Interstates and Autobahns

Global Medtech Innovation and Regulation in the Digital Age

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UCLA Biodesign is a healthcare technology innovation hub at the University of California Los Angeles. Uniting stakeholders across the healthcare ecosystem, UCLA Biodesign seeks to transform medicine through the development and translation of novel technologies. The advancement of industry research and thought leadership are central to UCLA Biodesign's mission. UCLA Biodesign collaborates with industry partners and the medical community to support innovations that will deliver improved value and outcomes to patients worldwide. An annual innovation fellowship at UCLA Biodesign supports training and leadership development in collaboration with the UCLA David Geffen School of Medicine, UCLA Anderson School of Management, UCLA Clinical and Translational Science Institute, and UCLA Health.

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Introduction

UCLA Biodesign has led an industry study of medtech and digital health regulation and its impact on innovation in US and global strategic markets. This work examines the experience and perspectives of medical and digital technology companies with the US Food and Drug Administration (FDA) and other leading global regulatory bodies from January 1, 2010, through December 31, 2021. Recognizing the additional downstream mechanics of market access and the role of reimbursement agencies, we also examined key questions surrounding existing and forward-looking perspectives on reimbursement.

During this period, the medtech industry collectively and consistently invested over 7% of its annual global revenues in R&D, amounting to more than $300 billion. US private venture capital funding in digital health alone increased significantly, from $1.1 billion in 2010 to $29.1 billion by 2021, and US private funding for medical devices has averaged around $4 billion per year during the same time frame. As innovators deployed huge amounts of capital to bring new, more connected and digitized medical products to market, what were their expectations of the regulatory community?

In response to the rise of digital innovation and the expansion of medical technology, the FDA has implemented new programs, special designations, and guidance for companies launching new medical products, especially with regard to digital health—for example, software as a medical device (SaMD)—as well as principles and white papers for artificial intelligence and machine learning (AI/ML) offerings. Advances in technology, along with regulatory and reimbursement programs and policies associated with the 21st Century Cures Act, the FDA Safety and Innovation Act, and the unbundling of remote patient monitoring reimbursement, have contributed to a rapid expansion of digital health throughout the decade, ushering in a new era of innovation.

No known research sheds light on how the FDA has managed the convergence between medical devices and digital health and whether today's programs are maintaining pace with the exponential acceleration in technology. Other agencies around the world have experimented to various degrees in these areas, but implementation of new policies historically lags technology and business model innovation. Consequently, there is a need to understand whether the metrics used to gauge regulatory requirements are up to date, whether new regulatory initiatives underway are effective, and how markets can provide clear guidance in the emerging science of digital health. In this report we establish timely benchmarks across various regulatory pathways, designations, therapies, and products, with primary emphasis on US 510(k), De Novo, and premarket approval (PMA) trends, along with somewhat more limited comparative information on the European Union's CE mark, Japan's Pharmaceuticals and Medical Devices Agency (PMDA), and China's National Medical Products Administration (NMPA).

Our findings are based on a survey of 104 company leaders who provided commentary and data on 105 novel medical devices, technologies, and software of any risk class that have achieved regulatory clearance or approval within the FDA.[1] Many of these products also sought EU CE mark, Japan PMDA, or China NMPA approval in the period from 2010 to 2021; we have captured these experiences and data as well. In the US, we have evaluated the experience of novel products with PMA, 510(k), and De Novo regulatory pathways, as well as special designations.

Of the technologies represented, 85% are new products in their respective portfolios rather than line extensions or updates, 60% incorporate digital technology, and the majority are first in class. To maintain an emphasis on innovative technology in areas of high unmet need, products that attained FDA Breakthrough Device designation in the US were eligible for participation even if they had not received FDA clearance or approval.

The intended audience for our research is medtech industry stakeholders, including public and venture-backed manufacturers, regulatory bodies such as the FDA and its counterparts at the Centers for Medicare and Medicaid Services (CMS), and early- and late-stage investors and bankers. It is important to note that our survey results are retrospective. In addition to the survey questionnaire, our research included 104 in-depth interviews with industry representatives.[2] Our interviewees shared feedback on industry best practices, as well as guidance for regulatory and reimbursement agencies that we have included in the report. Our primary goal is to inform the discussion and encourage adoption of practices across industry and governing bodies that will accelerate and support medtech innovations that offer meaningful improvement in the lives of the patients they serve.

1. Two Class I, 88 Class II, and 15 Class III devices.
2. One of our 105 respondents completed the survey but was not available for an interview.

Key Findings

The US market has emerged as the preferred launch site for new medical technology. The pattern, which holds across large and small, venture-backed, private, and publicly traded companies, represents a sea change for the industry. Historically, medtech companies preferred to launch in Europe because they viewed EU product registrations as more straightforward. In our survey, 53% of respondents say they are deprioritizing the CE mark relative to US FDA approval.

The FDA has responded more effectively to advances in innovation than regulatory authorities in Europe. Overall, 79% of respondents agree that the FDA is responding well to advances in medical technology, with industry looking to the FDA's Digital Health Center of Excellence as a positive development that offers greater clarity and guidance on evolving regulatory pathways. On the narrower topic of whether authorities are adapting to changes brought about by digital technology, 64% of respondents say that the US is managing well versus only 34% who say that Europe is.

The EU's Medical Devices Regulation (MDR) slows the pace of innovation. Nearly half the products in our survey had been launched in EU markets; but 89% of companies sponsoring these products say they will prioritize US regulatory approval going forward. In fact, 23% of respondents with successful CE mark products say they will pursue Japanese and Chinese registration prior to EU clearance. Respondents overwhelmingly view new MDR rules as complex and unpredictable, making it less appealing to develop and launch novel products in Europe. Other factors, including Brexit and intense reimbursement pricing pressure, may also reduce the attractiveness of pursuing the CE mark.

The median cost from initial concept to US 510(k) clearance for novel medical products was $3.1 million, while De Novo products posted a median cost of $5.0 million (data not available for PMA).[3] Cost is dictated by many factors, including but not limited to the inherent novelty of the design, whether clinicals are required, and whether the product consists of software or hardware. The range for 510(k) clearance was $0.2 million to $41.0 million; De Novo products ranged from $0.8 million to $91.0 million. Consequently, average costs alone convey little meaning.

Median time from concept to FDA decision for novel medical products was 31 months for 510(k) and 66 months for De Novo. Minimum and maximum times from concept to approval were reported at 2 to 132 months for 510(k) and 18 to 240 months for De Novo. The wide range in elapsed time reflects differences in starting points for various innovators, with some concepts percolating for years before initiating a formal development project and others proceeding straight from conceptualization to project stage.

Average regulatory review time (pre-MDR) to CE mark for novel medical products remained lower at 3.2 months versus 3.9 months for US 510(k) clearance. Although the average EU regulatory approval process was faster for products in the sample, it is important to bear in mind that this was a retrospective study. Consequently, the results do not fully reflect the impact of European MDR requirements, which went into effect in May 2020.

The FDA's Breakthrough Device designation is widely perceived as an important new program that provides a fast track for medtech innovation. The FDA granted 561 Breakthrough Device designations during the study period, almost all of them since 2019, including nearly one-quarter of our survey respondents. Although only 32 Breakthrough Devices have received FDA clearance to date, 88% of respondents agree that guidance is extremely clear or somewhat clear, 75% believe the program will lead to earlier patient access, and more than half believe it enables more flexible study design.

Increasing product innovation incorporating artificial intelligence and machine learning necessitates greater clarity on regulatory requirements and more reviewer expertise. The FDA has approved 343 AI/ML devices since 1997, more than half of them in 2019 and 2020. Median cost and review times for 16 AI/ML products seeking 510(k) clearance in our sample were reported as $9.1 million and 37 months.

Respondents have a less favorable view of the predictability of regulations for digital products than they do of the pathway for standard medical technology. In our survey, 62% of respondents find the US pathway for regulatory approval of standard medical technology predictable, versus 22% who view EU registration similarly. The figures with regard to digital product offerings fall to 33% for the US and just 15% for the EU.

3. Of our total sample of 105 products, 63 510(k) and 13 De Novo products achieving clearance reported full cost data.

The FDA's Progress

Share of respondents who agree that the agency is responding well to advances in medical technology.

Continental Divide

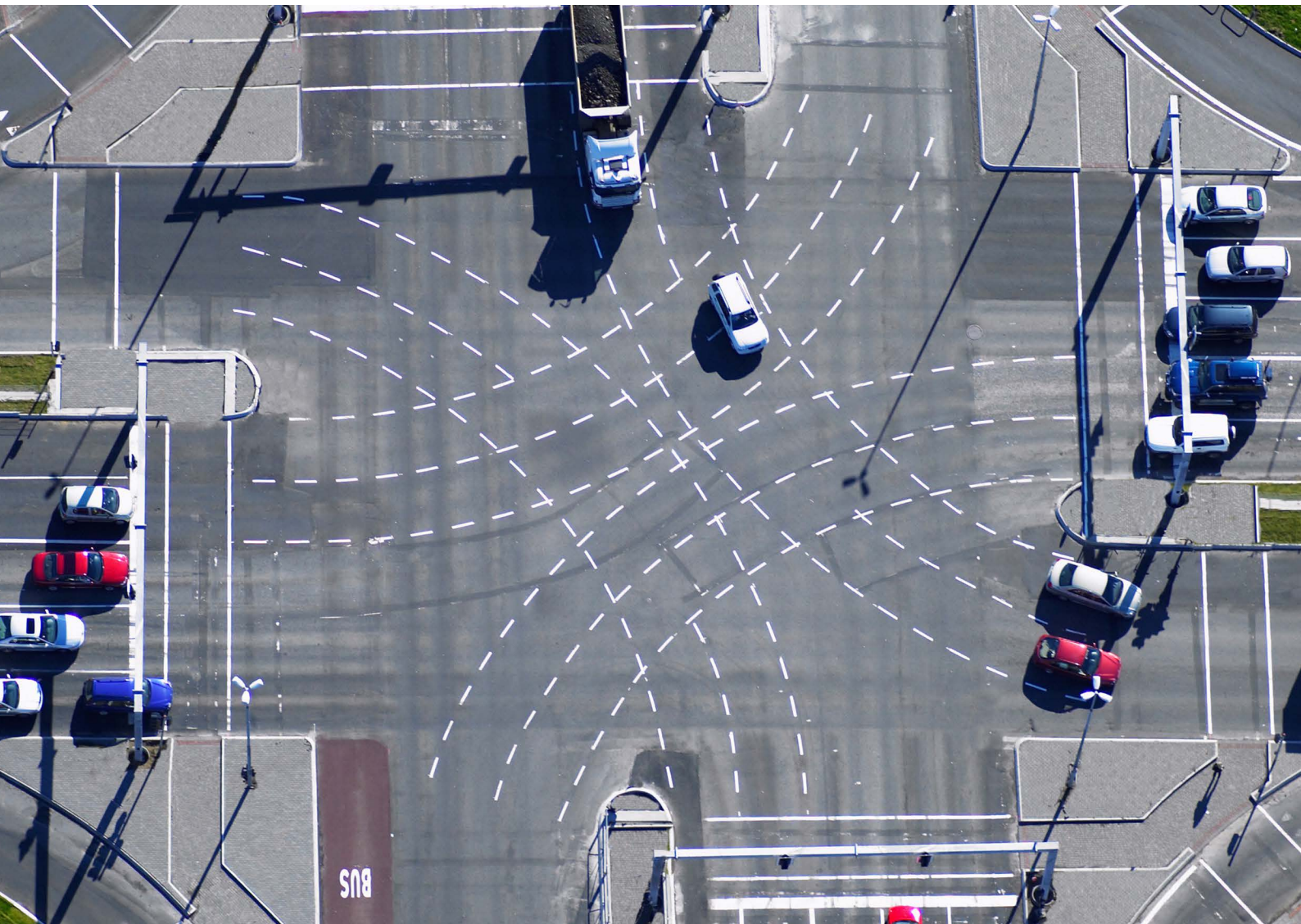
Share of respondents who say they will prioritize US regulatory approval.

For many smaller and venture-backed companies, raising capital hinges on a US-first market strategy in anticipation of the shift in the EU regulatory landscape. Early-stage companies advancing first-in-class medical and digital technology are heavily exposed to evolving regulatory patterns, requirements, and programs. Clear, predictable approval pathways are critical for small and venture-backed medtech firms, which must manage their burn rate carefully to instill investor confidence and raise follow-on funding. The FDA's Q-Submission (Q-Sub) process was used extensively by respondents (69 out of 105), and overwhelmingly by De Novo and PMA applicants (37 out of 40).

Reimbursement is less predictable for digital medical products. In the US, 63% of respondents see the path to reimbursement for digital medical products as unpredictable, versus 45% for traditional products. In the EU, 50% of respondents view reimbursement for digital offerings as unpredictable, compared with 30% who feel the same about standard medtech products.

Reimbursement emerges as the leading barrier to medical innovation across all companies. In our study, 55 of 73 CEOs and regulatory leaders view reimbursement as the key impediment to innovation, eclipsing concerns about regulatory approval. Only 40% of respondents believe that CMS decision criteria for benefit coverage and payment for medical technologies is clear. Leaders broadly called for greater coordination between regulatory and reimbursement agencies and for the creation of a separate reimbursement classification for digital products.

Methodology and Limitations of the Study



This Institutional Review Board–exempt research project was designed to collect information from medtech and digital health executives about their perceptions and experiences with the US FDA, EU CE mark, Japanese PMDA, and Chinese NMPA regulatory processes, as well as the reimbursement processes within these regions. UCLA Biodesign solicited input on survey topics from the FDA, the Medical Device Manufacturers Association, the Advanced Medical Technology Association, the Regulatory Affairs Professionals Society, and a variety of other relevant stakeholders, including but not limited to Octane, UCSF Health Hub, the Colorado Bioscience Association, the Global Center for Medical Innovation, the Medical Device Innovation Consortium, and the Medical Alley Association. (For a complete list of organizations that provided input to the study, see the Acknowledgments.)

The research team leaders at UCLA Biodesign facilitated all surveys over live virtual interviews. The survey team posed questions and recorded responses throughout each interview via Qualtrics. Survey recruitment took place through the associations and groups mentioned above, as well as through digital channels using the UCLA Biodesign website. Survey participants were screened to ensure they represented entities that had successfully registered a novel medical product (FDA Class I [nonexempt]/II/III or international equivalents) during the period from 2010 to 2021 via the 510(k), De Novo, or PMA pathway or under their equivalent in the EU, Japan, or China. In total, the survey reflects the experience of 105 successful product registrations or approvals undertaken by 102 discrete companies. (See Exhibit 1.) In most cases, there was one respondent per company or product. In certain instances —such as in the case of a large publicly traded multinational company with different executives responsible for regulatory versus reimbursement—multiple people were interviewed to obtain a full perspective.

All 105 products included in the survey identified the US FDA's Center for Devices and Radiological Health (CDRH) as the primary center for regulatory review. (See Exhibit 2.) All products were considered novel technology, necessitating at a minimum a 510(k) clearance (nonexempt) for US market registration. Approximately half of the products in the survey had achieved CE mark; a minority had obtained Japanese and/or Chinese regulatory approval. In addition, 24 of the 105 products had received US FDA Breakthrough Device designation. Of the 84 products classified as medical devices by CDRH, 47 were interoperable digitally enabled medical devices, and 37 were standard (that is, nondigital) devices. The remaining 21 technology products were regulated as standalone software/digital products, combination products, in vitro diagnostic products, or radiation-emitting electronic products. Across medical specialties, the largest number of products were reviewed under cardiovascular (28), followed by neurology (15), radiology (13), orthopedic (10), gastroenterology and urology (7), anesthesiology (6), and general and plastic surgery (6); the remaining 20 products were distributed across ear, nose, and throat; obstetrical and gynecological; general hospital; hematology; ophthalmic; microbiology; physical medicine; chemistry; and dental.

Exhibit 1 - Survey Respondents

Headquarters location

- US: 90 companies
- EU: 9 companies
- Other: 3 companies

Funding

- Publicly traded: 20%
- Private: 80% (including 59% VC funded)

Role

- CEOs: 65
- Regulatory leaders: 30
- Other: 10

Sources: BCG and UCLA Biodesign.

Exhibit 2 - Products Covered in the Survey

US FDA regulatory pathway	Risk class	CDRH classification	Global regulatory experience
510(k): 65	Class 1: 2	Medical device: 84	US FDA: 105
De Novo: 25	Class 2: 88	Standalone software/digital: 13	EU CE mark: 49
PMA: 15	Class 3: 15	Combination product: 4	Japan PMDA: 17
		IVD: 2	China NMPA: 6
		Radiation-emitting electronic product: 2	

Sources: BCG and UCLA Biodesign.

UCLA Biodesign collaborated with the Boston Consulting Group (BCG) on this research study. BCG helped create the questionnaire and validated the study methodology, analytics, and key findings. BCG also provided an industry expert to write this report in partnership with UCLA Biodesign. In order to preserve confidentiality and anonymity between those who participated in the study with the research team at UCLA Biodesign, BCG was not provided access to the individual participant responses. The study was conducted out of UCLA Biodesign and certified as exempt from IRB review per 45 CFR 46.104 category 2 (IRB#20-001604). All companies gave consent to participate in the study. Participants were assured that responses would be kept confidential and would remain anonymous. Responses are reported in aggregate.

Study Limitations

There are a number of important limitations to the study, and these should be taken into consideration when reviewing the key findings:

- **Selection bias may be present.** Although efforts were made to distribute the study through associations in the US, Europe, Asia-Pacific, the Middle East, Africa, and Latin America, there may be some selection bias.
- **Participation was voluntary.** Some companies chose to participate because the topics of regulatory and reimbursement requirements were important to their experience. Others opted not to participate for fear of retribution from regulatory authorities for expressing any concerns. Other companies were unavailable at the time of the study or stated that they did not have all of the information necessary for participation readily available.
- **Other sources of potential bias may be present.** Study authors may have direct or indirect relationships and industry affiliations. Likewise, study participants may harbor certain biases based on their personal or professional experiences with the FDA and other regulators.
- **The survey sample size may be too small to yield a representative result.** The study aimed to represent the experience of a wide array of companies and medical technologies, but the number of respondents who answered individual questions varies. Some questions were not relevant to all respondents, and some respondents did not provide specific information for all questions. In particular, a number of companies declined to provide information about time and cost to reach registration or approval because they viewed this information as confidential. Likewise, numerous regulatory pathways are available to medical products (for example, 510(k), De Novo, Breakthrough Device, PMA, with or without clinicals), and the number of observations in the sample declines as the number of categories expands. The resulting findings are therefore not directly comparable to conclusions from earlier studies, nor can they be used to generalize the overall experience for novel medical products, particularly on the topic of time and cost for various forms of regulatory clearance.
- **Reported data may not be internally comparable.** Although the researchers took care to define metrics consistently, companies self-reported data on the time and funding required to achieve premarket and postmarket stages, and they may have differing interpretations of these milestones.

- **Survey findings were augmented with publicly available data.** Self-reported funding benchmarks were compared with data analyzed from resources such as the FDA's publicly available database of medical device clearances and approvals, and the NIH National Library of Medicine's ClinicalTrials.gov database.

- **The study did not specifically review postmarket experience for the sampled products.** While development and regulatory costs and time to market are of tremendous importance in an innovation-driven industry like medtech, the regulatory authorities must necessarily concern themselves with safety and efficacy over the life cycle of approved products. Our study does not provide information on whether the products included in the sample are of comparable safety and efficacy to products approved before, during, or after our study time frame.

Despite these limitations, this is the first study in more than ten years that attempts to provide an industry-wide perspective and benchmarks on the industry's experience with regulatory and reimbursement programs, processes, and authorities in the US and the global regulatory theater.

Discussion

The following sections highlight the key findings of our research and share the experiences and perspectives of medtech companies that participated in the study.

Medtech Companies Find New Pathways to Regulatory Approval

The medtech industry plays a vital role in the global economy and in global health. Medtech companies generated worldwide revenues of approximately $550 billion in 2021, with the US market comprising 40% of the total and the EU accounting for another 27%. Within the US, medtech employment has increased in recent years, growing 4.1% annually from 2014 to 2019, and directly employs nearly 400,000 people across 15,000 companies at an average salary of $88,000. Indirectly, the industry is responsible for nearly 2 million jobs in the US.[4]

Medtech products run the gamut from simple swabs and bandages for dressing minor wounds, to highly sophisticated implants and hospital equipment that provides life-sustaining treatment, to AI software used to detect underlying medical conditions. Advanced medical products are often connected and interoperable, and increasingly the underlying offering is the SaMD itself. Technological advances and new revenue models, particularly in the digital arena, are having a profound impact on the medtech industry.

Regulatory agencies ensure the safety and efficacy of and access to existing and emerging medical technology and digital health offerings. Their structure and remit varies, as does their performance in helping industry companies bring new products to market in a predictable manner, at a cost and in a time frame that allow investors an acceptable return. (See Exhibit 3.) The increasing prevalence of digital offerings, including AI/ML and SaMD, challenges regulatory agencies to keep pace with the rapid evolution of technology. In this regard, the FDA has clearly outperformed its international peers, and intriguing data from this study suggests that the US has emerged as the most hospitable market for the burgeoning field of digital health offerings.

Exhibit 3 - Regulatory Pathways in Leading Medtech Markets

	US	Europe	Japan	China
Agencies	FDA	Competent authorities and notified bodies (e.g., DEKRA, BSI, TUV)	PMDA	NMPA: high risk and/or imported products Provincial bureau: moderate- to high-risk domestic products Municipal bureau: low-risk domestic products
Product classifications	Class I: low risk Class II: moderate risk Class III: high risk	Class I: not measuring or sterile Class I: measuring or sterile Class IIa Class IIb Class III	Class I: general (low risk) Class II: specified control (low to moderate risk) Class II: controlled (moderate risk) Class III: highly controlled (moderate to high risk) Class IV: highly controlled (high risk)	Class I: low risk Class II: moderate risk Class III: high risk
Clearances and approvals	510(k) Pre-market notification: low to moderate risk De Novo: novel products of low to moderate risk Premarket approval (PMA): moderate to high risk Humanitarian device exemption (HDE): limited exemption for high risk	CE marking certificate	Todokede: premarket submission for low risk Ninsho: premarket certification for moderate to high risk Shonin: premarket approval for moderate to high risk	Record filing certificate (Class I) Registration certificate (Class II & III) [Imported products require record filing and registration with central NMPA office] Domestic products are reviewed by different levels of NMPA, based on class (Class I = city; Class II = provincial; Class III = central)

Sources: BCG and UCLA Biodesign.

4. "The Economic Impact of the Medical Technology Industry," AdvaMed, August 2021.

A Decade of Innovation

In November 2010, Stanford University professor Josh Makower and his colleagues released a report titled *FDA Impact on US Medical Technology Innovation*, with support from the Medical Device Manufacturers Association, the National Venture Capital Association, and PricewaterhouseCoopers. The study, based on a survey of more than 200 medical technology companies, compared FDA and CE mark regulatory experiences during the period from 1999 to 2009. The authors concluded that the regulatory pathway to market in the EU versus in the US was more predictable (85% versus 22%), reasonable (91% versus 25%), and transparent (85% versus 27%). They also found that 75% of respondents cited the overall experience with EU regulatory authorities as excellent or very good, while only 16% assigned one of those ratings to the FDA.[5]

Under pressure from industry and other stakeholders, the FDA undertook a series of actions to improve its responsiveness while upholding its role as guarantor of patient safety and product efficacy. One critical move already underway was the reauthorization and overhaul in 2007 of the Medical Device User Fee and Modernization Act (MDUFMA II) , which enabled additional staffing investments, and enhancements to FDA regulatory processes in the digital age. Beyond these typical pathways, the FDA and other agencies may also place special controls—performance standards, postmarket surveillance, patient registries, special labeling requirements, premarket data requirements, and specific guidelines—on certain device categories in order to ensure safety and efficacy in real-world settings.

The number of yearly 510(k) clearances has come down from its 21st-century high point in 2002, but by 2014 the average review time had reached its present level after a steady climb. PMA trends show considerable variation from year to year, with no clear pattern in the number of approvals. However, average review time has declined markedly from 2013 to 2020. (See Exhibit 4.) The De Novo pathway, introduced in 1997, was revamped to permit a direct pathway to device clearance without the need to first submit a 510(k), and the results have been very impressive. Whereas only 49 devices were considered De Novo from 2000 to 2009, the number increased to 239 devices in the next decade, ranging from a low of 3 in 2010 to a high of 44 in 2018. (See Exhibit 5; Exhibit 6 shows PMA approvals during the same time period.)

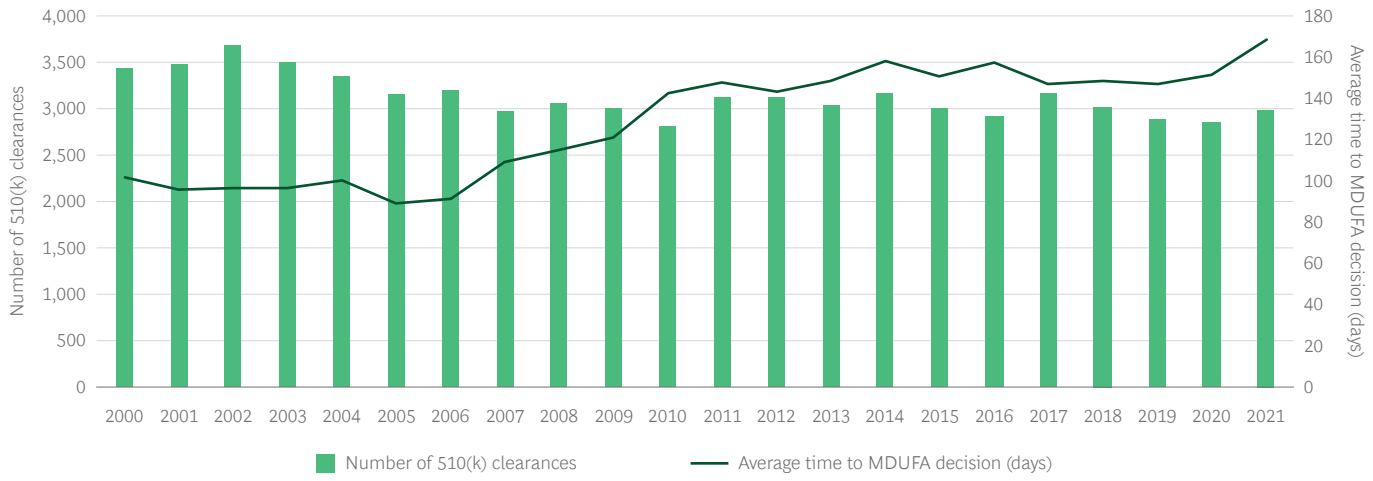
During the past decade, the rise of digital solutions has profoundly changed how companies, including those in the medtech sector, conduct business. Private venture capital funding for digital health solutions during this period has soared. While R&D for established medtech companies climbed to more than $40 billion in 2021 and private funding for the sector has added another $4 billion per year for the decade, venture capital backing for digital health exploded from just over $1 billion in 2010 to $29.1 billion across 729 unique deals in 2021.[6] (See Exhibit 7.)

5. J. Makower, A. Meer, and L. Denend, "FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies," November 2010.
6. B. Evans, M. Zweig, and A. Krasniansky, "2021 Year-End Digital Health Funding: Seismic Shifts Beneath the Surface" Rock Health, January 2022.

"Companies used to go to the EU to test and commercialize new products, because it had lower barriers to entry. Now companies are finding that it's more attainable to get clearance in the US due to continued uncertainty in the EU."

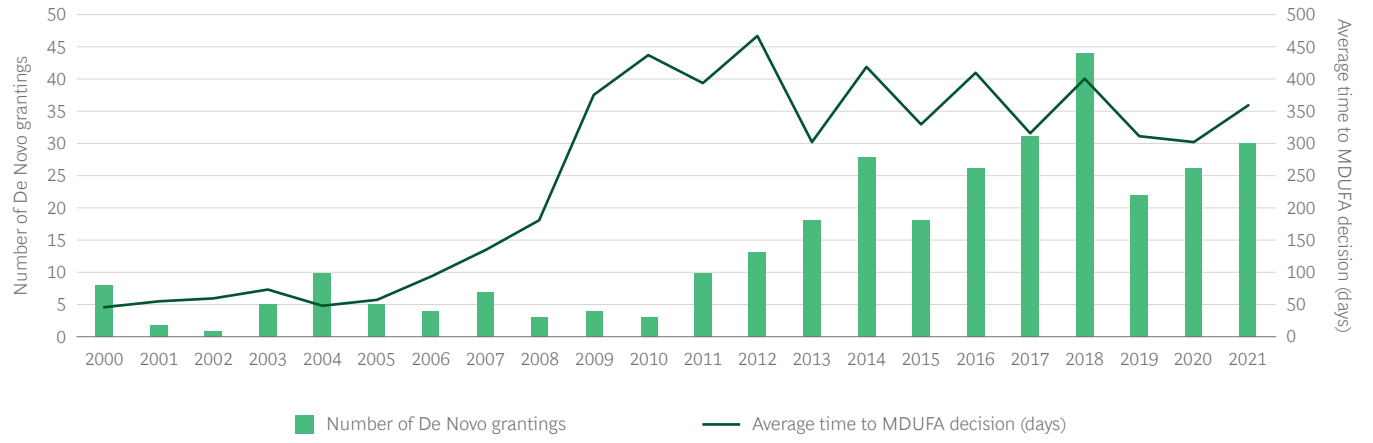
—CEO, publicly traded neurology device company

Exhibit 4 - 510(k) Clearances, 2000–2021



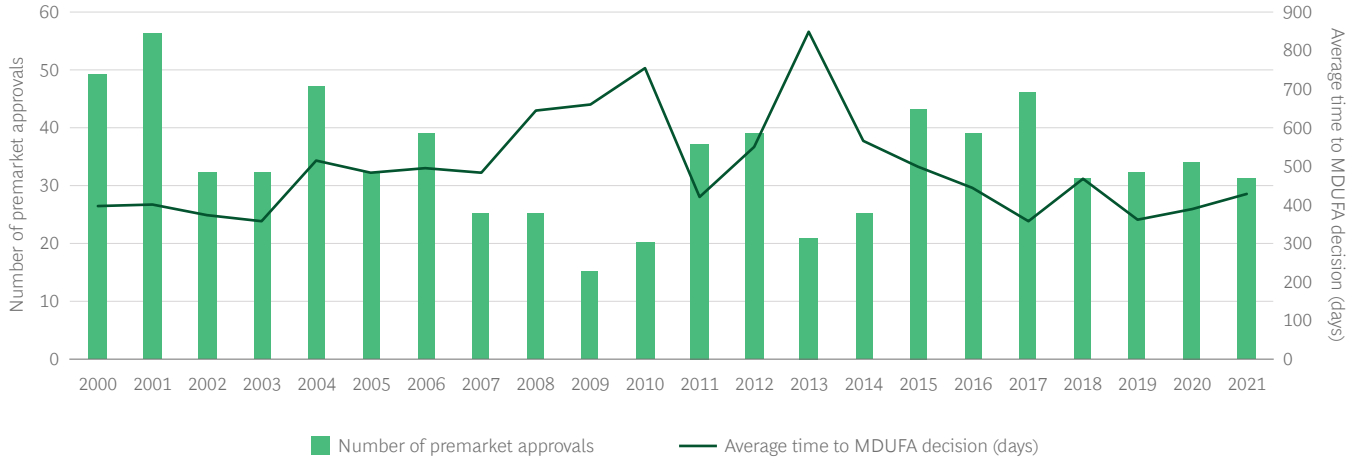
Source: FDA.

Exhibit 5 - De Novo Clearances, 2000–2021



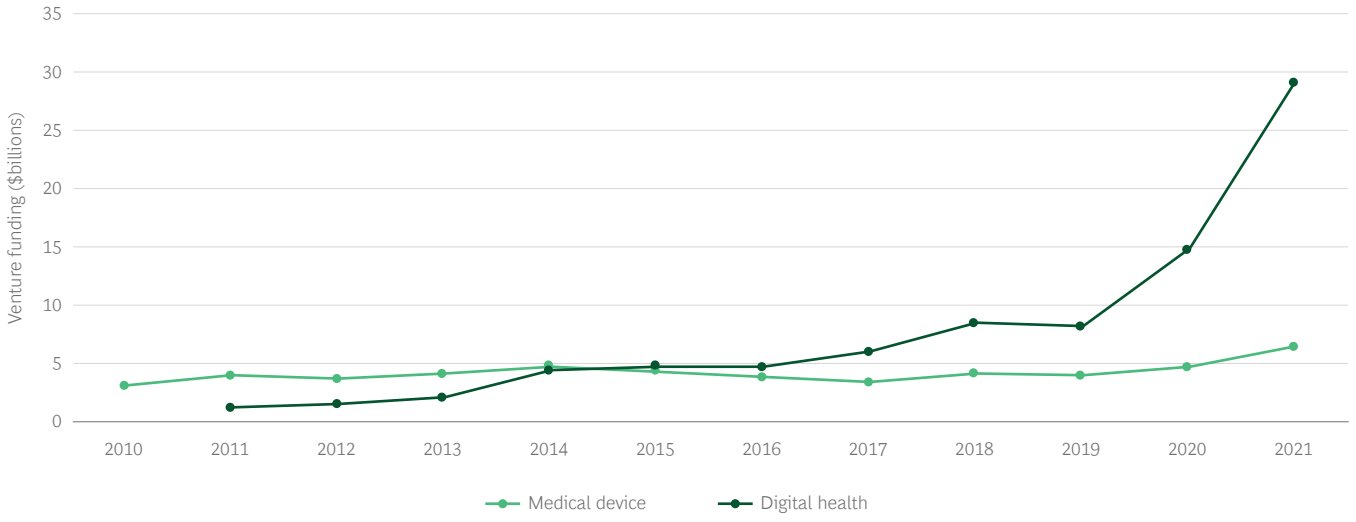
Source: FDA.

Exhibit 6 - Premarket Approvals, 2000–2021



Source: FDA.

Exhibit 7 - Digital Health and Medical Device Venture Funding, 2010–2021



Sources: Medical device funding data provided by Silicon Valley Bank. Digital health funding data provided by Rock Health.

Note: Some overlap may exist in funding reported between medical device and digital health categories.

In 2012, Congress passed the FDA Safety and Innovation Act (FDASIA) to provide a risk-based regulatory framework for mobile apps, health IT, and software. In 2016, the 21st Century Cures Act amended the definition of *medical device* to include more-specific criteria for software regulated as a medical device. The FDA released its Digital Health Innovation Action Plan in 2017; in 2020, it launched the Digital Health Center of Excellence to guide new programs, policies, and support for digital innovation.

While the FDA has introduced new programs and policies to address the emerging needs of medtech and digital health, no study has been conducted to examine the impact of these changes, nor has there been a comparative study between US FDA and EU CE mark regulatory experiences during this time period for medical and digital technologies.

The Road Ahead: Looking Beyond 2021

Medical technology companies often face a choice about where to pursue initial registration or approval to market their products, weighing such matters as the total addressable market and competitive intensity, as well as the predictability, cost, and duration of the regulatory review process and the level and likelihood of reimbursement. Country of origin plays an important role, too, as companies based in the West typically opt first for US or EU registration, while their Japanese and Chinese counterparts begin in their domestic markets. Because market capitalization of public companies and the availability of equity and venture funding are heavily skewed toward Western markets, US and EU regulatory bodies tend to get the first look at emerging medical technology offerings.

> **Historically, the CE mark has been the preferred route for novel medical technology registration, since its processes were faster, cheaper, and more predictable. The situation is now reversed.**

"The structure of the 510(k) pathway and the guidance documents is well done. It is clear for the most part. . . . The approaches to software design changes, when to use other pathways in the 510(k) framework, when to use an abbreviated path—these are all clear in the guidance documents. This aids regulatory leaders in informing their teams and leadership on the path forward."

—Regulatory leader, US publicly traded cardiovascular device company

Historically, the CE mark has been the preferred route for novel medical technology registration, since its processes were faster, cheaper, and more predictable.[7] The situation is now reversed. The FDA's introduction of key programs to clear backlogs (Medical Device User Fee Amendments), accommodate novel trial designs (Innovation Pathway, Expedited Access Pathway), encourage innovation (Breakthrough Device designation), and offer guidance for digital offerings (Digital Health Center of Excellence) demonstrates a commitment to providing swift access to life-enhancing, life-extending, and lifesaving technologies.

The introduction of MDR in the EU was intended to ensure patient and provider safety. Laudable as its objectives are, most medtech respondents viewed product registration and approval under MDR as cumbersome and uncertain. Common complaints centered on the cost and time of re-registering current SKUs, as well as on expectations for clinical studies and language translation requirements. Smaller companies expressed these sentiments most strongly, while some executives from multinational medtech companies were more circumspect, speculating that MDR may indeed elevate the average quality of products on the market in the EU by reducing the number of undercapitalized new entrants. Moreover, they observed, future US and global contract opportunities may require the same metrics that MDR now compels, giving EU-compliant products and companies a competitive edge once again.

Nevertheless, survey respondents overwhelmingly view US FDA regulatory pathways as more predictable than the EU CE mark for novel technologies—at least in the next five years. (See Exhibit 8.) For traditional medical device registrations, 62% of respondents saw the FDA's guidance as highly or somewhat predictable, whereas only 22% of participants expressed comparable views of the CE mark. The pathway for digital technology appears less certain in both markets, but 32% of respondents considered the FDA pathway predictable, versus only 15% who felt the same about the CE mark. (See Exhibit 9.)

Among the executives polled, 52% said their companies would deprioritize the CE mark as a result of their views on the risk and reward associated with EU markets, versus only 4% who said European registration would receive a higher priority beyond 2021. The pattern held even for the 14 non-US-domiciled companies polled. Eleven respondents said they would deprioritize EU registration, while three predicted no change in their approach to commercializing new products.

7. J. Makower, A. Meer, and L. Denend, "FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies," November 2010.

"MDR is killing innovation."

—CEO, European cardiac medical device company

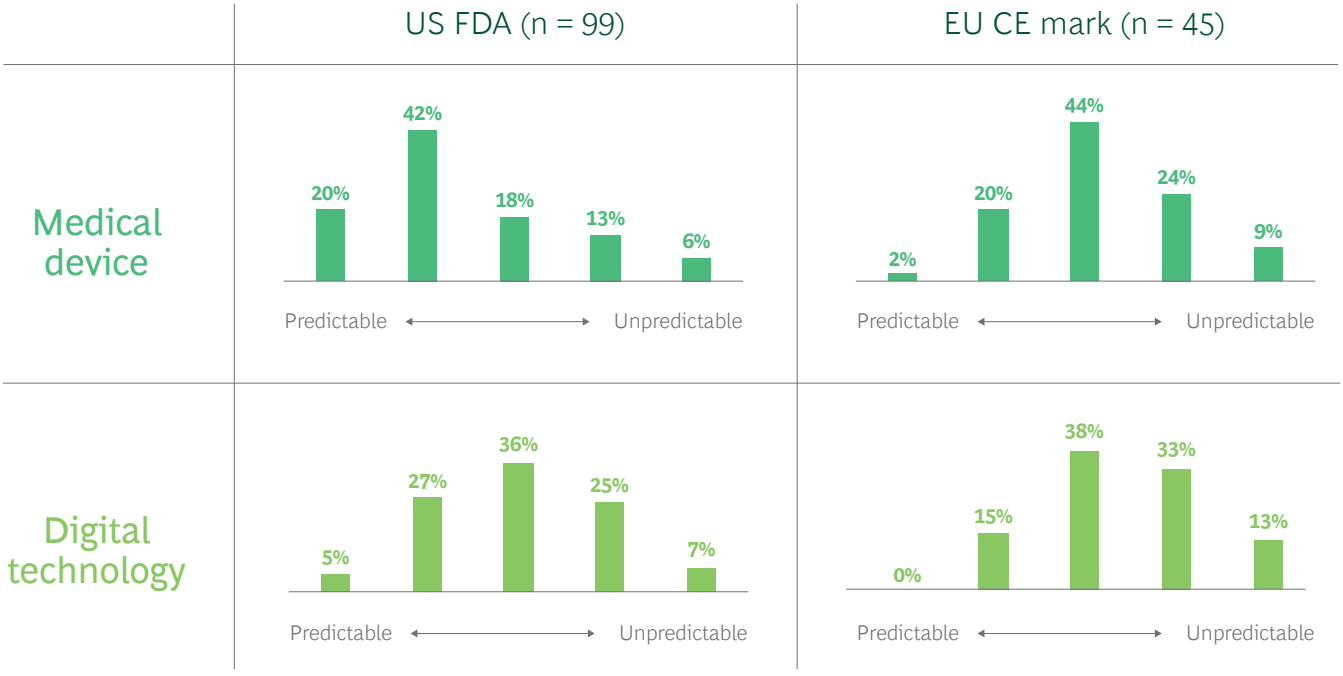
Exhibit 8 - Priority Markets

Prioritized order in which companies will pursue regulatory approval

First: United States | Second: Europe | Third (tie): Canada and Australia/ New Zealand | Fifth: Japan | Sixth: China

Sources: BCG and UCLA Biodesign.

Exhibit 9 - Predictability of Global Regulatory Pathways



Sources: BCG and UCLA Biodesign.

Note: Respondents were asked to rate predictability on a scale from 1 ("unpredictable") to 5 ("predictable"). Because of rounding, the percentages given do not always add up to 100%.

The fading allure of CE marking may be partially attributable to ongoing and significant budget-induced price pressure. The post-Brexit world presents yet another looming and complicating factor for European medical product registrations. Although the UK established transitional guidelines that recognize and accept CE marking through June 2023, the country has issued its own regulations for UK Conformity Assessed (UKCA) markings, along with separate requirements for Northern Ireland. Some of the UK regulatory changes—such as a digital formulary and integrated reimbursement solutions—may prove prescient and especially helpful for software-only companies. That said, creating a separate review process for one of the largest European markets lessens the overall value of the CE mark and will likely change the risk-reward equation over the next decade as medtech companies roll out their new offerings. For EU residents, the likely impact will be delayed access to new and improved medical technology.

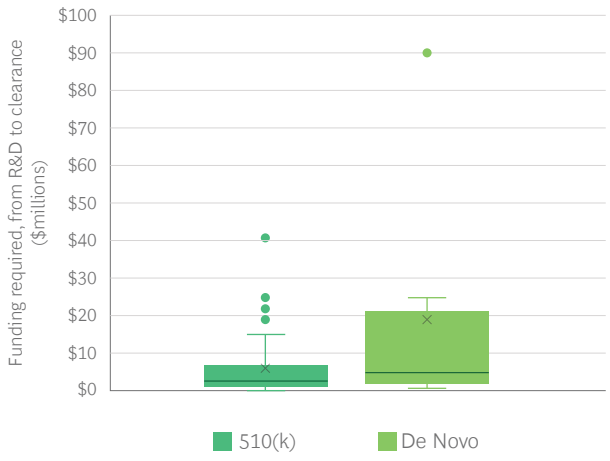
Medtech Innovation: Cost and Time

Competing in an innovation-driven industry with exacting requirements for patient access and safety requires ample funding and rigorous study. Depending on the class of device and whether a predicate product has already made it to the market, clinical trials may or may not be required. The rapid rise of digital applications and connected products adds a layer of complexity that regulators must assess. Thus, the cost and time required to bring products to market can vary quite widely.

Averages alone convey little information in such a diverse set of product types and regulatory pathways. For the 510(k) products on which we have detailed cost information (n = 50), the minimum cost from concept to clearance was just $0.2 million as compared with a maximum of $41.0 million. The cost for half of the 510(k) clearances in our data set fell into a range from $1.2 million to $6.8 million, with a median total cost of $3.1 million. For the 13 De Novo products in our cost study, the corresponding minimum and maximum figures were $0.8 million and $90.0 million, with 50% of the sample landing in a range from $2.0 million to $21.0 million and with a median reported cost of $5.0 million. (See Exhibit 10.)

Total time from concept to clearance likewise shows a wide distribution, with 510(k) clearance occurring in as little as 2 months and as long as 132 months. The middle 50% of the distribution experienced a total time to clearance of 18 to 43 months and a median elapsed time of 31 months. For De Novo products, the minimum approval time was 18 months and the maximum was 240 months. The middle 50% of the De Novo products observed received clearance in 45 to 99 months, with a median duration of 66 months. (See Exhibit 11.) The broad time frame for both may reflect differing interpretations of the concept stage, with some inventors musing on ideas for years or decades before initiating a formal development project, and others proceeding straight from an R&D brainstorming event to the new product development queue.

Exhibit 10 - Funding Required, from Concept to Clearance ($Millions)



	510(k)	De Novo
Average	$6.1	$17.8
Maximum	$41.0	$90.0
Third quartile (75%)	$6.8	$21.0
Median	$3.1	$5.0
First quartile (25%)	$1.2	$2.0
Minimum	$0.2	$0.8

Sources: BCG and UCLA Biodesign.

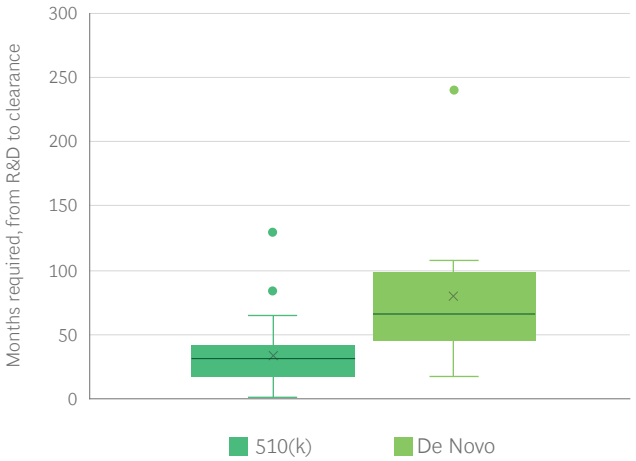
The study did not provide a head-to-head comparison of total development costs and time to market for products achieving CE mark before 510(k) clearance. However, we can evaluate average review time from first communication through clearance in the EU and the US for 22 products in our sample that reached the market in the course of the study. For these products, CE marking still came faster, at 12.1 months versus 16.4 for 510(k). Actual regulatory review time (submission to decision) incurred a narrower gap of 3.9 months for a 510(k) versus 3.2 for CE marking. (See Exhibit 12.) It should be noted, however, that these are retrospective views that do not consider the impact of MDR on CE mark speeds.

The 2021 UCLA Biodesign/BCG study of 105 products includes 21 offerings from publicly traded companies, with the balance from companies generating less than $5 million in annual revenues. For all the positive feedback about FDA initiatives to improve regulatory efficiency and adapt to digital product requirements, many smaller companies in the sample voice ongoing frustration.

For all the positive feedback about FDA initiatives to improve regulatory efficiency and adapt to digital product requirements, many smaller companies in the sample voice ongoing frustration.

Precommercial and venture-backed medtech startups must focus on their burn rate—the amount of cash that they on hand have to cover operating expenses before their products reach the market. With typically only months of cash on hand, smaller companies still face tremendous challenges when dealing with FDA officials whose time horizons too often do not comport with their own. Because smaller companies are disproportionately responsible for digital innovation, regulatory agencies in the US and the rest of the world must determine how to accommodate time-sensitive requests that could make the difference between a novel product reaching the market or being shelved due to regulatory waiting time.

Exhibit 11 - Time Required, from Concept to Clearance ($Millions)



	510(k)	De Novo
Average	33	80
Maximum	132	240
Third quartile (75%)	43	99
Median	31	66
First quartile (25%)	18	45
Minimum	2	18

Sources: BCG and UCLA Biodesign.

Exhibit 12 - Approval Time for Products That Achieved Both FDA 510(k) and CE Mark Clearance

Months required

	First communication to submission	Submission to decision	Total
510(k)	12.5	3.9	16.4
CE mark	8.9	3.2	12.1

Sources: BCG and UCLA Biodesign.

Note: n = 22 products that achieved both FDA 510(k) clearance and CE mark with all data reported for FDA and CE marking communication, submission, and decision dates.

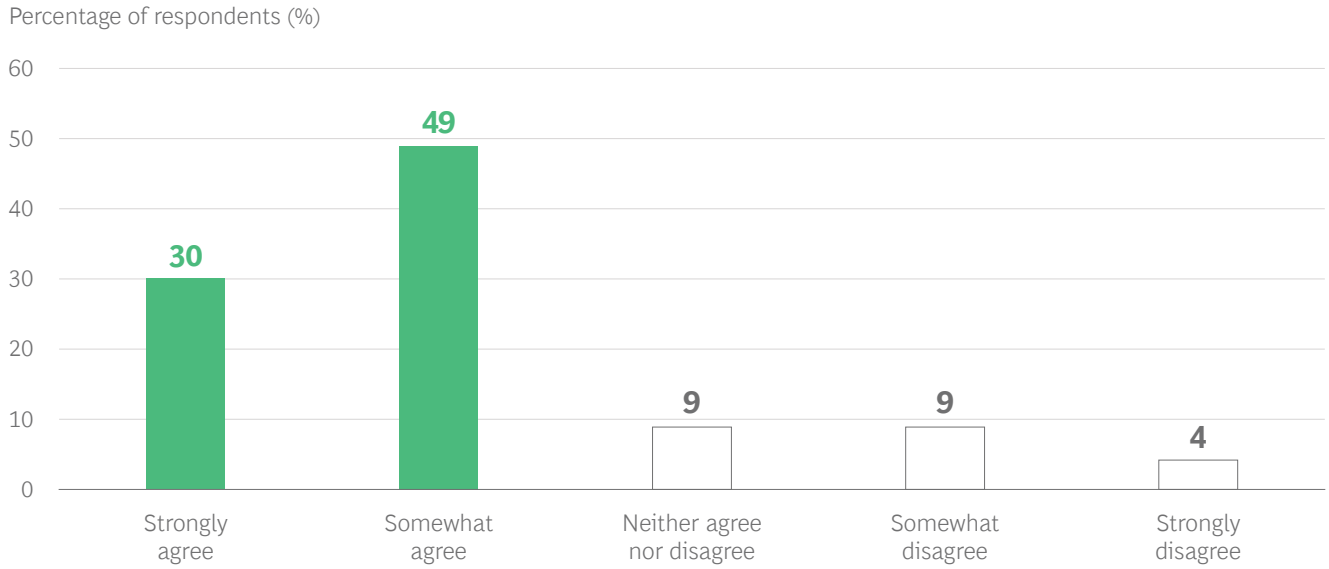
US FDA Programs Assist Growth of Medtech and Digital Health

The US FDA's emergence as the regulatory agency of choice for medtech innovators offers a positive example of how government regulators adapt to secular change in the industries they serve. Throughout the past decade, the agency has made draft guidance and white papers available for review and commentary, leading to a greater understanding of FDA regulatory pathways. Although challenges remain, particularly around reimbursement and support for innovation, it is worth visiting several key programs that the FDA has introduced within the past decade. Feedback from our survey respondents, as well as empirical evidence, suggests that these programs have supported innovation and, by extension, helped patients.

Respondents to the survey gave the US agency high marks for keeping pace with advances in the industry. A total of 79% agreed that the FDA has responded effectively to the challenges of technological change in the past decade, versus only 13% who disagreed. (See Exhibit 13.) The strong showing represents a departure from perceptions of the FDA during the 2000–2010 period and raises the question of how the US regulatory authorities achieved this turnaround. Our research indicates that much of the success is attributable to key programs instituted in the past ten years.

Exhibit 13 - FDA Response to Innovation

79% of respondents agree that the FDA has responded effectively to advances in medical technology innovation over the past ten years



Sources: BCG and UCLA Biodesign.

Note: Because of rounding, the percentages given do not add up to 100%.

Medical Device User Fee and Modernization Act (MDUFMA II)

One of the changes for which the FDA deserves credit actually took place in 2007. The Medical Device User Fee and Modernization Act (MDUFMA II) generated $287 million in fees over the course of the next five years, augmenting federal funding for the agency and allowing the FDA to commit to meaningful performance goals and to report on their success on a quarterly basis. In addition to imposing stricter time limits for PMA and 510(k) decisions, the User Fee program allowed the FDA to support small businesses by waiving PMA submission fees for first-time applicants with less than $30 million in revenue, and it steeply cut 510(k) application fees for businesses with less than $100 million in sales. Foreign entities could qualify as small businesses under the program, lowering the risk for innovators from around the world to introduce their technology in the largest global market. Moreover, the FDA agreed to make its fee program more predictable by introducing a clearer schedule of assessed fees and improvements to its interactive review system, along with third-party inspections.[8]

FDA Innovations, 2010 to 2020

Our survey collected feedback on three important FDA innovations: the De Novo direct pathway, Breakthrough Device designation, and the Digital Health Center of Excellence. Other new programs, such as Parallel Review and the Payor Communication Task Force, were not specifically covered in the questionnaire but came up as positive developments in some follow-up interviews.

8. "Medical Device User Fee Amendments 2007 (MDUFA II)," FDA, 2017.

De Novo Pathway Gains Traction

The De Novo pathway, introduced in 1997, allows classification of novel, low-to-moderate risk devices as Class I or Class II products under 510(k) requirements, rather than forcing them to submit to the stricter standards applied to Class III devices. The 2012 FDASIA created a direct pathway to market for De Novo products—obviating the need to first obtain 510(k) clearance.[9] The De Novo pathway accounted for 25 of the 105 products covered in our survey. This pathway tends to run longer and cost more than traditional 510(k) clearance, but it represents a major step forward for innovators who would otherwise face the more expensive and time-consuming process of applying for a PMA. Smaller companies particularly value the De Novo pathway, which offers a process for ongoing dialogue with the FDA. Larger companies, taking note of the time to approval and the uncertainty of the process for De Novo, may opt for a PMA in spite of the added cost and accept the additional entry barrier that comes with this route to market.

Breakthrough Device Designation Drives Innovation

Following on the heels of FDASIA, the 2016 21st Century Cures Act codified into law an expedited review program for so-called Breakthrough Devices that, per the FDA, "provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions." The FDA grants this designation during the Q-Sub—an interactive program designed to provide guidance to companies seeking clearance or approval before they submit their applications. Once a Breakthrough Device designation is granted, the manufacturer has more opportunity to discuss and receive feedback on its application, with the FDA applying its least burdensome provisions to streamline the path to market while maintaining safety and efficacy standards.

9. "Food and Drug Administration Safety and Innovation Act (FDASIA)," FDA, 2012.

"[Our] company's experience with De Novo was positive. Where companies can go wrong [with it] is, when a company does not design and execute a robust clinical trial, then it's difficult for the FDA to make decisions on limited or insufficient data."

—VP, venture-backed company

Although only 32 Breakthrough Devices have received FDA clearance to date, the program has quickly gained popularity, with more than 80% of designations occurring since 2019.[10] (See Exhibit 14.) The 24 successful Breakthrough Device applications in our study cohort took, on average, 81 days to FDA designation. Of this total, 75% felt the program would lead to quicker patient access to novel technologies, and 52% applauded the way the designation creates more-flexible arrangements for clinical study design. (See Exhibit 15.) The most significant concern about the program was the Biden administration's decision to uncouple Breakthrough Device designation from CMS reimbursement, which has been seen as an important determinant for venture-backed companies seeking investment. On a more fundamental level, respondents worry about whether the FDA will be able to define and uphold criteria to guarantee that the Breakthrough Device designation continues to be a meaningful distinction. For now, however, 88% of respondents felt that the guidance documents for the designation are clear, although interview feedback uncovered a concern that the FDA has adopted an unwritten rule requiring clinical data before granting a Breakthrough Device designation. To avoid confusion, any such rule should be written and promulgated.

Head Start on Digital Health Regulation in the US

In 2017, MDUFA IV committed resources to the FDA to address the emerging needs of digital technology by establishing a digital health unit within CDRH. In addition to establishing a centralized and dedicated digital health unit, the FDA published a Digital Health Innovation Action Plan, which initiated a cascade of guidance for software, new regulatory approaches for digital technology, and growing agency expertise.

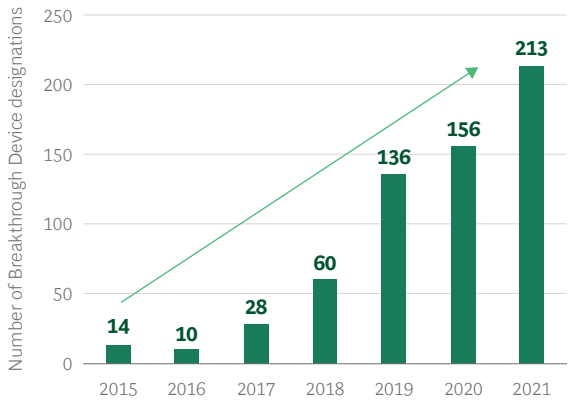
Beginning with the rollout of the FDA's digital health software pre-certification pilot program (Pre-Cert), the agency kicked off a dedicated effort to develop a regulatory model that would streamline regulatory oversight for software-based medical devices. A cohort of nine companies was selected to help inform an agile approach for evaluating the software developer's systems for software design, validation, and maintenance. Insights from Pre-Cert 1.0 have spurred a working model for evaluating and monitoring SaMD across the product life cycle.

Most recently, the FDA's Digital Health Center of Excellence was established in 2020 as a continuation of the agency's efforts to keep pace with the evolving needs of the marketplace. Although the program was still in its design phase during our survey period, respondents were broadly aware of the initiative and supportive of its goals. Its objectives—to bring greater digital expertise to review meetings, to create more guidance for AI/ML software, and to provide clarity on appropriate clinical evidence required—help fuel the belief that the FDA is responding effectively to advances in digital technology innovation. Among our survey respondents, 64% rated the FDA positively on this topic, while only 34% felt that EU regulatory authorities were doing enough to support digital health innovation. (See Exhibit 16.)

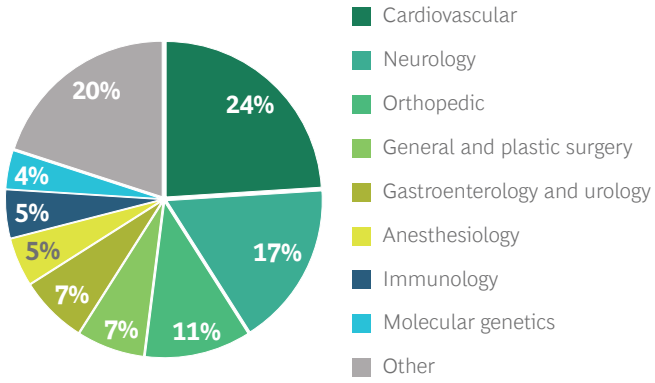
10. M. Eydelman. FDA panel presentation, Octane Medtech Forum, October 28, 2021.

Exhibit 14 - Annual Breakthrough Device Designations

Growth in annual Breakthrough Device designations since 2015



Where are Breakthrough Device innovations emerging in medtech?



Source: FDA.

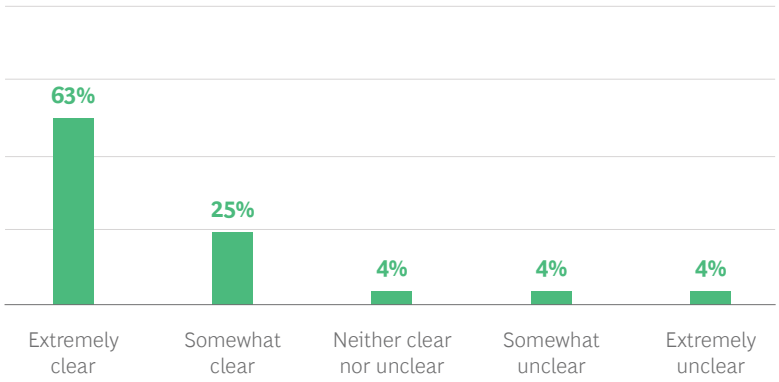
Note: FDA data on 617 Breakthrough Device designations as of December 31, 2021.

Exhibit 15 - Breakthrough Device Designation Provides a Clear Pathway to Accelerated Approval, According to Respondents

75% of respondents believe the designation will lead to **earlier patient access**

52% of respondents believe the designation enables more flexible clinical study design

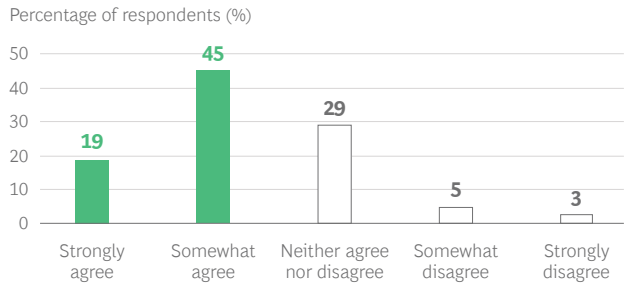
How clear are guidance documents for companies that receive a Breakthrough Device designation?



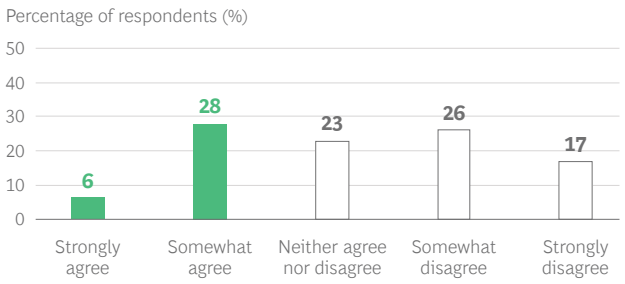
Sources: BCG and UCLA Biodesign.

Exhibit 16 - EU and US Responses to Changes in Digital Technology

64% of US respondents say that the FDA has responded effectively to advances in digital technology innovation



34% of EU respondents say that European regulatory authorities have has responded effectively



Sources: BCG and UCLA Biodesign.

Note: Because of rounding, the percentages given do not always add up to 100%.

Regulation, Reimbursement, and Innovation: An Industry Perspective

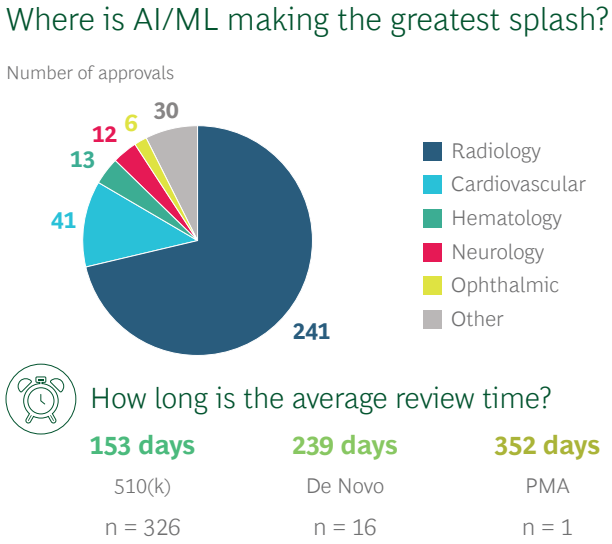
The ongoing digital transformation of industry has already had a profound impact in the medical technology arena. Real-world evidence comes in every day from standard sources such as medical-grade monitors and from an expanding constellation of apps focused on specific patient groups and supported by ubiquitous smartphones and wearables. Unstructured data from these many sources can be tapped to power AI algorithms that self-correct via ML. But the regulatory framework in which companies operate can help or hinder these advances, in the latter case by raising barriers to innovation. Most importantly, rolling out new technology remains a risky undertaking for the developer—and investor funding for promising new projects will always hang in the balance over questions of whether, when, and how patients and providers receive reimbursement.

Artificial Intelligence and Machine Learning Storming the Market

AI and ML surged into the medical technology space in the latter half of the past decade. FDA approval of AI/ML devices numbered in the single digits through 2015 before vaulting to more than 100 in 2020. In fact, in 2018, the FDA approved more AI/ML devices in a single year than it had in the agency's entire history. And the pace continues: as of this report, the FDA had approved 343 AI/ML devices, more than half of that number in 2019 and 2020.[11] (See Exhibit 17.)

11. "Artificial Intelligence and Machine Learning (AI/ML)-Enabled Medical Devices," FDA, 2021.

Exhibit 17 - AI/ML Medical Devices



How long is the average review time?

153 days	239 days	352 days
510(k)	De Novo	PMA
n = 326	n = 16	n = 1

Source: Data based on UCLA analysis of FDA's reported list of regulated AI/ML-enabled products.

[1] Data for 2021 reported up until June 2021. Total AI/ML-enabled devices for 2021 not available.

Historical AI/ML Approvals

Unsurprisingly, most early approvals for AI/ML devices have come in the field of radiology, where the massive computational power of machines can interpret and discern minute patterns to define ever-improving algorithms for patient care. Accordingly, radiology indications for AI/ML devices represent a staggering 241 out of 343 approved tools. Other major fields represented include cardiology, hematology, neurology, and ophthalmology, with a combined total of 72 approvals.

AI/ML Study Respondents

Our survey respondents included 29 entities that had received approval for AI/ML devices, representing nearly 10% of all such approvals as of September 2021. The FDA required human studies of various types for 22 of the 29 products, with about half running a pivotal trial. Reported survey data on 16 successful 510(k) registrations showed minimum, median, and maximum R&D expenditures of $0.6 million, $9.1 million, and $41.0 million, respectively, while the corresponding concept-to-clearance times were 6, 26, and 132 months (there was insufficient data to break out De Novo and PMA details).

While applauding the agency for the strides it has taken, respondents questioned whether the FDA will develop the capacity and capability to handle future submissions for AI/ML. As a percentage of total 510(k) submissions, AI/ML represents a relative handful today. But if the exponential growth continues, respondents wonder whether the FDA will be able to keep pace.

As this question plays out, the FDA will also have to contend with the defining question facing AI/ML: how to regulate locked versus adaptive algorithms. A locked AI/ML product applies a static set of logical rules to real-world information. A regulator can query the logic to assess its safety and efficacy. An adaptive product, on the other hand, updates the logical sequence that the product pursues to arrive at a solution, forcing regulators to assess whether the future outcomes will be safe and effective.

To date, the question has been largely hypothetical, since the FDA has approved just one adaptive algorithm. Recently, the FDA issued guiding principles for good machine learning practices to inform the development of safe and effective AI/ML-enabled medical devices, but no official guidance has been provided to the industry. Although the FDA has published a discussion paper with a request for industry feedback, the regulatory framework for AI/ML remains in its infancy.[12]

12. "Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan," FDA, January 2021; "Good Machine Learning Practice for Medical Device Development: Guiding Principles," FDA, October 2021.

Greater Clarity and Guidance for Digital Health Products Required

Although the FDA can justifiably claim success in supporting digital health innovation, important work remains to be done. Interview feedback raises questions about the specific role that the Digital Health Center of Excellence plays in review and approval of devices. Respondents call for more technical expertise and greater capacity to handle the Q-Sub process for digital products, and more clarity on data requirements, clinical testing expectations, study design, endpoints, and post-approval processes for digital and software devices, especially those that incorporate AI/ML.

Company Maturity Poses Unique Challenges to Medtech Innovation

Setting aside digital and AI/ML concerns, respondents noted a number of other regulatory measures that serve as innovation hurdles. Smaller and venture-backed companies emphasize the importance of establishing a dialogue with the FDA via the Q-Sub process, while their larger counterparts are often comfortable proceeding straight to application submission for their more straightforward 510(k) candidates. Burn rate emerges as the primary barrier to innovation for smaller companies, which suffer disproportionately from common issues such as when the FDA swaps out a lead reviewer or postpones a Q-Sub meeting. Similarly, the abandonment of the Medicare Coverage of Innovative Technologies (MCIT) program for Breakthrough Devices deprives precommercial companies of a critical investor credential—a national reimbursement coverage guarantee upon approval.

Reimbursement Questions Loom Largest for All Innovators

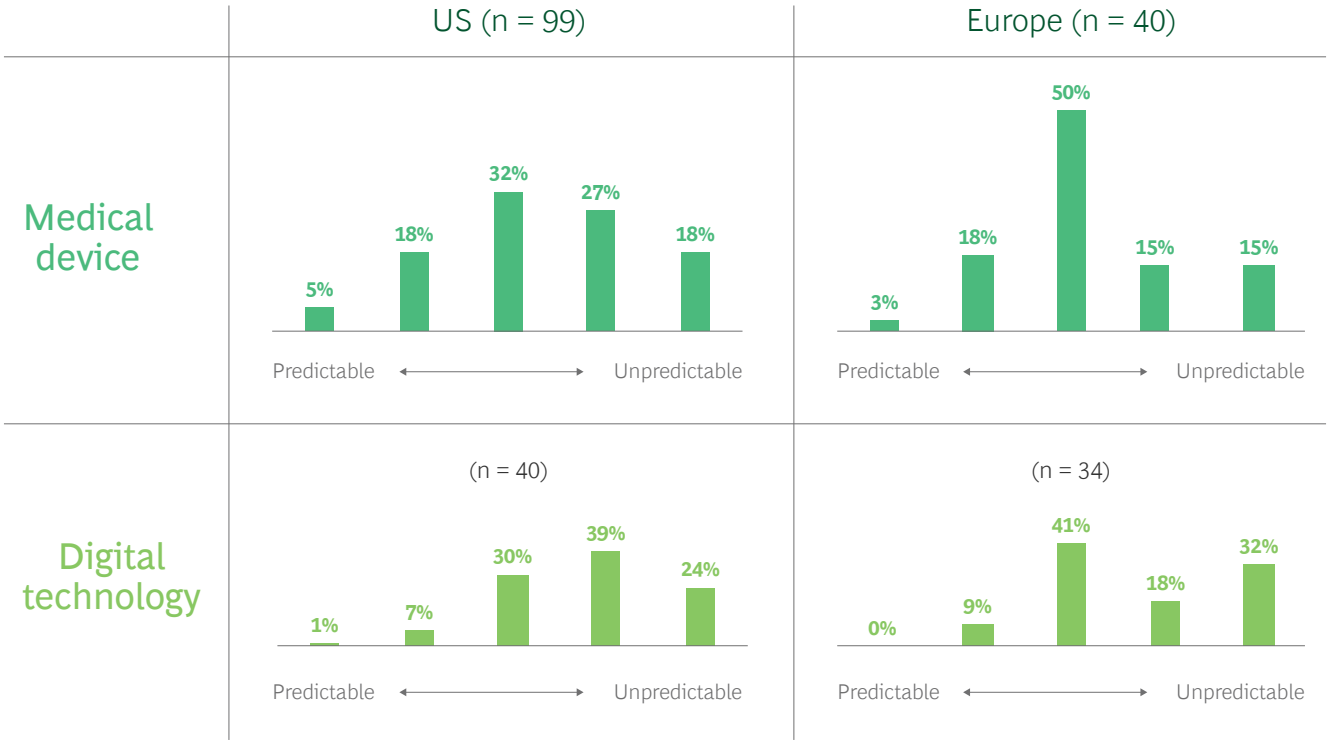
In our survey, 72% of respondents cited reimbursement as the leading barrier to innovation. Just 16% felt that the US regulatory process represented the biggest hurdle; and another 11% cited other concerns, including early-stage investment, technology adoption by hospitals, and specific factors involving targeted patient populations.

The topic of reimbursement dogs advances in digital health across the globe. (See Exhibit 18.) Although visibility into reimbursement is not particularly high for standard (nondigital) medical devices (24% in the US, and 21% in the EU), few companies developing digital health offerings have confidence in their ability to predict whether and how their products will be reimbursed once approved (8% in the US, and 9% in the EU). Executives in our survey called for greater coordination between regulatory and reimbursement agencies to alleviate this problem.

"The current [US] reimbursement system and processes are designed for traditional medical devices. The system needs to be updated for digital health technologies."

—CEO, venture-backed European company

Exhibit 18 - Predictability of Global Reimbursement



Sources: BCG and UCLA Biodesign.

Note: Respondents were asked to rate predictability on a scale from 1 ("unpredictable") to 5 ("predictable"). Because of rounding, the percentages given do not always add up to 100%.

By far the largest share of commentary about reimbursement centered on a perceived lack of communication and coordination between the FDA and the Centers for Medicare and Medicaid Services (CMS), the US agency responsible for federal reimbursement decisions covering seniors and low-income citizens. Of note, 41 of our 73 CEO respondents viewed CMS reimbursement as the leading barrier to patient access to novel technologies. Another 14 CEOs saw private-payer reimbursement as the core challenge, making reimbursement the leading concern among CEOs by a wide margin. By contrast, only four CEO respondents saw the FDA regulatory process as the biggest barrier to innovation. Overall, only 40% of respondents believe that the CMS decision criteria for benefit coverage and payment for medical technologies is clear. Respondents cite the route to reimbursement for digital health offerings as being particularly opaque, calling for greater coordination across FDA, CMS, and industry.

Feedback for Medtech Industry, Regulators, and Reimbursement Agencies

In addition to collecting data on the experience of companies seeking clearance and approval for 105 medical products over the past decade, our research team conducted 104 in-depth interviews with company executives. We also conducted 27 interviews with leaders of industry; trade associations; and representatives of the FDA and other regulatory agencies. The objective of these conversations was to go beneath the study's empirical findings and gain greater insight into how industry and regulators can work together most effectively to smooth the path for novel medical technologies to benefit patients in the US and beyond. We summarize our observations in three categories: best practices for industry competitors, feedback for the FDA, and recommendations to CMS.

Medtech Industry Best Practices for Regulatory Approval and Reimbursement

We have several recommendations for companies to adopt as best practices.

Preparing for FDA Submission. Survey respondents generally find FDA guidance documents helpful in determining the right pathway for US regulatory clearance or approval. As a first step, companies should determine whether their new device has a suitable predicate, which will dictate baseline submission requirements and inform expectations about coverage, coding, and reimbursement. In addition, devices with a clear predicate may opt out of the Q-Sub process, whereas others seeking regulatory approval will generally find this step helpful. The consensus view in our peer interviews was that companies typically hire or consult seasoned regulatory experts with experience in handling innovative pathways such as De Novo, Breakthrough Device designation, and digital products. In all FDA submissions and discussions, companies should take care to use only reputable data sources and credentialed testing sites. Third-party reviewers can provide great leverage, too, especially if they have preexisting relationships with the FDA—but outside experts cannot know the product, the basic science, and the data as well as the innovator does.

Communicating and Collaborating with the FDA. Companies should be aware that all information submitted to or discussed with the FDA becomes part of the public record. Thus, it is critical to be clear, articulate, and concise in all communications with the FDA. Companies are advised to engage the FDA early in the review process to educate the agency on the product, science, and data and to help reviewers make informed decisions. If practicable, companies should establish a working relationship with the lead reviewer that will permit a frank discussion about submission requirements and expectations before submitting a regulatory application.

Maximizing Q-Sub Meetings. Q-Sub meetings were used for 69 of the 105 submissions covered in our survey—overwhelmingly for De Novo and PMA pathways (37 of the 40), and for about half of the 510(k) applications (32 out of 65). The primary reasons cited for using Q-Sub meetings were to gain input on the regulatory pathway, to seek guidance on clinical study protocol and design, and to align on indications for product use. Executives suggest using multiple Q-Sub meetings if necessary, and to set an agenda of three to five topics for each session. Bringing in regulatory consultants and clinical experts who can comment on prior reputable studies will help guide proposals for clinical study design, animal studies, testing requirements, and other considerations. Finally, companies should not expect any decisions from the FDA in the Q-Sub process—the program exists as a communication channel only.

Special Considerations for Regulatory Pathways. Regulatory pathways pose challenges that are specific to each type:

- The De Novo pathway opens an avenue for FDA consideration of novel products that have no predicate, and it allows the sponsor to explain the supporting science and data behind the technology to the FDA. Some companies may be tempted to forgo De Novo granting due to a perception that the timeline to clearance may be longer for it than for a standard 510(k). They should also take into consideration, however, the possibility of an even longer time to market if the FDA determines that their device is not substantially equivalent (NSE) to any currently marketed products. Under De Novo consideration, companies should expect to brainstorm with the FDA on clinical requirements and testing to create a pathway to a successful product clearance. De Novo applicants will use the Q-Sub process and should define the product's indication very carefully, as this will affect multiple aspects of preregulatory and postapproval requirements, including clinical trial protocol design, testing, and labeling.

- Like the De Novo pathway, the Breakthrough Device designation provides an opportunity for more frequent and open communication with the FDA, as well as priority access to market. If accepted into the Breakthrough Device program, companies would do well to pursue it. MCIT via CMS also offers access to reimbursement upon approval, although the program is slated for termination in 2022.

- Premarket Approval (PMA) applications pursue the most intensive US regulatory pathway, with a target FDA review time of 320 days. Actual time to a decision may be longer or shorter, depending on such variables as whether the FDA issues a request for information (RFI), a change in the lead reviewer, and slow or fast company response time. Consequently, survey respondents suggest that companies budget an FDA review time of at least one year. Interviewees suggest that companies invest in first-time approvals to educate the FDA on pipeline products, as this will pay dividends downstream. Lastly, the sponsor's relationship with the FDA can affect the timeline for any application. Given the long timelines involved in a PMA, selecting the right regulatory leader is one of the most important talent decisions a medical device company can make.

Managing Regulatory Approval and Reimbursement. In the US, gaining regulatory approval generally represents a separate step from reimbursement. Too often, interviewees say, companies (especially smaller, newer entities with more-limited resources) fail to start the reimbursement planning process early enough to anticipate clinical and economic data requirements that are best met through the clinical study process. Respondents suggest that planning for reimbursement should occur in parallel with developing a regulatory strategy to accelerate commercial readiness and revenue generation once approved.

Medtech Industry Feedback for the FDA

The company leaders we spoke with had several recommendations for regulators.

Improving the Submission and Review Process. Executives in our survey note that changing lead reviewers can be quite disruptive to a regulatory application, as can the underlying variability in individual reviewers' processes, skill sets, and core knowledge. Industry respondents generally support the FDA's move to standardize record keeping so that new reviewers are properly apprised of past considerations and decisions taken, but they suggest that the FDA could do more to reduce staff turnover, lead reviewer attrition, and lost communication. One notable idea that surfaced was a suggestion that the FDA appoint a cadre of senior "floating" reviewers to work across various product teams and be in a position to step in and assume the lead role when required.

Clarifying Guidance for Digital Solutions. The FDA's guidance for software and digital health has improved over the past five years, providing considerably more clarity than international peer agencies offer. Still, industry seeks additional guidance to support innovative digital offerings, especially in SaMD and requirements for cybersecurity. The topic of clinical study design featured prominently in our interviews, with executives looking to the FDA for norms for dealing with digital solutions that may not require randomized, double-blind controlled trials.

Understanding Breakthrough Device Designation. The criteria for Breakthrough Device designation remain unclear to industry respondents. They say that written requirements outlining the information required to support a Breakthrough Device application would be quite useful. Meanwhile, respondents that have received such a designation appreciate the prioritization and enhanced communication, but they do not completely understand the ground rules for engaging with the FDA under the program. They also question whether the FDA intends to accelerate its actions and decisions for designated Breakthrough Devices.

Supporting AI/ML. Companies express concern that the FDA will not hire and train enough experts to keep pace with change in this field. AI/ML companies recommend establishing a data bank of case studies that can shed light on issues such as reducing AI bias, assessing the medical ethics of AI, evaluating the safety of locked and adaptive AI/ML algorithms, and updating those algorithms over time. Such a data bank might also provide guidance for piloting and implementing predetermined change control protocols. Industry respondents see an opportunity for creating AI/ML-focused reference standards for intended use (for example, detection, diagnosis, and treatment), risk to patient, type (locked versus adaptive), impact on real-time clinical care, and other factors.

Coordinating FDA and CMS Requirements. Industry respondents gave high marks to CMS and FDA for the MCIT program, which offered innovators greater clarity on a potential path to payback for their R&D investments. Although MCIT is being rescinded, industry respondents want regulators and reimbursement authorities to understand that decisions on which novel products to pursue depend equally on the probability of regulatory approval and on the market opportunity that these products represent. Accordingly, industry respondents express a clear desire for US regulatory and reimbursement authorities to harmonize their requirements.

Industry Feedback to CMS

Medtech companies also had several recommendations for government payers.

Address reimbursement as an impediment to timely patient access to innovation. Our survey suggests that the US has eclipsed the EU as the most favorable market in which to launch new medical technologies, largely on the strength of the FDA's measures to improve the efficiency of its core processes and its nimble response to the rise of digital health solutions, along with the favorable market fundamentals. Yet 72% of our survey respondents now perceive reimbursement as the biggest barrier to medical innovation in the US. In countries where a single agency handles regulatory approval and reimbursement, the path to payback once a product receives clearance can be far more straightforward (albeit often with narrow eligibility and low payment). Industry executives urge CMS to take note of the important connection between innovation and reimbursement. Specifically, survey respondents see the December 15, 2021, repeal of MCIT as a step in the wrong direction and urge CMS to replace that program with other measures to support medtech innovation for the benefit of the US patient population that it serves.

Increase the transparency and predictability of the reimbursement path for innovation. At present, no facility such as MDUFA establishes concrete processes and performance standards for CMS reimbursement decisions and decision-making processes. Moreover, CMS takes an annual and retrospective approach to reimbursement decisions, despite the fact that new technologies are approved throughout the year. Interviewees say the resulting lag time for benefit coverage affects new technology adoption. CMS reimbursement takes multiple forms, depending on where the product is used and whether the product is covered under a general code (for example, DRG) or directly reimbursed. The criteria and submission guidelines for each type of reimbursement may be difficult to interpret or entirely absent—as was the case for the New Technology Add-on Payment (NTAP) and New Technology Ambulatory Payment Classification (APC), less than six months before the 2022 application deadline. Companies request that CMS establish more-streamlined, structured, and transparent processes for attaining reimbursement, with decision criteria, data standards, performance targets, and opportunities for dialogue with both industry and the FDA.

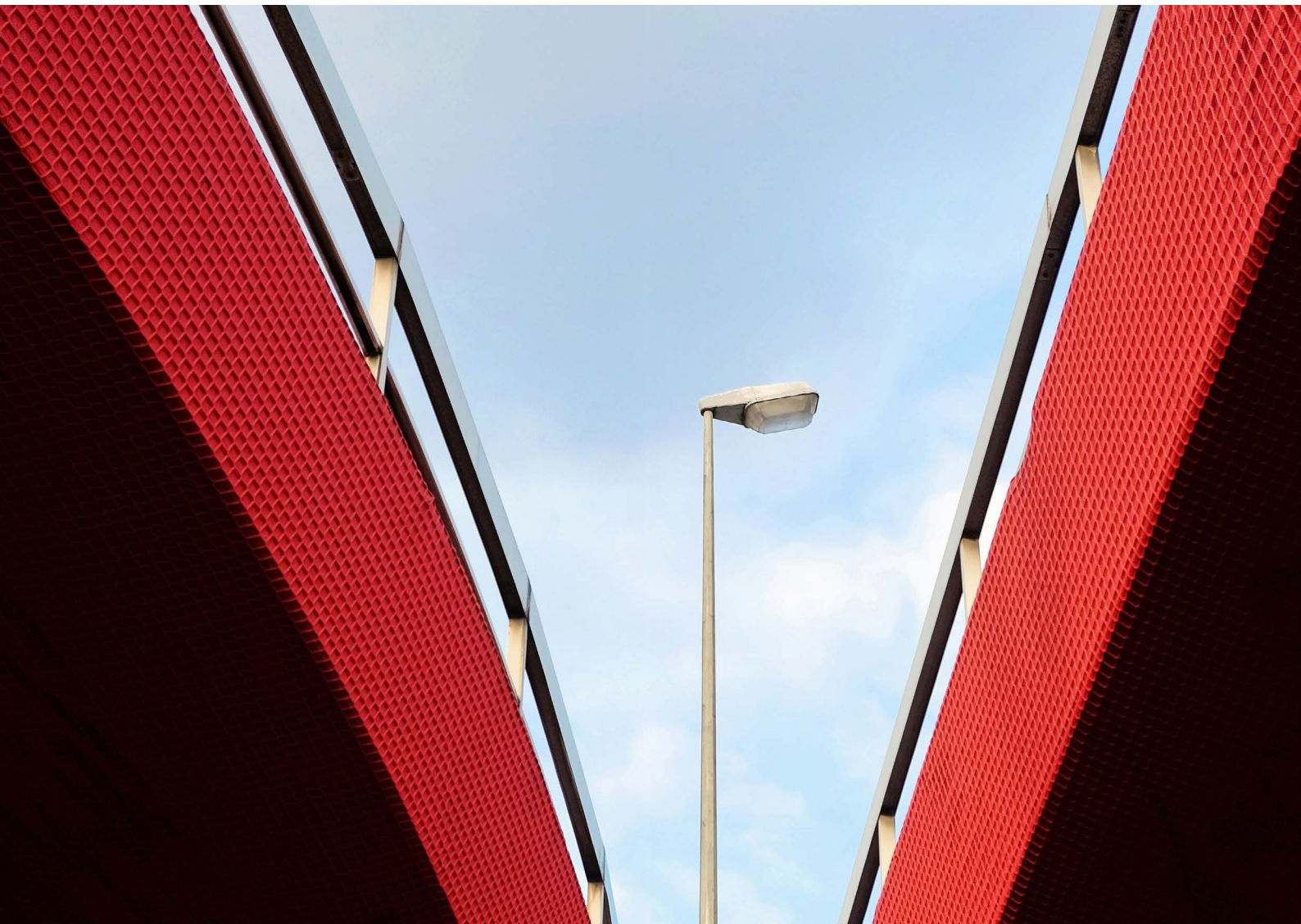
Modernize infrastructure and policy for digital health technology. Study participants called for clarity around existing criteria for benefit coverage and payment for digital health. Executives seek clearer guidance on how CMS makes decisions and what criteria and standards it will use for coverage and payment of digital health offerings. For instance, the substitution of AI for manual labor represents a potential cost savings for payers. Respondents ask what portion of those savings should accrue to the AI designers, which must first establish suitable algorithms and then continually update their offerings. Furthermore, industry experts suggest that CMS will need to expand hiring and emphasize digital expertise to improve both the capacity and the capability of specific approvals and policy decisions.

Enhance coordination between industry, regulatory, and reimbursement authorities. Industry respondents urge CMS to undertake a systematic review of how to work more efficiently with industry and the FDA to bring innovative products to market for the benefit of US patients. One idea for improving coordination between the FDA and CMS was a rotational leadership program that would bring rising talent into peer agencies. Such a program would help talented leaders identify critical handoffs and generate opportunities for more cross-agency cooperation while deepening CMS's understanding of digital and breakthrough technologies. Likewise, CMS could work with coding organizations to establish workshops with innovators and entrepreneurs to foster open dialogue on emerging technology solutions and realistic expectations for reimbursement.

"There needs to be a bridge between the FDA and CMS. Reimbursement shouldn't be the decider for clearance, but having it a part of the clearance decision, especially for novel technologies, is important. At some point, CMS needs to be in the room with the company and the FDA."

—CEO, venture-backed neurology company

Conclusion



The past decade was a period of profound change for the medtech industry as digital technology took hold, overturning legacy processes and ushering in exciting new possibilities for patients and caregivers. During this time, regulatory authorities and reimbursement agencies around the world had to redouble their efforts to recruit talent and upgrade their systems and protocols to accommodate new ways of doing business. Until now, no research has attempted to assess whether their measures are helping or hindering medtech innovation in the digital age.

Our study provides deep insights into these questions, concluding that the US FDA has emerged as the global regulatory agency most successful in promoting access to novel medtech products, especially digitally enabled or software-driven ones. Whereas a decade ago medtech companies strongly preferred to launch products in the EU due to a perception that the pathway to market was simpler and more predictable, the situation has reversed. In part, this reversal can be attributed to the EU's new MDR legislation and the challenges associated with Brexit. However, it is also clear that respondents hold a favorable view of several core FDA programs that promote innovation: De Novo granting, Breakthrough Device designation, and the Digital Health Center of Excellence.

One of the study's most important findings concerns the cost and time required to bring innovative products to market. Bearing in mind that a simple Class I device might cost less than $1 million from concept to launch in one year's time while a more complex Class II device can easily run into the tens of millions of dollars over two to three years, the ability of regulatory agencies to anticipate the demands of emerging technology and digital trends is critical to the pace of innovation. Of the 105 products included in our sample, 63 were digitally enabled. We observed that, on average, 510(k) clearances cost $6.1 million and took 33 months from concept to launch, while De Novo products cost $17.8 million and took 80 months to reach the market.

Although respondents praise the FDA for enhancing innovation and increasing the predictability of regulatory outcomes, they seek additional clarity and guidance on digital health. They worry even more about US reimbursement. Overwhelmingly, they view the repeal of MCIT, which paired Breakthrough Device designation with reimbursement, as a mistake. Smaller companies especially say that the need for predictable reimbursement as a precondition for raising venture funds poses a significant barrier to innovation.

Our findings conclude with a series of peer best practices as well as recommendations for regulators and reimbursement authorities. Despite the inevitable challenges involved in an innovation-driven industry, the past decade has been one of tremendous success for the medtech sector. Regulators deserve credit for their continuing efforts to adapt to the new reality of digital health, and the trend toward greater consultation between industry and regulatory authorities holds great promise for prospective medical products and the patients who stand to benefit from them.

Supplemental Data

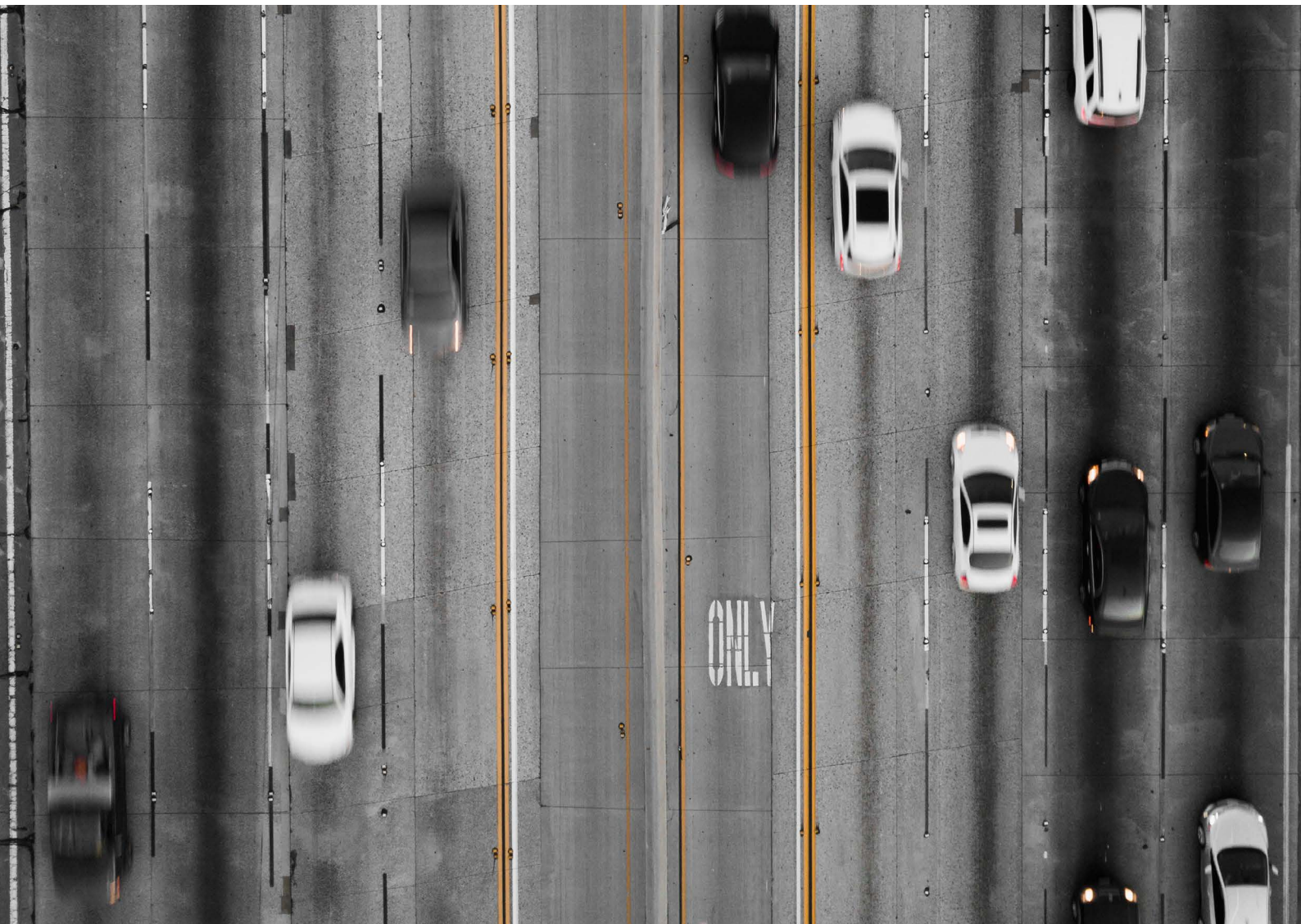


Exhibit 19 - Study Results Versus MDUFA Reporting for FDA Premarket Submission Review Time

	MDUFA performance Average time to MDUFA decision (days)[1]			Study[2] (days)
	2010	2015	2020	2010–2020[3]
510(k)	**154**	**135**	**126**	154 (n = 56)
De Novo	**781**	**278**	**258**	296 (n = 15)
PMA original	**419**	**294**	**251**	264 (n = 4)

Source: FDA.

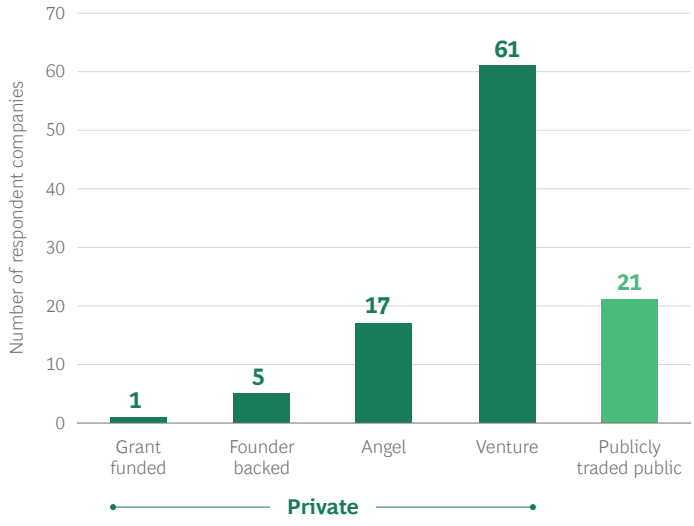
[1] MDUFA IV Quarterly Performance Report, August 3, 2021.

[2] Average time to FDA decision based on FDA database.

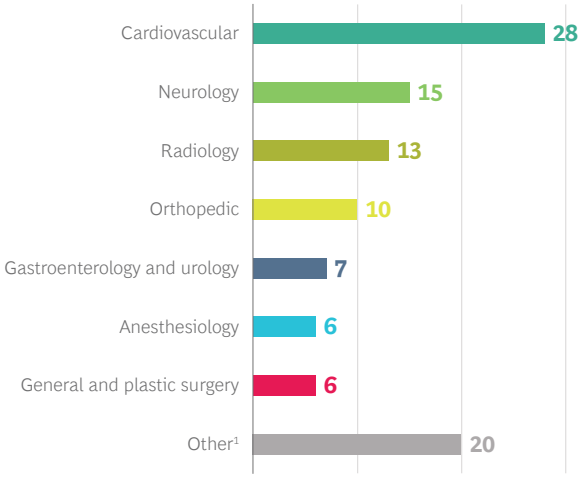
[3] Some of the 105 devices are not represented here, either because they are Breakthrough-designated devices whose approval is still pending or because they are devices approved in 2021.

Exhibit 20 - Participating Companies by Funding Stage and Medical Specialty

A majority (58%) of companies are venture backed



Medical specialty

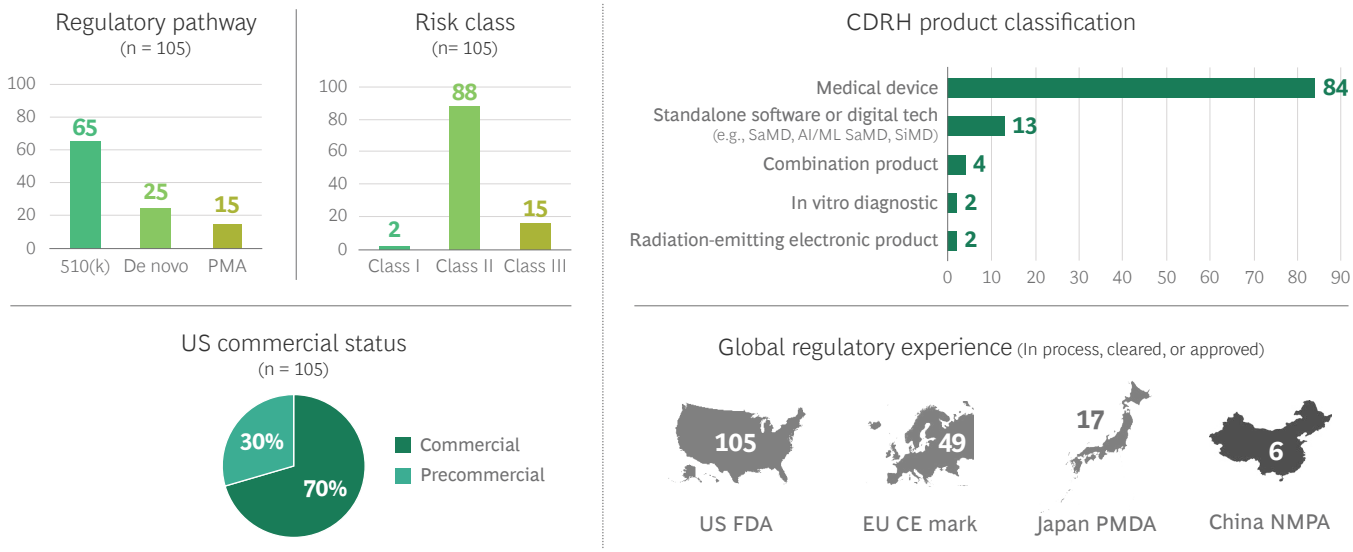


Sources: BCG and UCLA Biodesign.

Note: n = 105.

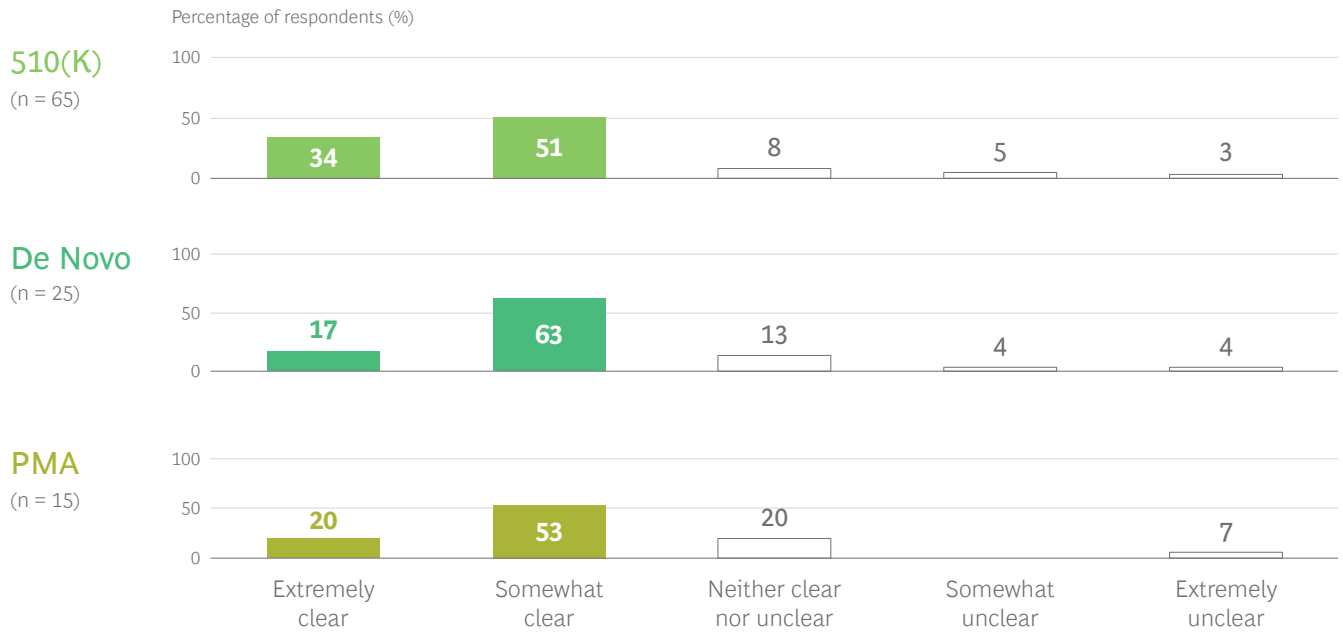
[1] Other medical panels represented in this study include ear, nose, and throat; obstetrical and gynecological; general hospital; hematology; ophthalmic; microbiology; physical medicine; chemistry; and dental.

Exhibit 21 - Products Represented in This Sample



Sources: BCG and UCLA Biodesign.

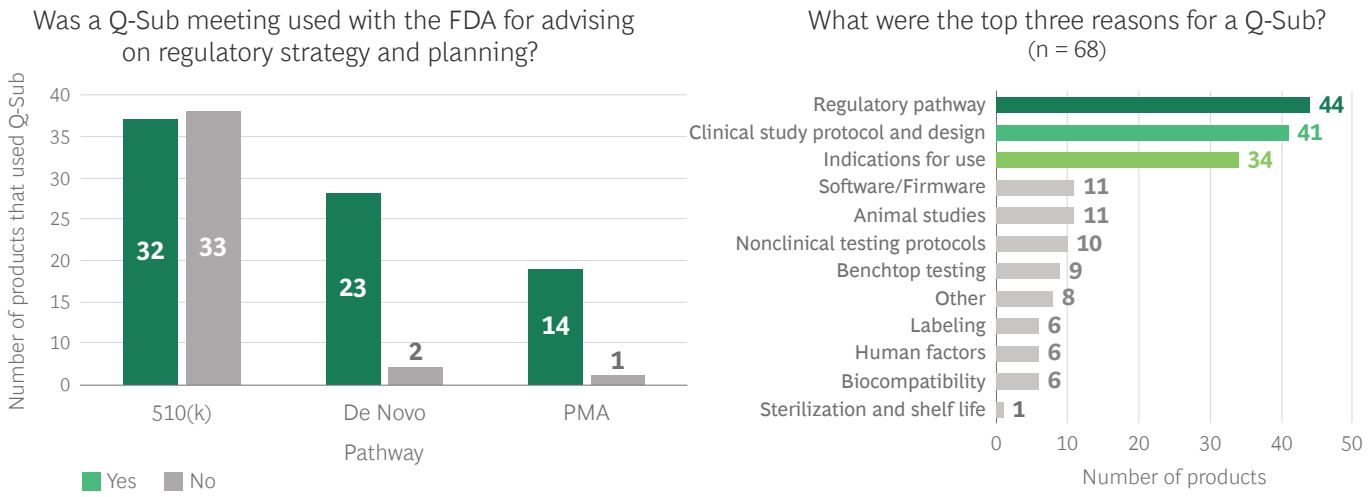
Exhibit 22 - Clarity of Guidance Documents



Sources: BCG and UCLA Biodesign.

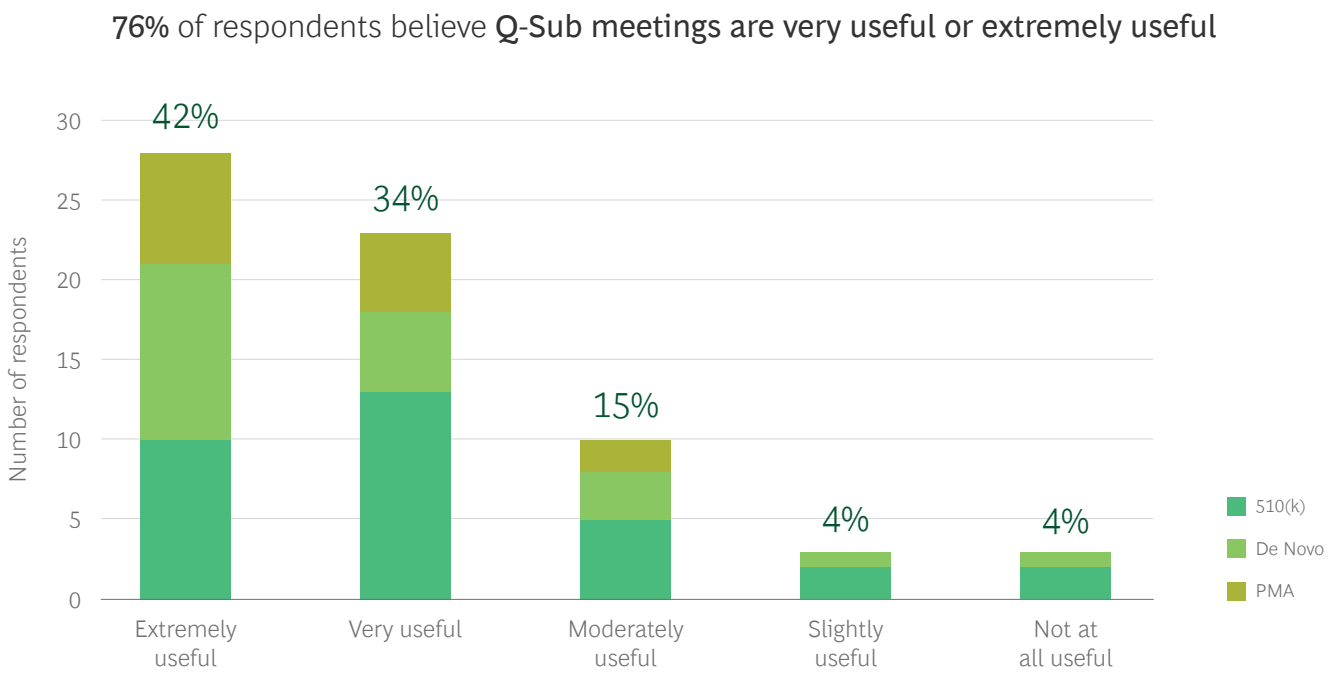
Note: Because of rounding, the percentages given do not always add up to 100%.

Exhibit 23 - Preregulatory Strategy: Q-Sub Process



Sources: BCG and UCLA Biodesign.

Exhibit 24 - Helpfulness of Q-Sub Meetings

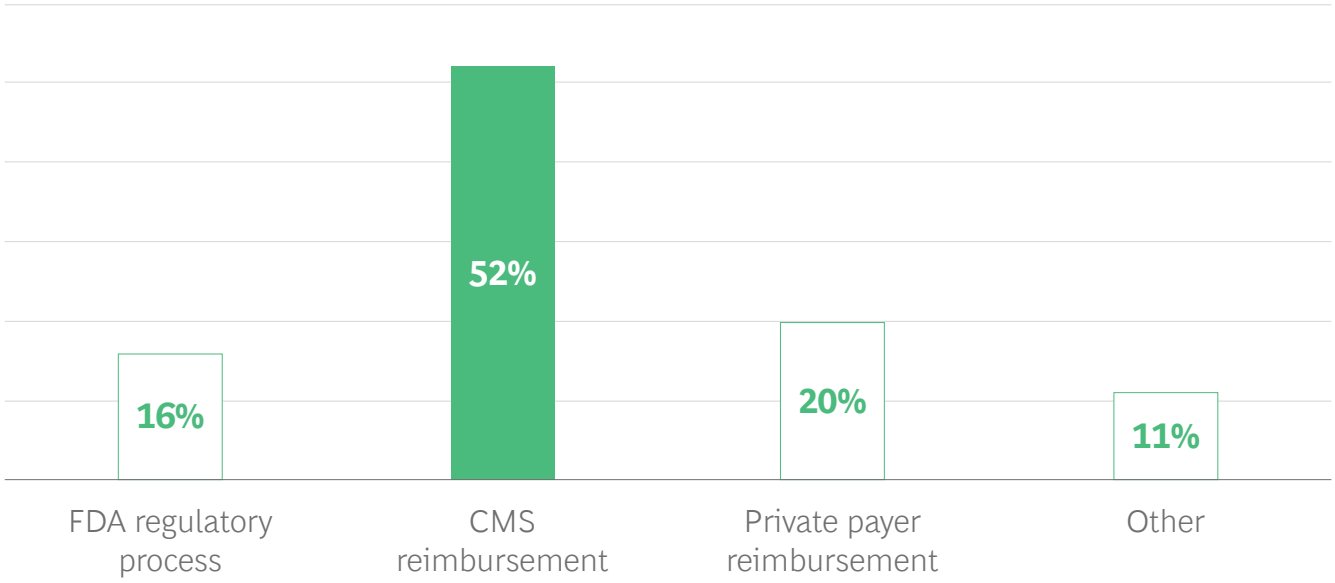


Sources: BCG and UCLA Biodesign.

Note: Because of rounding, the percentages given do not add up to 100%.

Exhibit 25 - Reimbursement as a Barrier to Innovation

A majority (72%) of respondents believe **reimbursement is the leading barrier** to patient access to novel medical technologies, relative to regulatory[1]



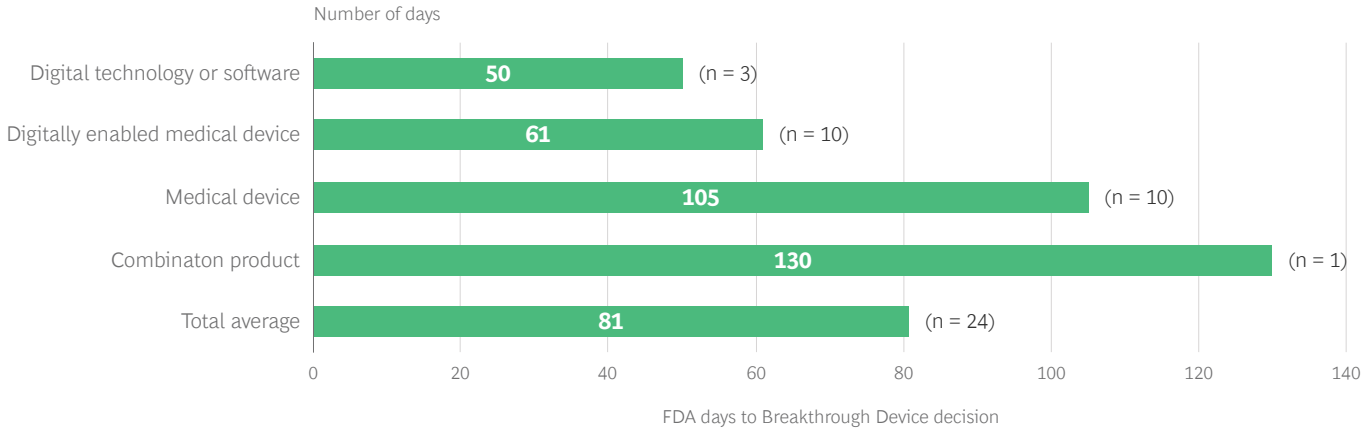
Sources: BCG and UCLA Biodesign.

Note: Because of rounding, the percentages given do not add up to 100%.

[1] 108 respondents were asked which activity was the greatest barrier to patient access to novel medical and digital technologies.

Exhibit 26 - Breakthrough Device Designation Approval Time

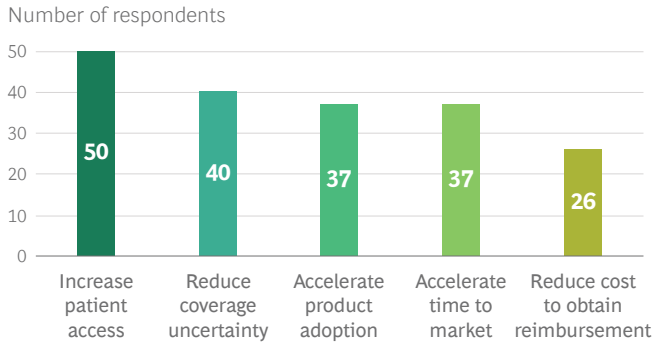
On average, **Breakthrough Device designations** required **81 days to be granted** (n = 24)



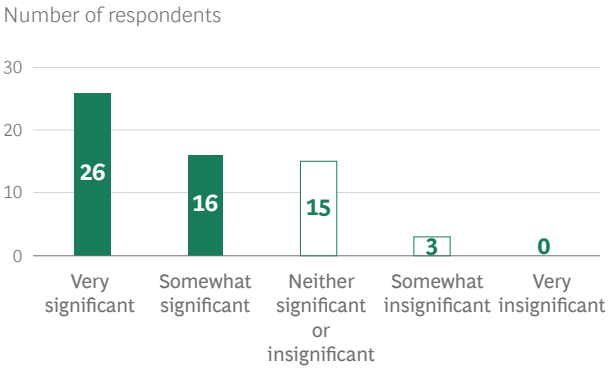
Sources: BCG and UCLA Biodesign.

Exhibit 27 - Benefits of Breakthrough Device Designation and Implications of MCIT Rescission

Increasing patient access is the leading perceived benefit of Breakthrough Device designation (n = 66)

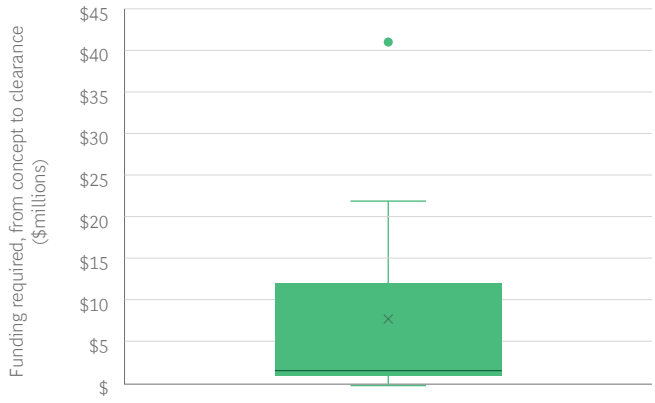


70% believe rescinding MCIT will have significant impact on patient access to breakthrough medical technologies (n = 60)



Sources: BCG and UCLA Biodesign.

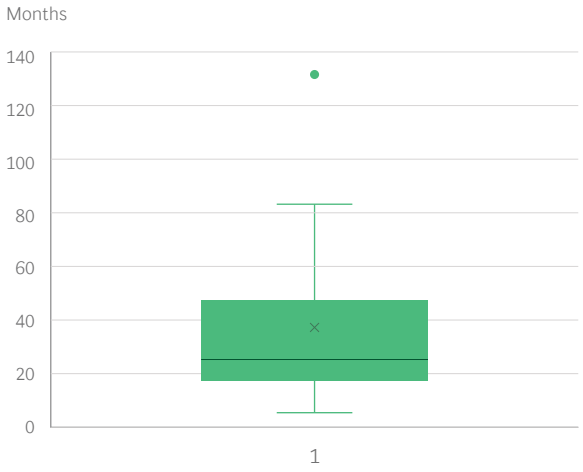
Exhibit 28 - Funding Required for AI/ML-Enabled Devices with 510(k) Clearance



	510(k)
Average	$8.6
Maximum	$41.0
Third quartile (75%)	$10.8
Median	$2.8
First quartile (25%)	$2.0
Minimum	$0.6

Sources: BCG and UCLA Biodesign.

Exhibit 29 - Time Required for AI/ML-Enabled Devices with 510(k) Clearance

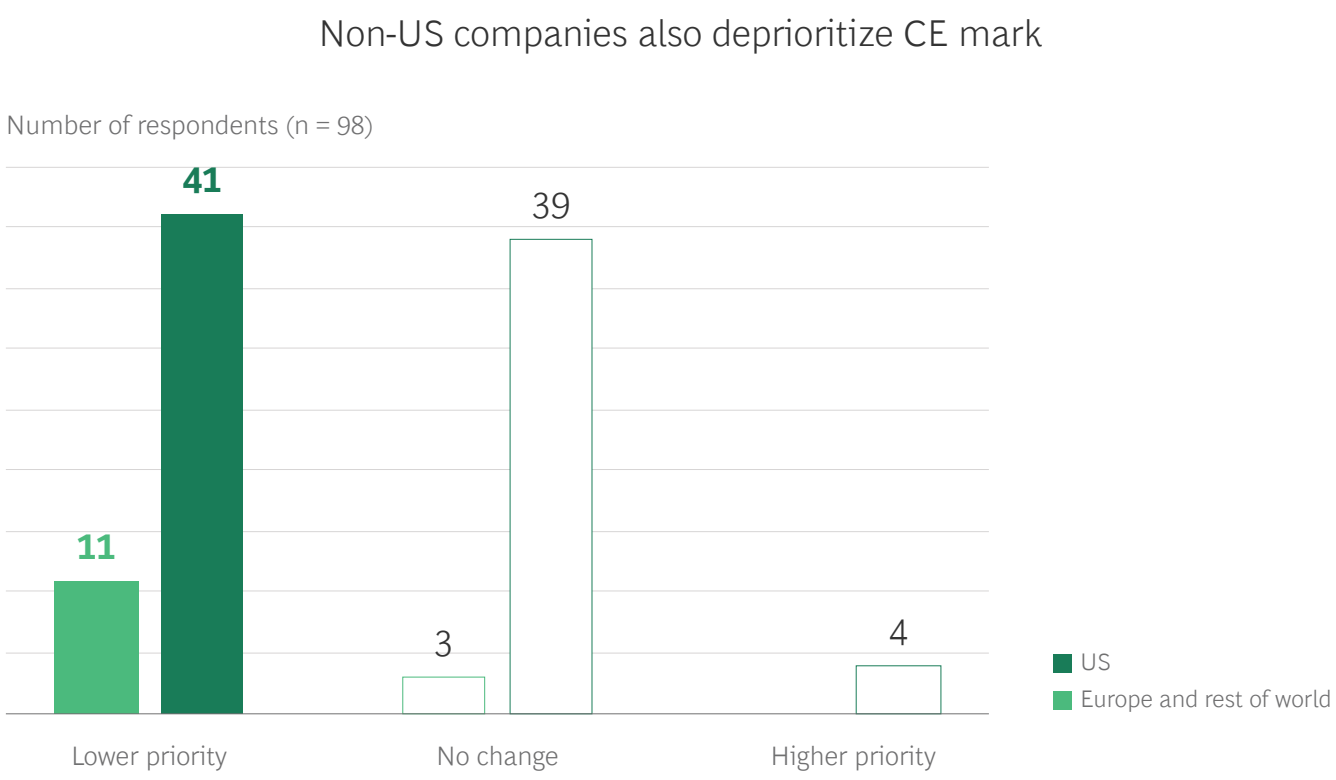


	510(k)
Average	37
Maximum	132
Third quartile (75%)	45
Median	26
First quartile (25%)	18
Minimum	6

Sources: BCG and UCLA Biodesign.

Note: n = 16.

Exhibit 30 - Prioritization of EU Versus US by Headquarters Location



Sources: BCG and UCLA Biodesign.

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