

Does FDA Funding Increase Drug and Medical Device Innovation?

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Introduction

The US FDA receives funding through the general fund and user fees. Additional funding comes from the regulated industries. Specifically, the drug industry funds FDA through the Prescription Drug User Fee Act (PDUFA), and the medical device industry funds FDA through the Medical Device User Fee Act (MDUFDA). Both acts are considered a success for requiring FDA to improve approval time for drugs and devices. However, decreased approval times have not resulted in more drug and device innovation.

In fact, the same number of products are still submitted for approval to FDA. They are just approved more quickly. FDA does not have an incentive to actually increase innovation—its only incentive is to meet its MDUFA and PDUFA approval times to keep its funding flowing.

The expense of putting drugs and devices through this system is almost unimaginable. The cost of bringing low- to medium-risk 510(k) medical devices to market averages \$31 million, \$24 million (75 percent) of which is dedicated solely to attaining FDA approval

within an average of about six months.¹ Any significant improvement to the device requires reapplication.² For higher-risk medical devices where there may be significant health gains, the costs are about \$94 million, \$75 million (80 percent) of which is dedicated to attaining FDA approval.³

For drugs, the situation is much worse. It costs an average of \$2.6 billion simply to get a drug through the FDA process and onto the market. This does not include postmarket monitoring, the terms of which are laid out by FDA upon approval.⁴ These costs have increased from about \$1 billion between 1983 and 1994.⁵

In addition, the primary laws governing devices and drugs are now 40 and 50 years old,

respectively. These laws, in conjunction with other incentives, attenuate progress in the device and drug arenas. As one congresswoman describes it, “Health research moves at a rapid pace, but the federal drug and device approval process is in many ways a relic of another era.”⁶ Yet we continue to increase the funding and authority for FDA and assume that we will somehow boost innovation in medical products (drugs and devices) despite the growing obstacles. This has not happened.

FDA has grown in both resources and statutory authority, and to continue those increases, it must meet user fee goals and avoid bad publicity.

FDA Funding

Concerns Relating to User Fees

FDA and industry initially opposed user fees, first considered in the 1950s. Early discussions focused on drugs, for which FDA began getting user fees in 1992. Earlier objections cited the disproportionate burden user fees would impose on “the poor and the elderly” through higher drug prices.⁷ FDA’s Center for Drug Evaluation and Research (CDER) maintained that user fees for Investigational New Drugs would function as a tax and discourage innovation.⁸

There was also considerable concern about FDA’s sluggishness in approving drugs relative to counterparts in other countries—the “drug lag.”⁹ A key reason industry began to support user fees was that “the [New Drug Approval] review times were so long, and the cost of an NDA was therefore so large, that if an NDA was approved even one month quicker, it would reduce the cost of the NDA by more than the user fee.”¹⁰ These fees have been

widely declared a success, particularly by FDA, in reducing “the total time it takes to make decisions.”¹¹ However, *speedier approvals do not necessarily equal speeding up innovation*. In fact, establishing performance goals that avoid unintended consequences, or that satisfy more fundamental goals like increasing the rate of innovation, is notoriously difficult.

Economist Robert Heilbroner provided an apocryphal story about managing incentives through central planning in the Soviet Union. He wrote that “If the output of nails was determined by their number, factories produced huge numbers

of pinlike nails; if by weight, they produced smaller numbers of very heavy nails.” The ultimate goal of producing more nails that are actually useful is never achieved.

Heilbroner’s point is not that incentives created by government do not work. They do, but they do not necessarily incentivize the desired outcome. Although it appears that PDUFA and MDUFA have met their approval goals with respect to timeliness, just as with the satirical nail factory, the ultimate goal of more medical product innovation is not achieved.

FDA's Budget Increases

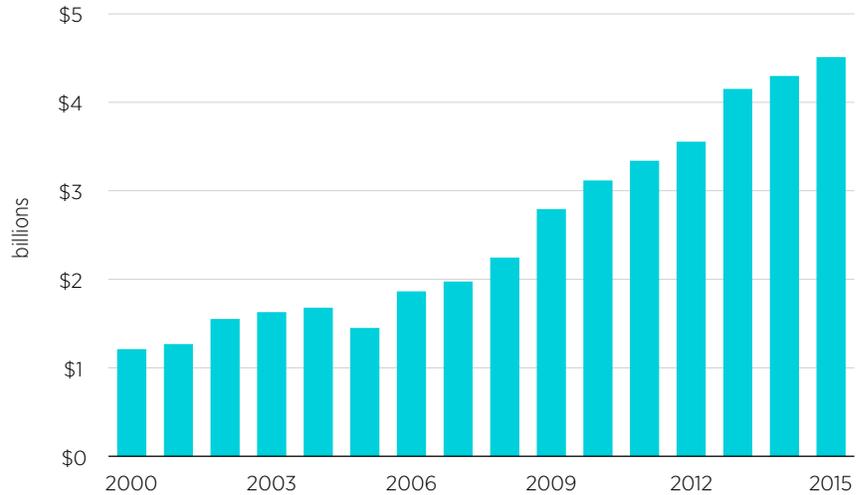
FDA funding increases have been largely uninterrupted for the last 15 years. Fees from the drug and devices industries help FDA's funding grow more rapidly than that of agencies that depend on general funding alone.¹² FDA's 2017 requested

budget increase for drugs and devices (no increase requested for biologics) is \$26,294,000.¹³ The bulk of that increase (87 percent) would come from user fees. Figures 1, 2, and 3 show the growth in FDA budgets.

Figure 1

Total Funding (FDA Overall)

Sources: FDA, *Justification of Estimates for Appropriations Committees, 2009–2017*; data for 2000–2008 provided by FDA Office of Budget.



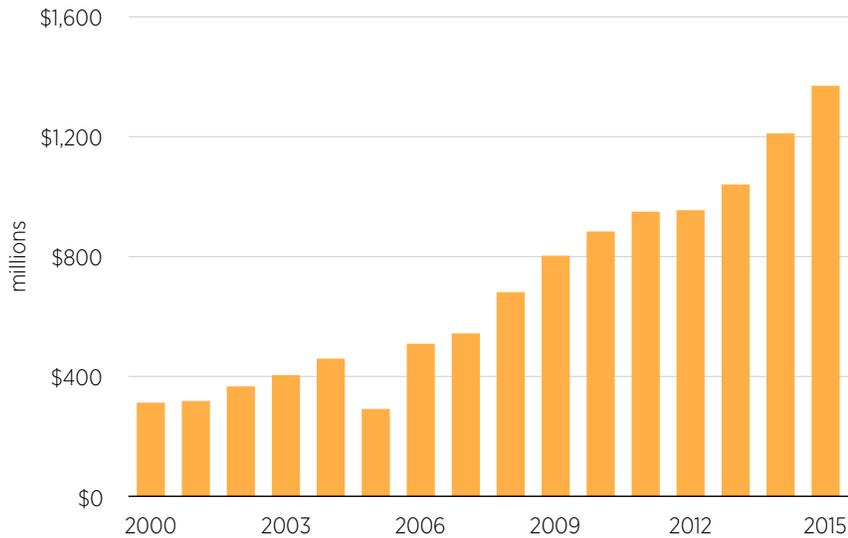


Figure 2

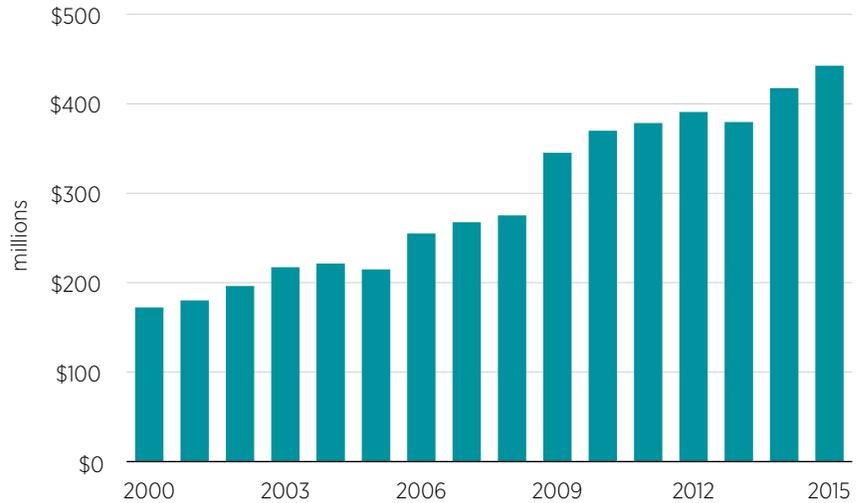
Human Drug Funding (2000–2015)

Sources: FDA, *Justification of Estimates for Appropriations Committees*, 2009–2017; data for 2000–2008 provided by FDA Office of Budget.

Figure 3

Devices and Radiological Health Funding (2000–2015)

Sources: FDA, Justification of Estimates for Appropriations Committees, 2009–2017; data for 2000–2008 provided by FDA Office of Budget.



Specific Sources of Funding for FDA's Drug Activities

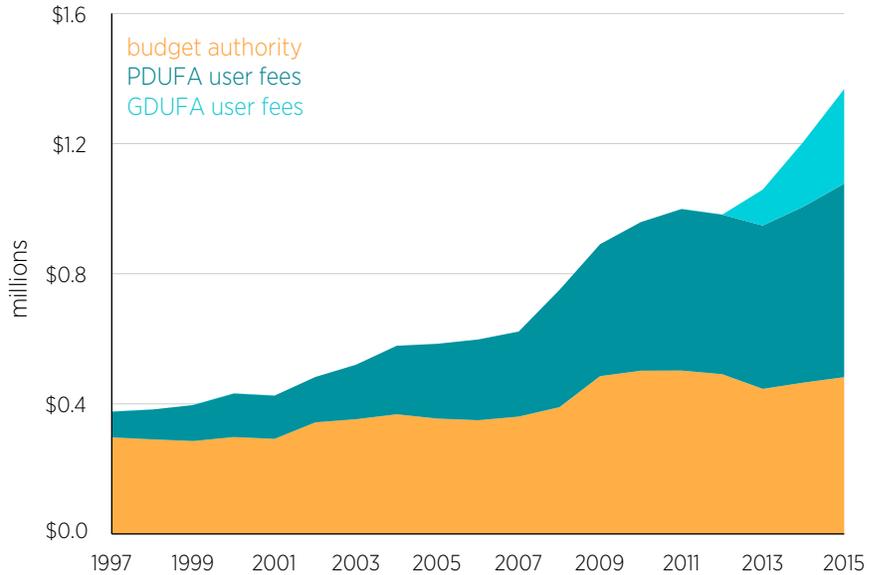
FDA also reports on the sources of funding for the Human Drugs Program. Virtually all of the funding comes from three sources: the program's budget authority plus user fees provided under either the PDUFA or the more recent Generic Drug User Fee Amendments (GDUFA). Inflation-adjusted funding by source since 1997

is plotted in figure 4. Budget authority made up most of the funding until fiscal year (FY) 2013, when it was surpassed by PDUFA, and funding from GDUFA also began that year. In FY 2015, budget authority made up 35 percent of spending, with PDUFA accounting for 44 percent and GDUFA 21 percent.

Figure 4

FDA Human Drugs Program: Real Spending by Source of Funds, 1997–2015

Sources: FDA, *Justification of Estimates for Appropriations Committees*, 2009–2017; data for 2000–2008 provided by FDA Office of Budget.



Meeting PDUFA Goals

Spending Up, New-Drug Reviews Flat

FDA's Human Drugs Program provides assurance of the safety, effectiveness, and quality of pharmaceuticals. The work of the Human Drugs Program is carried out by FDA's Center for Drug Evaluation and Research, and fieldwork is done by FDA's Office of Regulatory Affairs (ORA).

FDA is required to report on how well it has satisfied the goals of the various PDUFA Agreements that detail the time allowed for reviewing

drugs and the percentage of drugs that must meet these deadlines. Each year, FDA reports the results in its *Justification of Estimates for Appropriations Committees*.

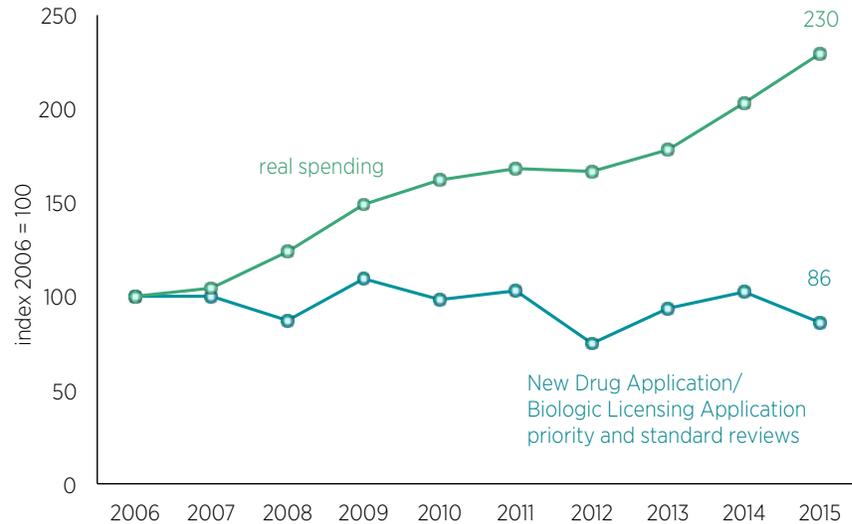
Figure 5 plots the number of New Drug Application (NDA) and Biologic Licensing Application (BLA)¹⁴ reviews conducted—the reviews that determine whether novel drugs (and biologics regulated by CDER) will be permitted onto the market.

Figure 5

FDA Human Drugs Program: Real Spending and NDA/ BLA Reviews Conducted

Note: This chart is an indexed chart relative to values in 2006.

Sources: Department of Health and Human Services; FDA.



FDA justification reports show that while annual real spending on the Human Drugs Program has more than doubled since 2006, the number of NDA and BLA reviews it conducts per year has not increased at all. FDA has managed to meet its PDUFA goals in two primary ways:

1. Because of the Orphan Drug Act,¹⁵ FDA has increased the percentage of orphan drugs that it reviews from 18 percent in 1995 to nearly 50 percent today. FDA approved less than 10 orphan drugs in the 1970s.¹⁶ Orphan drugs are niche drugs that address small populations (less than 200,000). These reviews come at the expense of drugs that would address population diseases like cancer, heart disease, diabetes, and Alzheimer's (unless these diseases are "broken up" by genetic biomarkers).¹⁷ FDA prefers reviewing these

drugs because they normally require less information (statutorily allowed), which decreases the amount of time it takes to review them.¹⁸

In addition, FDA views potential adverse events for drugs for common diseases as a "public health threat" and "intolerable." But FDA views adverse events for orphan drugs as "tolerable" and reviewing these drugs as a public health "opportunity" because adverse events from orphan drugs affect so few people relative to drugs for common diseases.¹⁹ Fewer people affected means less adverse publicity and berating from Congress.

2. Overall, FDA receives fewer drug submissions, possibly because reviewing nonorphan drugs requires much more information. The additional information that FDA requires includes larger trials with more clinical endpoints, contributing to the higher costs of bringing drugs to the market. In constant dollars, the total cost of bringing a new drug to the market was \$1.04

billion between 1983 and 1994, but by 2014 this cost had increased to \$2.56 billion (both in 2013 dollars).²⁰ Higher costs of FDA approval have discouraged investment in new drugs, particularly drugs for treating major diseases like cancer, heart disease, and Alzheimer's.

As seen in figure 5, despite a large increase in resources and faster reviews, there are not more new drugs and biologics on the market (see the appendix for additional information). Independent of the other ways FDA chooses to spend its growing resources, this should give pause to any request for further resources.

Where Is the Money Going?

Because PDUFA has provided FDA with more funding, one question is where the additional resources are spent, if not on drug reviews (particularly in the case of orphan drugs). One area is in postmarket patient safety and oversight of imported products (see table A1 in the appendix).

As recently as FY 2012, budget data for five “subprograms” comprising the Human Drugs Program was provided to Congress by FDA (per FDA's Office of Budget, such reporting has been discontinued). Figure 6 shows how spending on the Human Drugs Program was allocated by subprogram in

FY 2012. New Drug Review accounted for half of spending, with another 10 percent going to Generic Drug Review. The remaining two-fifths of spending went roughly evenly to Drug Quality and Post-market Safety Oversight, with a very small amount spent on Oversight of Drug Promotion.

Less of FDA's expenditures on drugs is going to fieldwork. In FY 2015, CDER accounted for 87 percent (\$1.19 billion) of Human Drugs Program spending, and ORA for only 13 percent (\$176 million). This is an increase from 1997, when CDER spent

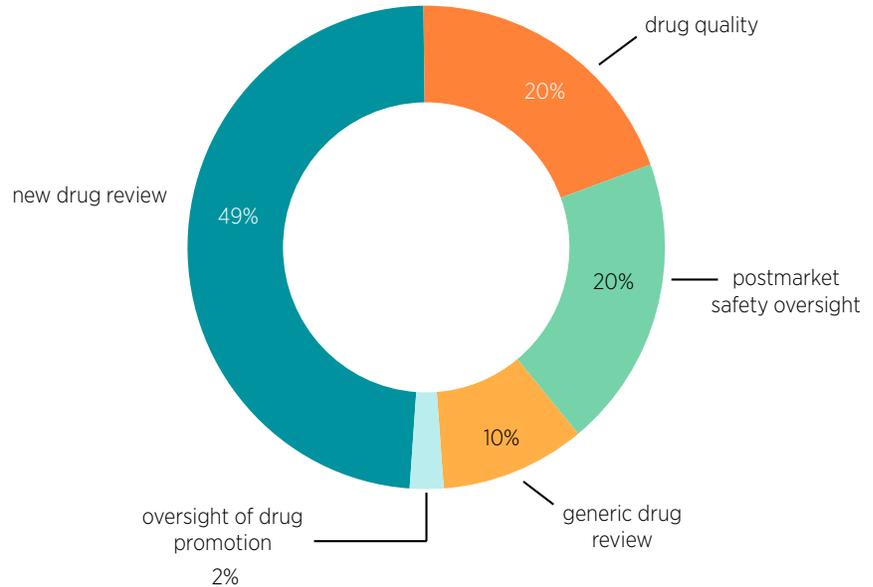
74 percent and ORA spent 26 percent. Since 2005, inflation-adjusted spending for the center has increased at an average annual rate of 9.5 percent, while inflation-adjusted spending in the field has increased at an average annual rate of 5.3 percent.

A better accounting of precisely how FDA allocates its budget among the different programs might provide a better understanding of how this allocation might be reprogrammed to encourage more submissions (to lower not just approval times but costs as well).

Figure 6

Allocation of Human Drugs Program Spending to Subprograms, FY 2012

Source: FDA, *Justification of Estimates for Appropriations Committees*, 2014



Meeting MDUFA Goals

Submissions

Similar to the Human Drugs Program, the purpose of FDA's Devices and Radiological Health Program is to provide assurance of the safety, effectiveness, and quality of medical devices. The work of the Devices Program is carried out by FDA's Center for Devices and Radiological Health (CDRH), plus fieldwork done by ORA.

Most observers, and particularly FDA, believe that user fees have been successful in helping

the Devices Program meet its performance goals in reducing “the total time it takes to make decisions.”²¹ But the evidence presented here suggests that increased spending on the Devices Program over the last decade has not yet led to an increase in the number of new-product applications and reviews.

Premarket Approval Applications (PMAs) for medical devices are for devices that are novel,

meaning there is nothing on the market like them. For example, the artificial pacemaker is a PMA medical device, as is a brain implant that allows a paralysis victim to move an artificial arm with only the brain.²² These are clearly innovations that policymakers want to encourage, and FDA is charged with ensuring there is a “reasonable” assurance of safety and efficacy for these high-risk devices.²³

However, reducing decision-making time is not sufficient to increase the rate of medical device innovations that cure or ameliorate health conditions. It appears to be the case, for instance, that fewer medical device inventions are being submitted to FDA even though they are getting

approved faster. The number of devices submitted for approval will be affected not only by the time required for a decision but also by the cost of the submission and the predictability of the decision.

Figure 7 plots the number of PMAs annually over the last decade and also shows inflation-adjusted spending on FDA’s Devices Program.

Annual real spending on FDA’s Devices Program increased substantially in 2009 and has increased again since 2013. It is now nearly 50 percent higher than in 2006 (with an additional 12 percent increase in user fees requested for 2017). But while the number of first-of-a-kind device applications spiked last year (to 72, from 43 in

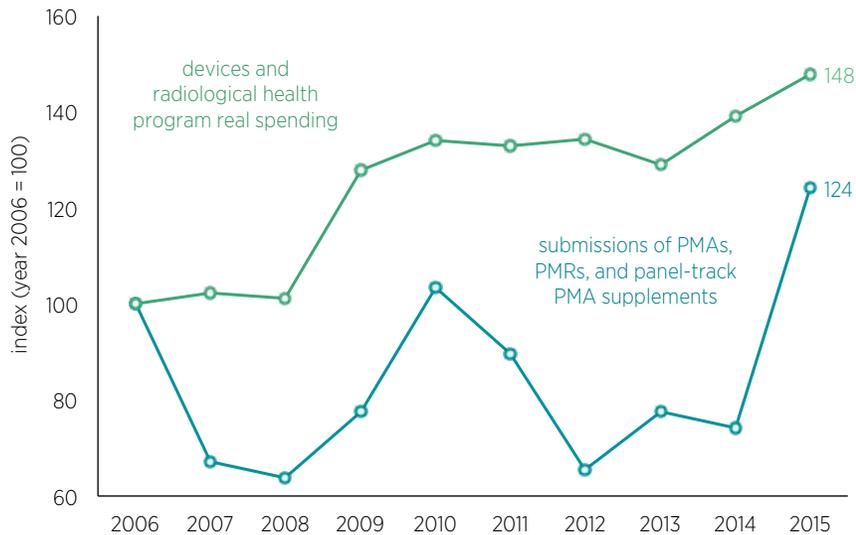


Figure 7

FDA Devices and Radiological Health Program: Real Spending and PMA Submissions

Notes: All years are fiscal years. Spending data is CPI-adjusted to April 2015 dollars.

Sources: FY 2015 spending data are from FDA, *Justification of Estimates for Appropriations Committees*, 2017. Spending data for earlier years provided by FDA Office of Budget. Submissions data are from FDA, *Performance Report to Congress for the Medical Device User Fee Amendments, FY 2006–FY 2014*; and FDA, *MDUFA III Performance Report*, February 18, 2016.

2014), in only two of the last nine years has the number of first-of-a-kind device applications been higher than it was in 2006.

So FDA has been obtaining substantially more resources to handle roughly the same number of device PMAs (although the number of PMA *supplemental* submissions was somewhat higher in the last five years than in the preceding five years). Resources may have been going to other activities, including increased examinations of imported

goods (conducted by ORA) and incoming Medical Device Reports (MDRs), which are user submissions regarding the safety of devices already on the market (see the appendix for details). But despite having more resources and FDA's Innovation Initiative, they have not “accelerated innovation focused on high priority unmet health needs.”²⁴

The overall decline in submissions is also illustrated in figure 8 for dollars invested in medical devices.

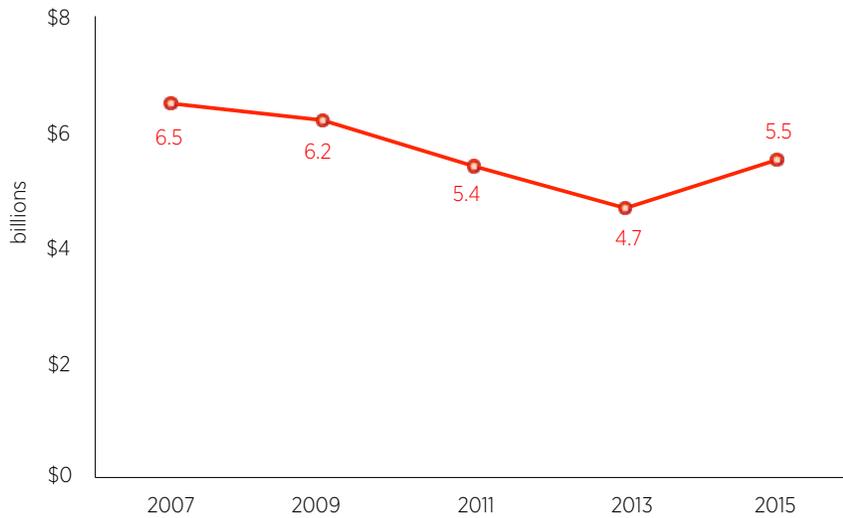


Figure 8

Aggregated Investment Dollars over Time

Source: PricewaterhouseCoopers, "National Aggregate Data, MoneyTree Report," accessed June 28, 2016.

More Pre-Submission Activity to Meet MDUFA Goals

Recent reporting by CDRH suggests that the average length of time it spends reviewing new-device applications has fallen over the past few years. The latest quarterly performance report from CDRH says that the average time to decision for novel devices, PMAs, has decreased markedly since reaching a 10-year high in 2009. The report also states that the average time to decision for devices that have similar predicates already on the market (510(k) Premarket Notifications, or 510(k)s) has fallen steadily from a peak in 2010.²⁵

In fact, for both PMAs and 510(k)s, interaction between CDRH and a device sponsor often begins long before the filing of a PMA or 510(k).²⁶ CDRH has for many years encouraged device makers to contact it with questions prior to filing an application. In 1995, CDRH outlined a process by which sponsors pursuing an investigational device exemption (IDE) could initiate such early interactions if they wished. In the following years, CDRH began to use this pre-IDE program to handle inquiries from sponsors looking for advance help with

other (non-IDE) submissions, including PMAs and 510(k)s. Then, under regulatory guidance published in 2012 and finalized in 2014, the pre-IDE process was substantially intensified and formally expanded to cover the major types of applications. It was rechristened the Pre-Submission Program. While using the program is not required, the guidance says that “Pre-Subs . . . are strongly encouraged in situations when specific questions arise which are not adequately addressed by existing guidance.”²⁷

Pre-submission interactions between CDRH and sponsors have grown enormously in the last decade. FDA reported in 2011 that the time spent

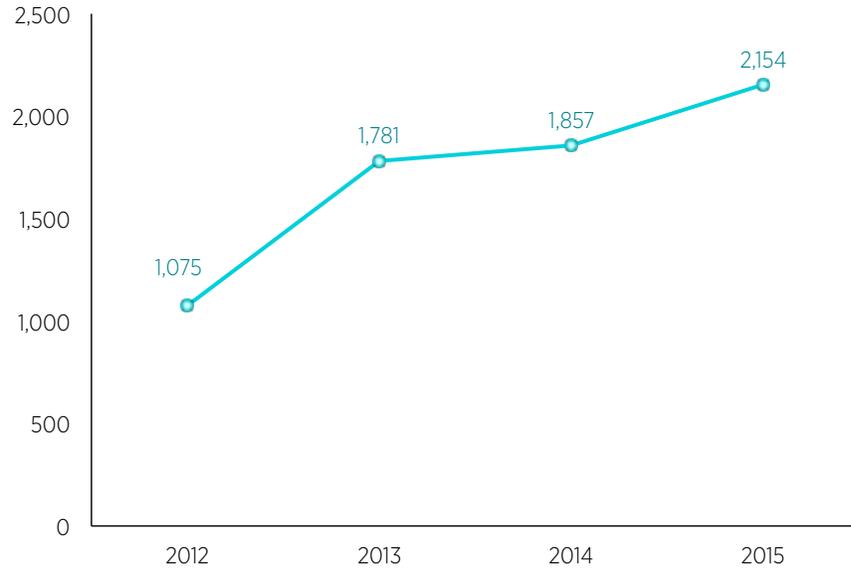
on such interactions had doubled between 2005 and 2010.²⁸ After the new guidance was drafted, FDA began to provide annual data to Congress on CDRH’s Pre-Submissions workload—which is, ironically, essentially a count of “Pre-Submission” submissions—in 2012. Between 2012 and 2015, as shown in figure 9, Pre-Submissions doubled again.

Certainly, the Pre-Submission Program involves some formalization of contacts that, in the past, also would have taken place informally pre-submission. But it also involves some movement of what once would have been *post-submission work* into what might be called “the pre-submission period.” Hence the dramatic increase in

Figure 9

FDA Devices and Radiological Health Program: Number of Pre- Submissions Submitted

Source: FDA, *Justification of Estimates for Appropriations Committees, 2014–2017*.



recent years. As a 2009 conference presentation from Hogan & Hartson LLP put it: “Pre-IDE process often saves subsequent IDE review time.”²⁹

The pre-submission period, while often very lengthy, is not counted in the average time to decision figures (required by MDUFA) reported by CDRH. The dramatic expansion

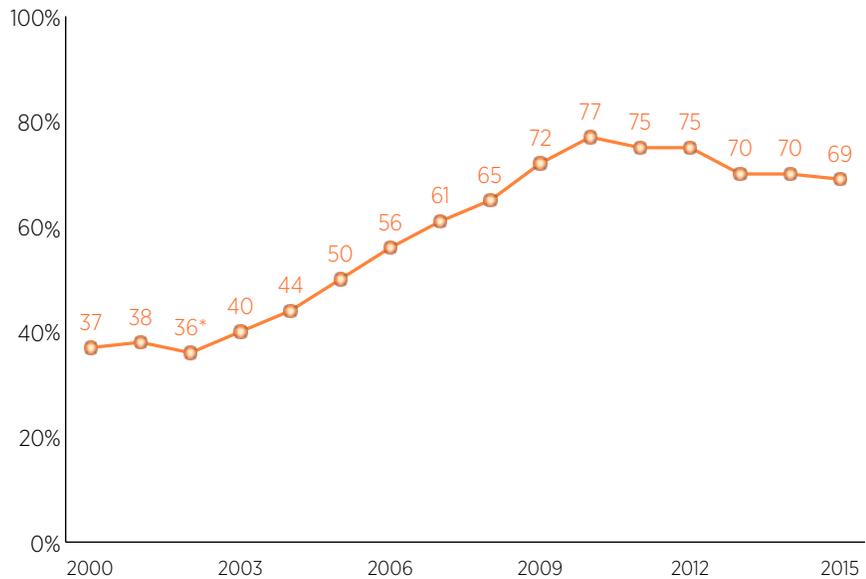
of the Pre-Submission Program that has taken place in recent years *should* have caused those CDRH-reported average time to decision figures to fall—not because of increased efficiency, but because much of the time that FDA and device sponsors spend working on the initial application has been moved off the (MDUFA) books.

Requests for Additional Information Post-Submission

Another impact of MDUFA is the expanded use of requests for Additional Information (AI) during the substantive review. When FDA asks a manufacturer for more information using an AI, the original MDUFA “clock” used to determine whether they have met their performance goals stops. However, as of the guidance issued in 2012 (MDUFA III), FDA began to share a goal with industry called “Total Time to Decision” that

does include AI requests.³⁰ To meet this goal, the final decision must be made within 100 days of the initial “accepted” submission.

As shown in figure 10, the reason for this goal is clear: the proportion of 501(k) applications with AI requests grew from 36 percent in 2002 to 75 percent in 2012. However, since the new goal was introduced, that proportion has only dropped down to 69 percent.



*Medical Device User Fee and Modernization Act of 2002

Figure 10

Percentage of 510(k) Applicants with Additional Information Requests

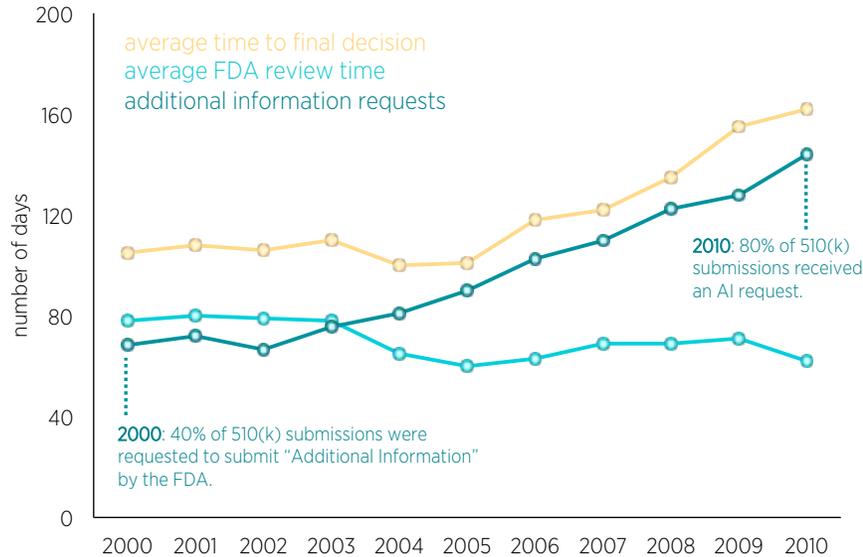
Source: FDA, MDUFA III Performance Report, November 9, 2015.

Although the MDUFA report itself does not provide analysis to explain what has driven the increasing percentages of AI requests, these numbers do fall in line with FDA's more rigorous approach to 510(k) application reviews.³¹ When 510(k) AI requests peaked in 2010, medical

device industry groups were lodging more sustained complaints about how burdensome FDA's registration process had become.³² Not surprisingly, figure 11 shows that the increase in AI requests coincides closely with the marked increase in total review time.

Figure 11

Additional Information (AI) Requests Lengthening Medical Device Approval Times, 2000–2010



Source: Government Accountability Office, "Medical Devices: FDA Has Met Most Performance Goals but Device Reviews Are Taking Longer," GAO-12-418, February 2012.

Summary

Congress continues to increase funding for FDA through both the general fund and industry user fees (and now, possibly, through mandatory expenditures) with the hope that performance goals and additional funding would increase FDA's performance and lead to an increase in innovations. Congress has continually tried to refine these goals, but FDA finds strategic ways to narrowly meet each goal while frustrating the original goal of improving health outcomes through innovation. As Manhattan Institute senior fellow

Peter Huber recently noted, "FDA's complex and costly review process for new drugs and devices makes it extremely difficult for new innovators to get their life-enriching medical services to market quickly."³³

To meet user fee goals, FDA has strategically found ways either to avoid being "on the clock" or to reduce its workload. Because of these strategies, modifying the goals of MDUFA and PDUFA and giving FDA increased resources has not resulted in more medical product innovation.

To incentivize innovation in medical products, FDA should decrease the percentage of products that must have premarket review or notification and, for those that remain, decrease the cost and time of review and rely more on postmarket mechanisms, particularly for effectiveness.³⁴

These solutions can be enacted as part of renewed user fees by insisting on accomplishing new performance measures prior to receiving new funds.

1. Remove more products from the system entirely, particularly low-risk products. It is not clear why an electric toothbrush is a medical device that requires

review or why every device improvement requires review. To free up resources, FDA should also consider removing low-risk drugs from the system that have already been reviewed for safety but for which new indications have been discovered.

2. Move to eliminate Phase III clinical trials or give conditional approvals (with more postmarket surveillance³⁵) and move those that remain toward intermediate endpoints.³⁶
3. Reduce the required size of clinical trials.³⁷
4. To the extent that performance goals remain, they should cover the moment of interaction with a manufacturer to the end and include all AI requests. They should also apply to 100 percent of submissions.
5. Introduce competition in reviews from the private sector, beginning with lower-risk medical devices.³⁸

APPENDIX

Table A1

FDA Human Drugs Program

Note: All years are fiscal years. Spending data is CPI-adjusted to July 2015 dollars.

Sources: Output metrics and FY 2015 spending data are from FDA, *Justification of Estimates for Appropriations Committees*, 2009–2017. Spending data for earlier years provided by FDA Office of Budget.

		Average 2006–2010	Average 2011–2015	Annualized Rate of Change
	Human Drugs Program Real Spending	\$763 million	\$1,129 million	+8.1%
New Drug Review Outputs	NDA/BLA Priority and Standard Reviews	169	157	-1.5%
	NDA Supplemental Reviews	3,041	3,116	+0.5%
Generic Drug Review Outputs	ANDA Actions	1,851	1,874	+0.2%
	ANDA Supplemental Actions	4,520	5,831	+5.2%
Patient Safety [postmarket] Outputs	Patient Safety Reviews	1,799	3,310	+13.0%
Field Activity Outputs	Import Physical Exams	4,028*	8,464	+16.0%

*Missing data for 2006; compensated by putting a double weight on 2007.

APPENDIX

Table A2

FDA Devices and Radiological Health Program

		Average 2006–2010	Average 2011–2015	Annualized Rate of Change
	Devices and Radiological Health Program Real Spending	\$339 million	\$409 million	+3.9%
Submissions	PMAs, PMRs, and Panel- Track PMA Supplements	48	50	+0.9%
	180-Day PMA Supplements	157	189	+3.7%
	501(k) Premarket Notifications	3,923	3,886	–0.2%
Field Activity Outputs	Import Physical Exams	10,061*	24,106	+19.1%

*Missing data for 2006; compensated by putting a double weight on 2007.

Note: All years are fiscal years. Spending data is CPI-adjusted to April 2015 dollars.

Sources: Field activity and FY 2015 spending data are from FDA, *Justification of Estimates for Appropriations Committees, 2009–2017*. Spending data for earlier years provided by FDA Office of Budget. Sources for submissions data are FDA, *Performance Report to Congress for the Medical Device User Fee Amendments, FY 2006–FY 2014*; and FDA, *MDUFA III Performance Report*, February 18, 2016.

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About the Author

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