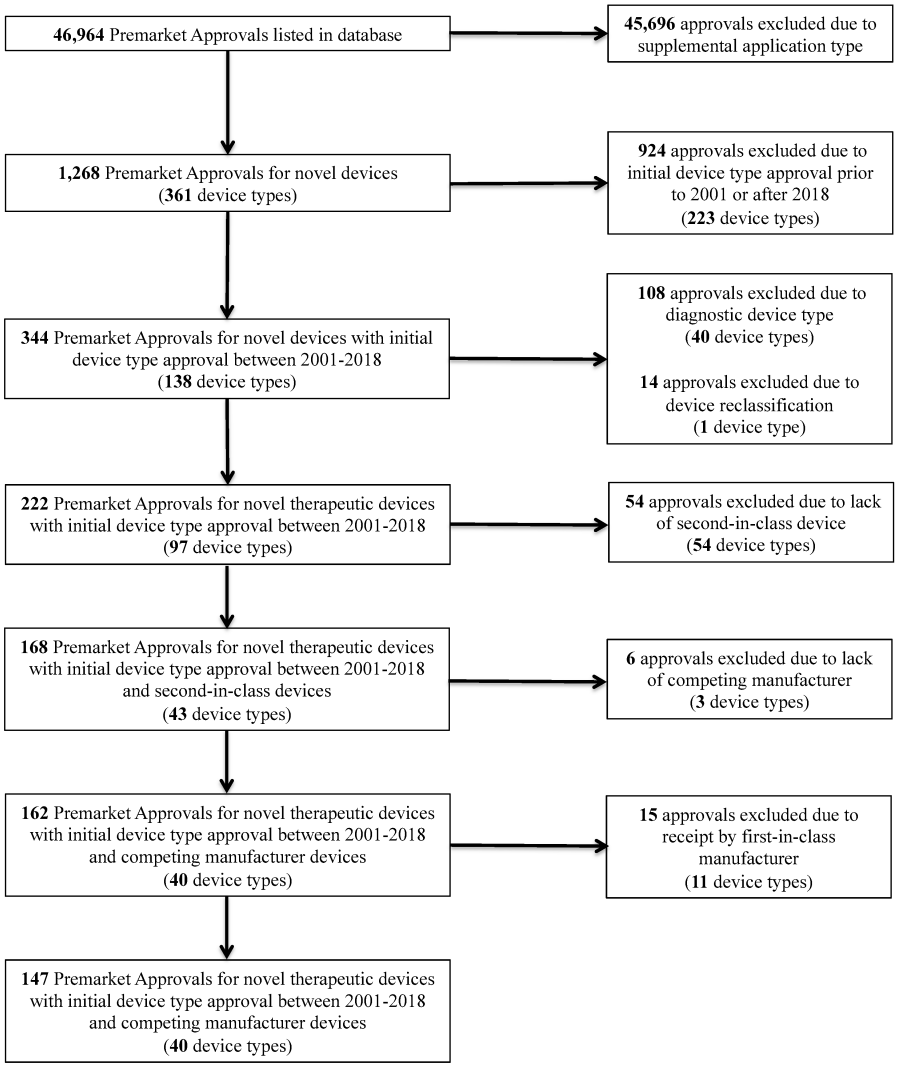
Supplemental Figure



Cohort of Novel High-Risk Therapeutic Device Types Receiving Initial FDA Premarket Approval with Subsequent Intra-Class Competition, 2001-2018

Caption: FDA denotes U.S. Food and Drug Administration. Non-wearable external defibrillators (1 device type, 14 approvals) were excluded because the FDA began requiring Premarket Approval for these commercial available (i.e., non-novel devices) devices in 2015 as a result of risk reclassification under the 515 Initiative.