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# Taking the Pulse of Medical Device Regulation & Innovation



# TAKING THE PULSE OF MEDICAL DEVICE REGULATION & INNOVATION

## Introduction

In 2011, as industry, the U.S. Food & Drug Administration (FDA), Congress and other stakeholders prepared to renew the medical device user fee program, California Healthcare Institute (CHI) and The Boston Consulting Group (BCG) initiated the *Competitiveness and Regulation* study, which analyzed trends in FDA product review processes and their impact on the medical technology innovation ecosystem.<sup>i</sup> The study was initiated in response to increasingly unpredictable timelines at the Agency and the global financial meltdown, which were undermining U.S. medical technology investment, innovation and competitiveness.

As *Competitiveness and Regulation* illustrated, concerns over increasing review times were well-founded. Medical device approval times at the FDA had slowed across the board. Comparing 2010 with 2003 through 2007, the first four years of the medical device user fee program, review times for lower-risk 510(k) devices and for novel, higher risk premarket approval (PMA) products had lengthened considerably. Indeed, FDA device review times were, on average, *slower* than they had been before the medical device user fee program.

If slower FDA approval times had increased safety, the debate might have ended there. However, *Competitiveness and Regulation* highlighted another important issue: the U.S. and the FDA are not the only options for medical technology innovators. Faced with increased regulatory uncertainty at the FDA, as well as investors who were downsizing and de-risking their portfolios in the face of the Great Recession, U.S. medical device companies were looking elsewhere.

By 2010, complex medical devices reviewed through the FDA's PMA process were being approved, on average, nearly four years faster in Europe. In addition, there were no demonstrable differences in safety or efficacy between devices approved in the U.S. and those green-lighted in Europe.<sup>ii</sup>

Despite often being developed in the U.S., proven, life-saving medical technologies were unavailable for American patients unless they traveled abroad.

In light of these findings, Congress, the FDA, the device industry and other stakeholders collaborated to find a solution. In negotiations with industry, the FDA agreed to implement new policies to improve the regulatory system's clarity, consistency and predictability. To fund these refinements, industry agreed to pay significantly higher user fees. Congress incorporated further improvements into the *Medical Device User Fee Amendments of 2012* (MDUFA III), part of the *2012 Food and Drug Administration Safety and Innovation Act* (FDASIA).

Have things gotten better? Has the FDA's medical device review process improved? Not surprisingly, the answer is not a straightforward yes or no. Real improvements are evident, yet there are still areas of concern. In some cases, it is simply too early to tell.

One dynamic does seem certain, however. The evidence is overwhelming that leaders at the Agency and, in particular, its Center for Devices and Radiological Health (CDRH) have worked to get processes, internally and with industry, back on track. Their leadership echoes the conclusion of *Competitive-*

*ness and Regulation*—working together, we can restore, support and sustain a rigorous, science-based Agency and efficient, transparent and predictable review processes to ensure safe and innovative treatment and technologies for patients in need.

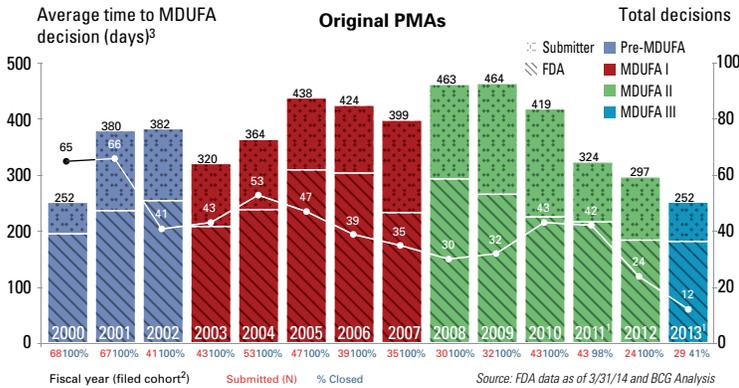
The commitment by Agency leadership was demonstrated in the development of this report, during which CDRH Director Jeff Shuren, M.D., and his senior team spent considerable time with us, providing unprecedented access to and answers about the data presented in the following pages. Our discussions were frank and candid, but most important, they were illuminating and constructive.

We know that change does not occur overnight. Improvements can vary across any agency as large as the FDA. But leadership matters. Dr. Shuren and his team deserve credit for many of the improvements we've seen, and it is up to industry, Congress and others to help ensure the progress continues. Where improvements have been slower or yet to be seen, we must continue to work together constructively to spur appropriate action.

We hope this report facilitates both.

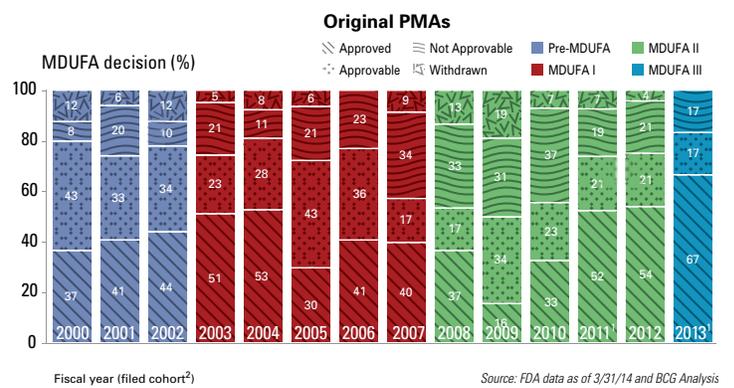
## Trends Indicate Declining Review Times for CDRH PMA's, Must Consider Impact of Pending Submissions

Figure 1



## Proportion of Approvals is Increasing, May Decrease as Pending Submissions are Closed

Figure 2



### Regulatory Review Overview

CHI created this report to provide objective data about the device review process. This information can help industry, policymakers and regulators assess where processes have worked well, and help them focus on areas that need improvement.

The report examines a number of issues that directly impact device approval, such as decision efficiency, process efficiency and outcomes. Specific measures include review times for both PMA's and 510(k)s; review backlogs; overall approval rates; division and review branch performance; and comparisons to EU timelines.

Notably, as a result of our discussions with the Agency, all data presented in this report is based upon submission cohorts<sup>1</sup>; *Competitiveness and Regulation* used decision cohort-based data. The advantage of submission cohorts is that these take as a starting point, the most recent submissions and assess their fate in a forward looking manner—submission cohorts therefore track more accurately the most recent progress and are not biased by past performance. The disadvantage is that early in the fiscal year, data is harder to interpret as many reviews will take a number of months, and in some cases data at year-end will also be incomplete if not all submissions have been decided on within 12 months.

### PMA Trends

PMA's represent the most complex, and often times most cutting edge of implantable, life-sustaining medical devices, such as heart valves, combination pacemakers/defibrillators and neuromodulation technologies. They are also the most expensive to develop and bring to market, usually requiring significant clinical studies and data for approval. In a typical year, only about 30 new PMA products are approved by the FDA.

In the lead-up to MDUFA III negotiations, PMA devices had seen a marked slow-down in approval times at the FDA over the first decade of the 2000s, as illustrated in *Figure 1*.<sup>2</sup> However, in 2010, as Dr. Jeffrey Shuren took the helm at the FDA's device center and Congress began a series of oversight hearings on Agency performance, that trend began to stabilize and reverse. Data suggests that the PMA classes of 2011 and 2012 will show the best overall review-time performance of the device user fee era. 2013 shows even further improvement, however, it is premature to determine given the number of products still awaiting a decision.

Signals of the turnaround for PMA's are also evident in the proportion of approved or approvable submissions (*Figure 2*), which has begun to rebound from the 2009 nadir, as well as the steep improvement in the Agency's backlog of pending decisions, down nearly half since 2010 (*Figure 3*).

## PROTECTING USER FEES

For more than a decade, drug and device makers have worked with the FDA to accelerate product approvals. To resolve this issue, industry agreed to pay significant user fees, providing extra resources to streamline the review process. In return, the Agency consented to a number of performance benchmarks.

These agreements, as codified in the *2012 Food and Drug Administration Safety and Innovation Act (FDASIA)* and other legislation, have helped improve Agency performance. Unfortunately, cuts to the FDA budget under the sequester limited the Agency's access to user fees.

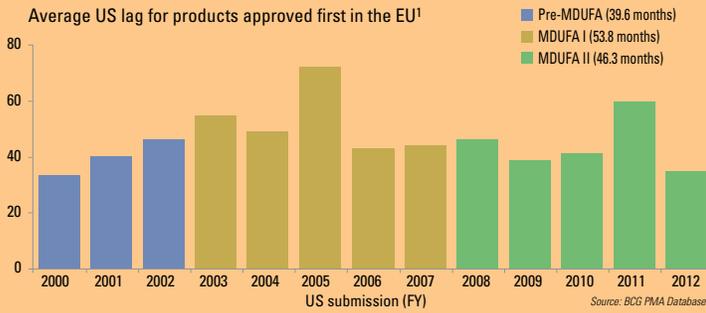
While Congress did not intend private, industry-paid dollars to be sequestered, the White House Office of Management and Budget (OMB) made the determination that they would be. This created an untenable situation in which industry continued to pay user fees along with their product submissions, but the FDA was unable to access the money.

In January 2014, when Congress passed a bipartisan spending plan, the sequester was rescinded for two years (FY2014 and FY2015) and \$85 million in total FDA user fees set aside during FY2013 were restored.

However, restoring these user fees was only the first step. The long-term threat posed by sequestration must still be resolved, or the continued viability of the FDA user fee model itself is at risk as the next round of industry-FDA user fee talks will begin under the cloud of the sequester's return. CHI, in collaboration with numerous industry organizations, patient groups, and others is working with Congress on legislation (H.R. 2725, the *FDA Safety Over Sequestration Act or FDASOS Act*) that will reverse OMB's determination and permanently exempt FDA user fees from sequestration.

## Despite Progress, Gap Remains Between PMA Approvals in US vs. EU

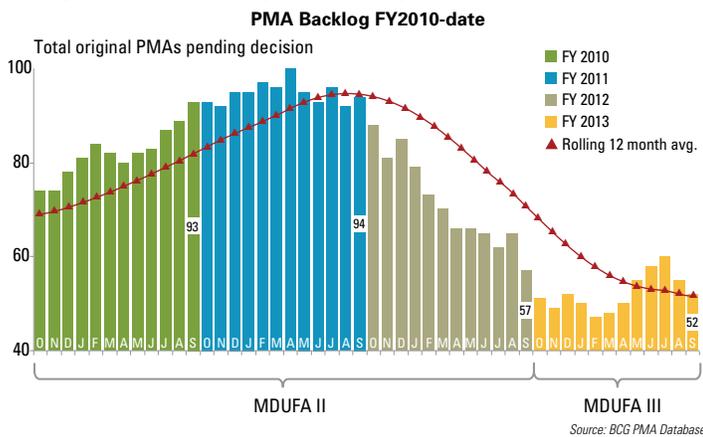
Figure 4



When comparing trends at the FDA with those in Europe (Figure 4), another sobering dimension is added: the 3-5 year lag between European and U.S. approval, which has seemingly always existed, hasn't improved during the user fee era.<sup>3</sup> Though processes and standards in Europe differ considerably from the FDA, and other factors are certainly also at work, Europe's regulatory environment continues to attract U.S. medical technology business, and all that goes with it—investment, R&D, engineering, subsequent design improvements and iterations, clinical trial infrastructure and other expertise. Only time will tell if recent improvements at the FDA ultimately have any impact on this gap.

## Significant Clearing in Backlog of CDRH PMAs

Figure 3



While these improvements are encouraging, it is also helpful to put these figures into context. For example, as shown in Figure 1, the number of PMA submissions has been trending down for some time. While not all the reasons for the decline are known, it does raise some concerns that warrant further consideration.

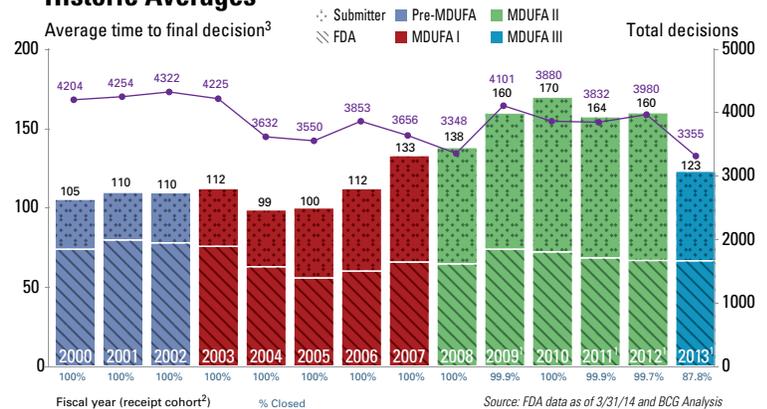
## 510(k) Trends

While PMA approval times seem to have turned the corner, the same cannot be said for clearance of 510(k) products, which represent that vast majority of devices (over 3,000 annually) reviewed by the FDA. As addressed in *Competitiveness and Regulation*, after holding steady between 2000 and 2006, 510(k) clearance times lengthened dramatically—review times in 2010 were 60 percent longer than in 2000 (Figure 5). Today, 510(k) review times continue to remain far higher, and processes are still viewed as less predictable, than during the pre-device user fee era.

There is at least one preliminarily encouraging sign for 510(k)s. Initial data suggests that clearance times have dropped slightly since 2010, and may drop further in 2013, although the cohort is still open. In addition, after climbing steadily since 2005 and peaking in 2010, the Agency's 510(k) backlog has begun to improve—especially for those pending for more than 90 days (Figure 6). However, by nearly any measure, there is still much work to be done before the 510(k) process is considered back on track.

## 510(k) Clearance Times Remain Longer than Historic Averages

Figure 5



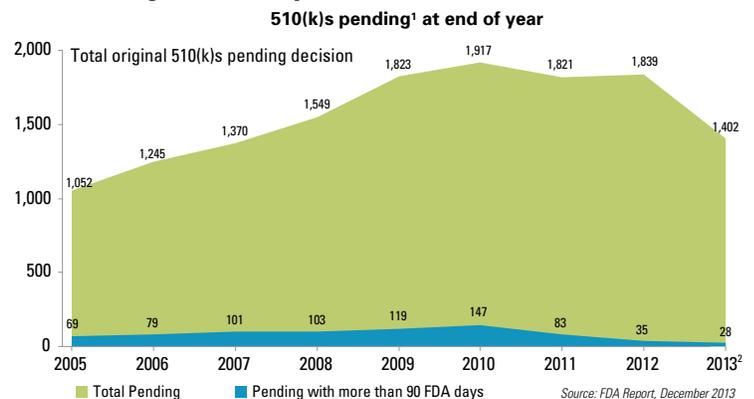
## De Novo Process

Introduced in the *FDA Modernization Act of 1997*, the de novo process seeks to accelerate clearance times by providing companies an alternative to the PMA path for low to moderate-risk devices. Since 1997, 106 de novo petitions have been granted, a tiny piece of the 52,000 510(k) clearances during the same period (Figure 7).<sup>iii</sup>

FDASIA included significant changes to the de novo 510(k) process to make the program more submitter-friendly and increase its use. Originally, de novo was a two-step process. After submitting a 510(k), if the device was ruled not substantially equivalent (NSE), the company could submit a de novo application within 30 days to reclassify it.

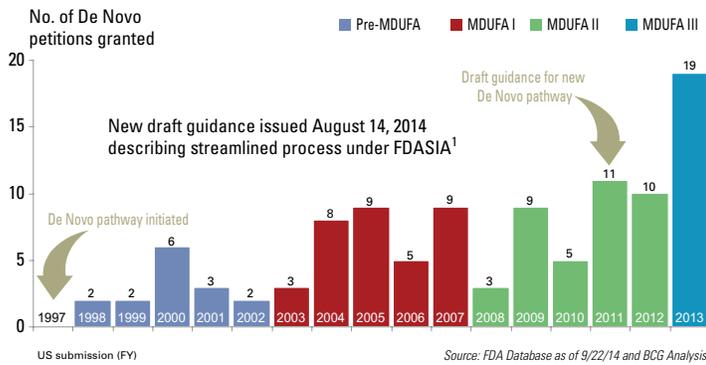
## Reduction in 510(k) Backlog, Primarily Those Pending Over 90 Days

Figure 6



## Increase in De Novo Petitions Granted in Recent Years, Expected Growth

Figure 7



Under FDASIA, the process has been simplified to one step. Rather than wait through a rejection, manufacturers can now submit a request for de novo classification from the start. This is an implicit acknowledgement that their device will require more testing and documentation than if they had pursued standard 510(k) clearance. The FDA has 120 days to issue a decision.

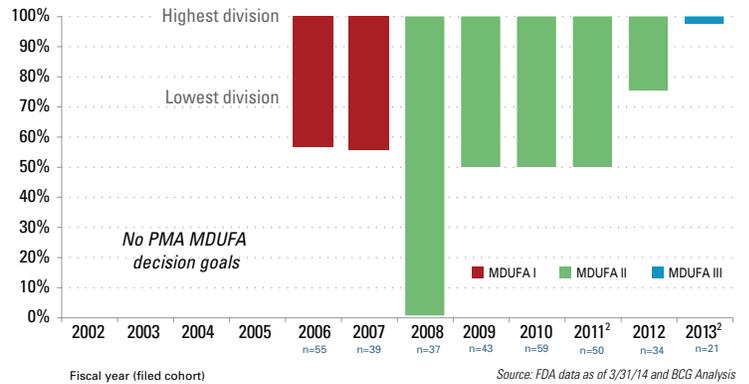
The number of de novo petitions granted has been slowly increasing since 1997 when the pathway was first introduced. For submissions in 2010 and 2011, ~10 petitions were granted, but in 2013 this number almost doubled to 19. It remains to be seen whether the new FDASIA guidance will further increase the use of this pathway.

### Does Performance Differ Across Review Divisions?

While aggregate data is informative, it often pays to take a closer look. For FDA device performance, we believe this means examining performance trends across review divisions and branches. Why? A key anecdotal theme heard from industry and investors alike has been that experience with the Agency can vary widely. Review of Product X may be characterized by quality communications, interaction and a timely decision; Product Y seems to have fallen into a black hole.

## Tightening in the Range in Division Percentages of PMA MDUFA Decisions Meeting Performance Goal<sup>1</sup>

Figure 8

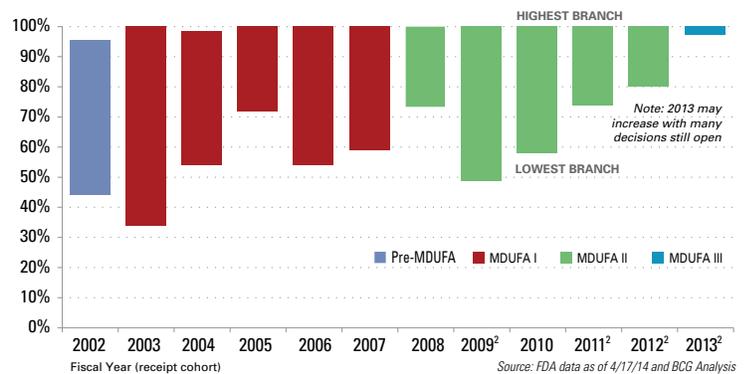


The data suggests there is some substance to these views. As shown in Figure 8, review divisions varied markedly in meeting their PMA MDUFA performance goals. Figure 9 shows similar variances across branches for 510(k) decisions. Encouragingly, the most recent years' data shows a trend towards narrowing those gaps.

A closer look at this and similar data may be helpful to Agency leadership, industry and Congress in identifying practices that may either be more broadly adopted across the Center, or conversely, become a focus for improvement.

## Tightening in the Range in Branch Percentages of 510(k) Final Decisions<sup>1</sup> Within 90 FDA Days

Figure 9



# CONCLUSION

The FDA is a critical linchpin in the medical technology innovation ecosystem. At the onset of this decade, however, the Agency and its review processes were viewed by industry and investors alike as increasingly unpredictable and inconsistent. Together, with the economic downturn resulting from the Great Recession, this period was viewed by many as a low point for the sector.

Recognizing the severity of the circumstances, industry, Congress and, ultimately, the leadership of the Agency were galvanized into action on a number of fronts, culminating in legislation that made a number of reforms and improvements to device regulatory review processes and mechanisms—paid for with a hefty increase in industry user fees. The early evidence suggests that this work is beginning to pay off, with PMA review times showing significant improvements and 510(k) times plateauing, though at a pace still far slower than historic standards.

However, there is still much more work to be done and, as we approach the next round of user fee negotiations, more to learn in order to ensure device regulatory review processes and accompanying performance measurements are best directed towards the Agency's twin goals: protecting patient safety and promoting patient health through timely approval of and access to innovative medical technologies.

## Footnotes

- <sup>1</sup> 510Ks are reported based on Receipt Cohorts, which is the later of: (1) the date on which FDA receives the required user fee; or (2) the date on which FDA receives an acceptable eCopy of the application. PMAs are reported based on Filed Cohorts, which is the date on which FDA receives an application (or an amended application) that FDA accepts for filing.
- <sup>2</sup> This figure shows MDUFA decisions. A similar analysis was conducted for final decisions and the trends look similar although the percent of cohorts closed for final decisions is lower.
- <sup>3</sup> Data assess the lag for products approved in Europe first and then approved in the US. Not for products approved in the US before Europe.

## Sources

- <sup>i</sup> Gollaher D, Goodall S. *Competitiveness and Regulation: The FDA and the Future of America's Biomedical Industry*. California Healthcare Institute and The Boston Consulting Group, February 2011.
- <sup>ii</sup> David S, Gilbertson E and Goodall S. *EU Medical Device Safety Assessment: A Comparative Analysis of Medical Device Recalls 2005-2009*. The Boston Consulting Group, January 2011.
- <sup>iii</sup> What You Don't Know About De Novo—A Primer For Medical Device Companies. [www.apivolutions.com/blog/medical-device/2011/03/what-you-dont-know-about-de-novo-a-primer-for-medical-device-companies](http://www.apivolutions.com/blog/medical-device/2011/03/what-you-dont-know-about-de-novo-a-primer-for-medical-device-companies), accessed February 14, 2014.

## Figure Notes

### Figure 1

- <sup>1</sup> Cohorts still open as of 3/31/2014, average times may increase; FY2011 cohort 98% closed (42 of 43) and FY2013 cohort 41% closed (12 of 29).
- <sup>2</sup> Date on which FDA receives an application (or an amended application) that FDA accepts for filing.
- <sup>3</sup> The total review time includes both FDA and Submitter days. FDA days are calendar days when a submission is considered to be under review at the Agency for submissions that have been accepted.

### Figure 2

- <sup>1</sup> Cohorts still open as of 3/31/2014, average times may increase; FY2011 cohort 98% closed (42 of 43) and FY2013 cohort 41% closed (12 of 29).
- <sup>2</sup> Date on which FDA receives an application (or an amended application) that FDA accepts for filing.

### Figure 4

- <sup>1</sup> US lag is the difference between the date of CE Mark in Europe and FDA approval in the US; only calculated for devices approved in the US with a reported CE Mark date in Europe; US CDRH data collected from monthly listing on FDA website of approved original PMAs (PMA numbers in the form of PXXXXXX); CE Mark date most commonly found in Marketing History section of Summary of FDA Safety and Effectiveness Data (other sources include press releases and company data); In the case when an approximate date is given, the most conservative assumption is made (e.g. May 2010 would be recorded as 5/31/2010 in the database).

### Figure 5

- <sup>1</sup> Cohorts still open as of 3/31/2014, average times may increase; FY2009 cohort 99.95% closed (4,101 of 4,103); FY 2011 99.97% closed (3,832 of 3,833); FY2012 99.67% closed (3,980 of 3,993); and FY2013 87.80% closed (3,355 of 3,821).

- <sup>2</sup> The date of receipt is the later of: (1) the date on which FDA receives the required user fee; or (2) the date on which FDA receives an acceptable eCopy of the application.
- <sup>3</sup> The total review time includes both FDA and Submitter days. FDA days are calendar days when a submission is considered to be under review at the Agency for submissions that have been accepted.

### Figure 6

- <sup>1</sup> Under review or on hold.
- <sup>2</sup> Excludes FY 2013 receipts that have not been accepted for substantive review.

### Figure 7

- <sup>1</sup> FDA Safety and Innovation Act, passed in 2012, eliminated the 510(k) equivalent requirement entirely, allowing medical device companies to apply for de novo status without the burden of proving substantial equivalence.

### Figure 8

- <sup>1</sup> Based on CDRH PMAs and PT Supplements that had a MDUFA decision subject to a performance goal; tier 2 goal was used if more than one MDUFA decision goal applied; FY 2005 had no MDUFA decision goal for non-expedited PMAs or for any PT supplements and is excluded from this comparison.
- <sup>2</sup> Cohort not complete—data may change.

### Figure 9

- <sup>1</sup> Based on SE and NSE decisions only; excludes Branches with fewer than 12 E/NSE decisions in a year (i.e., <1 per month).
- <sup>2</sup> Cohort still open as of 4/17/2014 include 2009, 2011, 2012 and 2013.

## About California Healthcare Institute (CHI)

CHI represents more than 275 leading biotechnology, medical device, diagnostics and pharmaceutical companies, and public and private academic biomedical research organizations. CHI's mission is to advance biomedical research, investment, and innovation through effective advocacy of policies to improve public health and ensure the continued vitality of the life sciences sector. CHI's website is [www.chi.org](http://www.chi.org). Follow us on Twitter @calhealthcare, Facebook, LinkedIn and YouTube.

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The Boston Consulting Group (BCG) is a global management consulting firm and the world's leading advisor on business strategy. We partner with clients from the private, public, and not-for-profit sectors in all regions to identify their highest-value opportunities, address their most critical challenges, and transform their enterprises. Our customized approach combines deep insight into the dynamics of companies and markets with close collaboration at all levels of the client organization. This ensures that our clients achieve sustainable competitive advantage, build more capable organizations, and secure lasting results. Founded in 1963, BCG is a private company with 81 offices in 45 countries.

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