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Health Policy Brief

21st Century Cures: The future of product innovation and approval

Executive summary

After almost three years of public meetings, debate, and consensus building, the 21st Century Cures Act (Cures Act) became law on December 13, 2016. The bipartisan legislation allocates a total of \$6.3 billion to advance biomedical innovation by funding basic science research at the National Institutes of Health (NIH) (\$4.8 billion) and allowing for innovation and flexibility for product regulation at the Food and Drug Administration (FDA) (\$500 million). Other provisions target health information technology (HIT) and public health priorities. The major Cures Act provisions that pertain to biopharmaceutical and medical technology product development, regulation, and approval include:*

- Striving for faster drug approvals using new classes of evidence and adaptive frameworks.
 Streamlines clinical trials using new drug development tools and frameworks; requires FDA to evaluate the use of real-world evidence (RWE) and ensure that patient experience is reflected in assessments of benefit/risk
- Communicating health care economic information among stakeholders. Expands the dialogue and provides flexibility on the economic evidence that biopharma and health care stakeholders can share
- Advancing medical device innovation. Adds clarity and updates to existing regulations; introduces regulatory flexibility for advancing devices that treat life-threatening conditions or small populations
- ^{*}To quickly access the goals of the provisions and implementation next steps, click on the bolded bulleted statements.

- Creating regulatory clarity for combination products. Provides clarity on assigning regulatory oversight to products that involve a combination of drugs, biologics, and devices
- Regulating medical software and HIT. Provides some boundaries on the types of software that will be excluded from FDA regulation; and advances interoperability of electronic health records (EHRs)
- Establishing a pathway for regenerative medicine. Updates the regulatory pathway for regenerative medicine products, bringing more products under FDA oversight and providing flexibility for more complex products

The Cures Act creates an opportunity for the FDA to apply recent advances in technology and analytics and scientific and evidentiary models to continue evolving regulatory programs. Moreover, the new administration's focus on reducing regulatory burden could spur agencies to move towards a more collaborative, adaptive approach to regulating therapies, and create regulatory flexibility that also supports patient access and public safety.

In many ways, the drug, device, and diagnostic development and approval process of yesterday is over. Life sciences companies (biopharma, medical device, and diagnostics companies) may risk being out of date and competitively disadvantaged if they are not pursuing the newer breakthrough, priority, or accelerated pathways included in the Cures Act and in some of the initiatives the FDA has developed in the past several years. As the industry strives to meet the evolving needs of stakeholders—patients, providers, and health plans this regulatory flexibility will likely be imperative to drive both regulatory approval and market access. To take advantage of the evolving regulatory landscape, our research and discussions with industry stakeholders suggest that life sciences companies should consider:

- Engaging in early discussions with the FDA to design clinical trials that incorporate surrogate endpoints and other tools to shorten drug development timelines
- Expanding capabilities to access, collect, and analyze RWE and patient experience data
- Continuing to work with the FDA, patient advocacy groups, and provider organizations to delineate pathways for patient and caregiver involvement
- Expanding the dialogue on economic evidence between biopharma and medical device companies and health care stakeholders, including payers
- Taking advantage of additional regulatory clarity by investing in breakthrough devices, point-of-care (POC) diagnostics, drug-device combination products, and regenerative medicine

 Advancing the conversation on the regulation of medical software in collaboration with the FDA and other industry stakeholders

The Cures Act builds on previous FDA initiatives to modernize the regulatory process

In an effort to modernize the regulatory process, the Cures Act builds on FDA initiatives already underway, including activities such as expedited review programs; working with life sciences companies to design efficient, flexible clinical trials; and helping speed development of potential treatments for rare diseases (see sidebar below). The Cures Act calls for collaboration among government agencies such as the FDA, NIH, the Department of Health and Human Services (HHS), the Office of Management and Budget (OMB), and the Reagan Udall Foundation to innovate processes and advance therapies.¹

The FDA has worked to implement six main expedited development and approval pathways

1.

Orphan Drug Act (1983) Diseases affecting <200,000 people per year

Fast Track (1988)

Potential to address unmet medical need; one Phase 2 trial sufficient

Accelerated Approval (1992)

"Meaningful advantage" over existing therapy; approval based on surrogate or intermediate endpoint "reasonably likely to predict clinical benefit"

Priority Review (1992)

"Significantly improve" safety or effectiveness; shorter FDA review (six months vs. 10 month standard)

Breakthrough Therapy (2012)

Preliminary clinical evidence with clinically significant endpoint(s); "substantial improvement" over existing therapy; benefits include intensive guidance to expedite development

The Food and Drug Administration Safety and Innovation Act (FDASIA) (2012)

Expands the FDA's authorities and strengthens the agency's abilities to safeguard and advance public health in a number of ways, including collecting user fees, promoting innovation, increasing stakeholder involvement in FDA processes, and enhancing the safety of the drug supply chain

The Cures Act allocates \$6.3 billion in funding for the NIH and FDA over the next 10 years, beginning in fiscal year 2017. The Act establishes the FDA Innovation Account and provides the agency with \$500 million to implement the initiatives laid out for faster drug approvals and updated guidance. The Act also creates the NIH Innovation Account and appropriates \$4.8 billion for:

- Cancer research (\$1.8 billion)
- Brain research (\$1.5 billion)
- Precision medicine (\$1.4 billion)
- Regenerative medicine (\$30 million)

Advancing federally-funded research

The Cures Act encourages the HHS Secretary to develop a network of scientists and public-private partnerships to come up with new approaches for addressing scientific, medical, public health, and regulatory science issues. The Act includes provisions that encourage translational medicine through greater data sharing among NIH-funded research and industry, and expands the scope of research that NIH can support. Further, it formalizes several key initiatives—such as the Cancer Moonshot and the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) initiative—by providing dedicated funding for each area. The Cures Act also contains provisions specifically aimed at advancing the Precision Medicine initiative.

Many health care stakeholders have voiced concerns around funding commitments, as the administration's blueprint budget released in March 2017 proposed \$5.8 billion in NIH funding cuts for fiscal year 2018. Many in the scientific community have warned that such cuts would blunt progress in improving the nation's health. The dollars that the Cures Act authorizes for NIH research initiatives represent an increase from NIH's current budget, after years of decline. Many had hoped that the funding included in Cures would, among other things, provide talented scientists and students with more opportunities in biomedical research and discovery in the US. However, Congress will still need to appropriate NIH funding every year and some stakeholders have expressed concern that competing priorities may slow the funding stream that the Cures Act provides.²

Among questions for life sciences companies: How should they invest their research and development (R&D) dollars across platforms, capabilities, and programs to keep up with scientific advances? How can they better collaborate and share data with NIH, the broader research community, and patient advocacy groups to advance the scientific understanding of disease? Biopharma and medical device companies increasingly are partnering with other health care stakeholders to address scientific and technological challenges, create greater efficiencies in R&D, and accelerate the development and delivery of new treatments. The Cures Act encourages more of these collaborations and creates an opportunity to expand the nature of these relationships.

Among questions for life sciences companies: How should they invest their R&D dollars across platforms, capabilities, and programs to keep up with scientific advances?



User fee reauthorization agreements important for FDA programs

Reauthorization of the current FDA user-fee programs, five-year agreements with drug, biologic, and device makers that provide about half of the FDA's annual budget, expire in the fall of 2017. These agreements have demonstrated that FDA and the life sciences industry can work together to reduce overall product development time by engaging earlier in discussions and pursing flexible approaches to developing data needed for product approval.³ Congress must review separate user-fee agreements for branded drug makers, generic drugs, biosimilars, and medical devices, and eventually package them into one bill. The user-fee programs provide additional detail and funding to support implementation of certain Cures Act provisions. Without the user-fee funding, the FDA would likely have to let hundreds of employees go, leaving the agency shortstaffed to approve new therapies.4

Currently, other legislative initiatives are taking precedence in Congress. Further, work on reauthorization spans two administrations—the former administration had reached initial agreements last year, but the current administration may have other priorities for the agreements. It is also unclear how the user-fee programs intersect with an Executive Order issued by the administration in early 2017 that requires a freeze on federal jobs. The impact to FDA hiring is unknown, since the law excludes jobs "necessary to meet public safety responsibilities," and hundreds of jobs are funded through user-fee agreements. If the hiring freeze applies (assuming the program is reauthorized), these jobs will be impacted and the FDA may not be able to fill the existing vacancies or move forward on implementing several Cures Act provisions.

Key Cures Act provisions and potential implications for life sciences companies

Enabling faster drug approvals using new classes of evidence and adaptive frameworks

The Cures Act includes several provisions intended to modernize the drug development and approval process. Several of these build upon existing FDA initiatives and investment areas, creating avenues for innovation and regulatory flexibility. Table 1 outlines the intent of the law, summarizes its provisions, and details next steps.

Table 1. Provisions to modernize clinical trial design, evidence development, and advanced therapies

Goal	Provision	Implementation next steps
Modernize the approach to clinical trial design and data analysis	Requires FDA to hold a public meeting and issue guidance documents to assist sponsors in incorporating adaptive designs and statistical (quantitative and qualitative) modeling into new drug applications	FDA to hold public meeting including representatives from industry, academia, patient advocacy organizations, consumer groups, and disease research foundations within 18 months; FDA to issue guidance no later than 18 months after the date of the public meeting
Incorporate tools to shorten the drug development process	Building on the 2012 Drug Development Tools Qualification Program, this provision establishes a review pathway for biomarkers and other development tools to help shorten drug development times, and makes additional information available on a biannual basis	FDA to issue guidance, in consultation with biomedical research consortia and other interested parties, on qualification of tools and framework for development of biomarkers within three years
Evaluate new sources of evidence in the post- marketing environment	Requires FDA to evaluate the use of RWE to help support the approval of a new indication for a previously approved drug and to help support or satisfy post-approval study requirements	FDA to create a framework in partnership with industry stakeholders for its RWE program within two years; in five years, FDA is to create guidance describing: (1) "the circumstances under which sponsors of drugs may rely" on RWE, and (2) acceptable standards and methodologies for collecting and analyzing RWE

Goal	Provision	Implementation next steps
Streamline applications for new indications	Allows FDA to rely upon qualified data summaries to support the approval of an application for a new indication of an already approved drug	Amends the Food, Drug, and Cosmetic Act and requires no further guidance be issued
Create incentives to study treatments in populations with high unmet needs	Reauthorizes Pediatric Rare Disease Priority Review Voucher (PRV) program, and requires a Government Accountability Office (GAO) study of all PRV programs Allows orphan drug grants to be used for observational studies Provides FDA with the flexibility to approve antimicrobial drugs based on a limited population if the drug treats a life-threatening infection	FDA to issue guidance, within 18 months, describing criteria, processes, and other general considerations for limited population antibacterial and antifungal drugs
Update clinical trial oversight	Streamlines institutional review board process for trials being conducted at multiple sites Provides FDA flexibility to waive or alter informed consent requirements for clinical trials with minimal risk	Requires that no further guidance be issued
Build on FDA initiatives to incorporate patient perspectives into the drug review process	 Requires FDA to report any patient experience data (data related to patients' experience with a disease or condition and patient preferences with respect to treatment, collected by patients, caregivers, advocacy organizations, drug manufacturers, or others) used during review of drug application at the time of approval Requires FDA to issue guidance on how patient experience data should be collected and used in the drug application review, and issue a report on: Its use of patient experience data and patient-focused drug development tools in regulatory decision making, which includes appropriate ways to collect data for use in regulatory decisions; How patients wishing to propose draft 	Requires FDA to publish a report on its use of patient experience data and patient focused drug development tools in regulatory decision making; series of reports to be published in coming years

guidance may submit document to FDA;How FDA will respond to patient experience

- How FDA plans to use relevant patient experience data in the drug review process

data submissions; and

Table 1. Provisions to modernize clinical trial design, evidence development, and advanced therapies

Source: 114-225 Public Law 114-255

Reactions and potential challenges to Cures Act provisions to modernize drug development and approval

Create regulatory flexibility that also ensures patient access and public safety. Some critics have suggested that the FDA's bar for approving drugs is set too high, with overly conservative regulatory requirements delaying patient access to needed treatments.⁵ However, many biotech executives have spoken out on the need to ensure safety and efficacy standards are met, and have lauded the FDA for its initiatives to partner with industry and speed approvals in the last several years. To get new treatments to patients as efficiently as possible, many in the life sciences industry are seeking less costly and faster ways to collect the data needed to demonstrate safety and efficacy. The ability to validate and use tools that serve as surrogate endpoints—such as biomarkers, and patient-generated data captured through new emerging technologies such as biosensors and apps-could help meet this goal. The Cures Act aims to continue efforts to validate these types of tools and new evidence sources. Further, proponents of the law suggest that allowing for more flexibility in the types of evidence, including RWE, required for the approval of new indications could help keep pace with and takes advantage of recent advances in data analytics.

Countering arguments that the drug approval bar is too high are those that say that the Cures Act's inclusion of data "summaries" and the lack of retrospective data transparency to verify or counter current results weakens the FDA standards in favor of industry.⁶ Before Congress passed the Cures Act, some critics had challenged the quality of material supporting medical claims when advocating for supplemental applications. For example, clinical studies supported only about a third of supplemental approvals.⁷

Flexible approaches to clinical trials, such as adaptive trial design (which allows modifications to clinical trial protocol as observations on outcomes are made), increase the potential that certain safety signals, or risks posed to populations not studied, may not be as clear during clinical trials pre-approval. However, flexible approaches often allow for quicker patient access to treatments and real-world data (RWD) collection. Many advocates of expediting the approval process suggest that making the product available to patients allows for observational studies that remove artificial controls included in randomized controlled trials. RWE, in these circumstances, could help to improve understanding of the health impacts of drugs. Regulatory flexibility that allows for drug approvals based on limited information often calls for greater surveillance programs following

a drug's launch—a trade-off that the Cures Act aims to address by creating an avenue to leverage RWE in the post-market drug studies.

Ensure that initiatives to incorporate patient experience data into drug and device reimbursement takes an inclusive approach. Full consideration of how drugs and medical technologies can create value, for example, traditionally has been excluded or not given appropriate weight in some of the existing value frameworks.⁸ This includes value drivers that take into account:

- Clinical utility and health outcomes associated with the product
- Impact on non-medical benefits for the patient or caregiver, the patient experience, and patient economics (such as out-of-pocket costs)
- Impact on revenues and costs for a provider, payer, or provider-sponsored plan
- Impact to the health care system at large and employers or the public as a whole

What considerations should be top of mind for life sciences companies?

Many provisions aimed at expediting drug development require the FDA to issue further guidance; however, the biopharma industry can take some next steps now to begin to benefit from regulatory changes.

Invest in the study and application of collaborative drug development tools. Expansion of the Drug Development Tool Qualification program supports the FDA's commitment to explore novel approaches to drug development. While the agency is expected to issue guidance on this topic, the industry can move forward with submitting letters of intent to evaluate tools. Biopharma companies should consider engaging in proactive conversations with the FDA early in development to understand which innovative tools might apply to their program and possibly expedite development—and get treatments to patients faster.

Expand capabilities required to access, collect, and analyze RWD. RWD—including data from claims, EHRs, surveys, registries, laboratory results, and potentially, wearable devices—can present an opportunity to link disparate data sources to provide a better understanding of the patient experience and what happens during an episode of care.



Figure 1. Status of RWE capabilities across life sciences companies

Source: Deloitte 2017 RWE Benchmark Survey

Deloitte's 2017 RWE benchmarking study, *Getting real* with real-world evidence,⁹ found that many biopharma companies are starting to invest in RWE capabilities and are exploring a number of use cases (see Figure 1). RWE can have several applications during the development process. For one, a more holistic view of a patient can speed-up trial enrollment. Further, stakeholders may use RWD as a control arm for clinical trials. This could drastically reduce the time it takes to execute a trial.¹⁰ In addition, many RWE use cases expand beyond drug development and approval: RWE can help demonstrate improvements in patient outcomes across large populations and support market access.

Many public-private partnerships such as the Reagan-Udall Foundation and others are becoming more important as a way to improve access to data and incorporate RWD into drug applications for new indications. RWD can have certain biases, and advances in HIT, standards, and methodologies need to continue improving for it to be widely accepted to support regulatory approvals. Leading practices on how to incorporate RWE into R&D will likely continue to emerge from public-private partnerships and other examples of multiple stakeholders working together to advance RWE use and interpretation.

The Cures Act presents an opportunity for biopharma companies and the FDA to discuss what the RWE framework could look like. Early and regular dialogue can help companies clarify how to take advantage of Cures-driven regulatory process changes as companies begin to build capabilities to access, integrate, and analyze RWD. As the volume, variety, and velocity of RWD continue to grow, the need for newer information management and analytics technologies will likely become even more apparent.

Leveraging incentives to develop drugs for specific

populations. Biopharma companies can already benefit from the PRV program and the expanded availability of grants for prospective observational studies. While the FDA is required to provide more guidance on the limited population pathway, companies can engage in dialogue with the agency now regarding products they would like to study under this approach. For example, studying an antimicrobial drug in a limited population can decrease the complexity of drug development, thus lowering the economic and regulatory burden for companies. Companies could also use narrower indications to promote novel contracting agreements and expedite market access.¹¹

Continue to work with the FDA, patient advocacy groups, and provider groups to delineate pathways for patient and caregiver involvement. The FDA

has placed increasing emphasis on incorporating patient perspectives into the drug review process, and has launched the Patient-Focused Drug Development Initiative under the fifth Prescription Drug User Fee Act (PDUFA V). The FDA has defined a patient reported outcome (PRO) as any status report on a patient's health condition that comes directly from the patient, without a clinician or other individual interpreting the patient's response. PROs typically include information about health-related quality of life (HRQL), symptoms, function (disability), satisfaction with care, adherence to prescribed medications or other therapy, and perceived value of treatment. Additional clarity on how the patient voice will be incorporated in FDA benefit/risk assessment decisions as a result of earlier initiatives, such as PDUFA V, as well as the Cures Act, will likely help these pathways continue to be productive. Achieving patient-centered drug development means life sciences companies must understand how patients define value, and design their drug development programs to demonstrate this value. Early engagement between the FDA and industry is now the model—life sciences companies might find themselves on an extended approval pathway if they do not adapt.

Communications among biopharma and stakeholders around health care economic information

The FDA has regulations regarding off-label drug marketing, including limiting drug companies' ability to proactively communicate some economic evidence. Part of the FDA Modernization Act of 1997, FDAMA 114 outlines what type of economic evidence can be shared, and with which stakeholders. The Cures Act aims to provide more clarity to biopharma companies on these details. Table 2 outlines the provision's goals, key provisions, and next steps.

Reactions and potential challenges to Cures provisions around health care economic information

Remove additional barriers to value-based contracting for both drugs and devices. As originally written, FDAMA 114 stated that health care economic information provided by a biopharma company to a formulary committee, or other similar entity, should be based on "competent and reliable scientific evidence" and would not be considered false or misleading if it "directly relates" to an FDA-approved indication.¹² As a result, many biopharma companies have been hesitant to proactively share economic information with health plans and providers in a way that would support valuebased contracts.

Goal	Provision	Implementation next steps
Provide flexibility on certain health care economic information communications (HCEI)	Provisions related to patient information and access to data clarify scope of permissible manufacturer communications regarding health care economic information to certain entities	The provision and new guidance offer potential for more and better communication between drug companies and health plans, although this will require careful monitoring by regulators
	One provision amends FDAMA 114 to provide increased flexibility for companies to communicate with formulary committees around the economic value of products	
	Broadens the evidentiary standard for HCEI communications to encompass clinical data and other assumptions that may include comparative analysis to other therapies or standard of care; also broadens the audience to include payers	
	FDA issued guidance shortly after the Cures Act passed ¹³ that addresses questions about the communication of HCEI by drug and device companies to formulary committees, including the statutory changes included in the Cures Act	

Table 2. Communication among biopharma and stakeholders around health care economic information

For example, biopharma companies may have to exclude indirect outcome measures such as reduced readmissions not studied in clinical trials. The Cures Act provisions and new FDA guidance change the clause on "directly relates" to simply "relates," allowing companies more flexibility to contract on a broader range of health outcomes. Further, the new guidance appears to allow companies more flexibility to make extrapolations in RWD analyses and in economic models.

These changes can be encouraging for biopharma companies that are seeking to enter into value-based contracts with payers (see sidebar below). However, both biopharma and device companies have also pointed to another regulatory hurdle that could hinder novel valuebased contracts: The federal Anti-Kickback Statute (AKS) prohibits entities from offering, soliciting, or accepting any type of gifts or remuneration in exchange for referring, ordering, or otherwise making arrangements for the provision of health care services payable by Medicare or Medicaid. Value-based agreements that include services offered by manufacturers—including those around data collection and analysis required to track outcomes—or incentives for providers to increase product utilization, such as adherence programs, might be considered inducements under this law.¹⁴

The industry has proposed safe harbors to allow for value-based contracting, but is waiting on a final rule from the HHS's Office of Inspector General (OIG).

What considerations should be top-of-mind for life sciences companies?

Expand the dialogue on economic evidence between biopharma and health care stakeholders.

The Cures Act and the FDA guidance expand the intended recipients of health care economic communications, from "a formulary committee or other similar entity" to:

- "A payer, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis, carrying out its responsibilities for the selection of drugs for coverage or reimbursement" (Cures) and;
- 2) "Drug information centers, technology assessment panels, pharmacy benefit managers, and other multidisciplinary entities that review scientific and technology assessments to make drug selection, formulary management, and/or coverage and reimbursement decisions on a population basis for health care organizations" (FDA guidance).

Making value-based contracting work in the real world

Biopharma, medical device companies, and health plans that have begun implementing value-based contracts in the private sector commonly cite several challenges to successfully executing such arrangements. These include:

- Determining the appropriate measures of value to link payment. Parties entering into a value-based contract should agree upon a definition of value that they can attribute to the drug therapy or device. This could include a demonstrated endpoint from clinical trials, an outcome that provider organizations are actively measuring under quality initiatives, or some other definition of value. Further, value should be defined according to the population sub-set that stands to benefit most from treatment.
- Controlling for non-treatment factors that can influence outcomes. Other variables that could impact the outcomes of drug or device use include patient factors such as co-morbidities and adherence; physician factors such as user errors with devices or

prescribing errors with drugs; and reimbursement factors such as the use of utilization management tools like step therapy or cost sharing.

• Capturing, integrating, and analyzing data.

Health plans and providers that enter into value-based contracts will likely need robust infrastructure to track individual patients, their treatments, and outcomes. Of note, this could be particularly challenging for device companies because traditional EHR and claims data sets do not capture device identifiers, though this is likely to change with industry-wide rollout of unique device identifiers. Validation and analysis would require collaboration and trust between the drug or device company and the health plan, and the companies should agree on methodology early in the process.

• Administrative burden to operationalize valuebased care. These arrangements require a different skillset and more resources to administer, monitor, and adjudicate. Lack of dedicated resources may hamper the ability to actually execute at scale. Stakeholders anticipate that this clarity will encourage biopharma companies to engage in a more robust dialogue around the economic value of treatments, and potentially allow for more value- or outcomes-based contracting (see sidebar on previous page).

Advancing medical device innovation

The provisions in 21st Century Cures related to device development and approval primarily add to existing regulations, providing updates and additional clarity. Many in the industry are particularly interested in provisions that clarify the device approval process and that introduce regulatory flexibility for POC diagnostics and advance devices that treat life-threatening conditions or small populations. Table 3 outlines these provisions and next steps.

Reactions and potential challenges to Cures provisions around advancing medical device innovation

Create regulatory flexibility that also ensures patient access and public safety. Some industry stakeholders are encouraged by some of the clarifying Cures Act provisions for devices, and the breakthrough device pathways it includes. Of note, the breakthrough device pathway builds upon the Expedited Access Program (EAP) that the FDA established in April 2014 and published guidance on in April 2015. The EAP aims to reduce the time to develop a device and expedite access for patients with serious conditions whose medical needs are unmet by current technology. The Cures Act increases the scope of products that the FDA may consider for an accelerated approval pathway.

Table 3. Provisions to advance medical device innovation

Goal	Provision	Implementation next steps
Clarify which devices require a 510K submission	Requires FDA to update lists regarding the appropriate regulation of Class I and Class II devices	FDA to update list of Class I and Class II devices 120 and 90 days, respectively, after the law's enactment
Improve existing medical device approval process	Improves classification panel review to ensure adequate expertise among members and allows for presentations by device sponsors	Requires FDA to assign staff to be available within a reasonable timeframe to address questions by institutional review committees concerning the conditions and clinical testing requirements applicable to investigational use of the device
Create regulatory flexibility for devices that treat life- threatening conditions or impact small populations	Establishes a breakthrough device pathway Provides FDA with the authority to apply the humanitarian device exemption to devices that treat diseases and conditions that affect up to 8,000 individuals in the US. Prior cap was 4,000	FDA to issue guidance on breakthrough device program within one year
Improves access to POC diagnostics	Requires that FDA update its existing regulatory guidance to clarify the criteria for waiving Clinical Laboratory Improvement Amendments (CLIA) requirements	FDA to issue guidance within one year that revises language to define "an insignificant risk of an erroneous result" to fulfill waiver requirements

Source: 114-225 Public Law 114-255

However, some critics of the law suggest that certain aspects, particularly the creation of a breakthrough device pathway, lower standards for device approvals and may put patient safety at risk.¹⁵ As discussed earlier, expedited approvals calls for robust post-market product performance monitoring (see sidebar below).

What considerations should be top-of-mind for life sciences companies?

Greater investment in medical technology

innovation. The new regulatory flexibility for devices that treat life-threatening conditions or limited populations could encourage greater investment in medical technology innovation. In recent years, venture capital investment in medical technology has declined, and growth in the number of startups has slowed.¹⁶ Industry stakeholders have cited the lack of regulatory certainty as particularly challenging in encouraging a robust innovation ecosystem in the device industry.¹⁷ The regulatory changes included in the Cures Act may reverse this trend. Large or mid-sized medical technology companies may consider taking advantage of this flexibility by entering into partnerships with companies that are developing life-changing innovations.

Generate data to support regulatory approval as

well as market access. Many in the medical device industry are facing increasing demands from health plans and providers for evidence demonstrating improved outcomes in order to justify providing patient access to products. Expedited regulatory pathways can leave companies with less evidence once products are launched; therefore, companies should consider investing early in evidence that supports coverage and reimbursement as well as regulatory approval. One strategy may be to take advantage of joint discussions with FDA and the Centers for Medicare and Medicaid Services (CMS) to help ensure that products will be available to patients once on the market.

Prepare for greater patient access to POC

diagnostics. This clarification of CLIA waiver requirements could advance POC diagnostics. Developments in biosensors and connected health technology are expanding opportunities for POC diagnostics to aid in prevention, early diagnosis, and chronic disease management. Analysts expect the POC diagnostics market to total nearly \$3 billion in 2021, up from \$2.13 billion in 2015.¹⁸ Companies can start to engage with the FDA now to understand the implications of CLIA waivers for POC products and to plan product investments accordingly.

RWE and medical device regulatory decision making

The Cures Act does not include language specific to applying RWE to medical device regulatory decision making but the FDA has already embarked on initiatives to consider RWE applications for medical devices, including issuing draft guidance in July 2016.¹⁹ The latest draft of the Medical Device User Fees Act (MDUFA), MDUFA IV, includes funding for 15 employees at FDA to evaluate the use of RWE in pre-market decision making (see sidebar: User fee reauthorization agreements important for FDA programs). In addition, the FDA is investing in a National Evaluation System for health Technology (NEST) to efficiently generate evidence to support provider, patient, and regulatory decision making. The FDA intends for this collaborative platform to synthesize and improve the quality of RWE from different sources, including clinical registries, EHRs, and medical billing claims.²⁰

Like biopharma companies, medical device manufacturers should consider investing in RWE capabilities to incorporate new sources of data into the device development and approval process.

Creating regulatory clarity for combination products

The life sciences industry is seeing a convergence of product types, including combinations of drugs, biologics, and devices. The FDA's Office of Combination Products (OCP) received 350 original pre-market applications for combination products in fiscal year 2015, a 10 percent increase from 2014.²¹ The Cures Act provides clarity on assigning regulatory oversight to these products. Table 4 describes specific provisions and next steps.

Reactions and potential challenges to Cures provisions to clarify combination product regulation

Clarity on combination product regulations is

welcome. In the past, determining a drug-device combination product's primary mode of action (PMOA) has been challenging. The Cures Act provides clarity to help companies better assess their risk/reward equation in developing these products. The PMOA determines which agency will have primary oversight of the product—the Center for Biologics Evaluation and Research, the Center for Drug Evaluation and Research, or the Center for Devices and Radiological Health. The FDA has been criticized by some for classifying many drug-device combination products as having a chemical PMOA if the product has any chemical action on the body. However, the Cures Act requires the agency to determine a single mode of action "expected to make the greatest contribution to the overall intended therapeutic effects."²²

What considerations should be top-of-mind for life sciences companies?

Take advantage of the opportunity to advance

combination products. The Cures Act allows for sponsor-agency to agree on "mechanism of action" studies which will determine the PMOA. The Act also clarifies a dispute process which allows sponsors to conduct studies and submit evidence to re-evaluate a PMOA determination. Industry sponsors should consider the trade-offs associated with investing in these studies, which could help to advance combination products but also delay product development timelines.²³

Goal	Provision	Implementation next steps
Improve regulation of combination products	Improves the regulation of combination products by requiring that the FDA meet with sponsors and agree early in development on how to best study the combination product to meet the standard for approval	Requires FDA to submit final guidance by December 2020 on the process for managing drug-device combination product pre-submission interactions, FDA's process for submitting feedback, and the information that must be submitted with a meeting request ²⁴
Increase opportunity for sponsor engagement in dispute resolution	Clarifies how dispute resolution works when the different centers of FDA do not agree	

Table 4. Provisions to clarify combination product regulation

Source: 114-225 Public Law 114-255

Regulation of medical software and HIT

Software technology is advancing at an exponential pace, and many companies are investing in health-related applications. Analysts state that the global digital health market reached \$51.3 billion in 2015, and will exceed \$379 billion by 2024, representing a 25.9 percent compounded annual growth rate from 2016 to 2024.²⁵ Many in the life sciences industry have been looking for clarity on how the FDA will regulate these products. As outlined in Table 5, the Cures Act begins to put some boundaries on the types of software that will be excluded from regulation.

The Cures Act also includes a number of HIT provisions to advance EHR interoperability and reduce administrative and documentation burdens. The Act encourages certification of HIT beyond the typical large hospital and clinic settings, such as certification of HIT for use at specialty providers and sites of service, to help ensure that more EHRs meet CMS standards for improved quality, safety, and efficiency. The Act also aims to promote interoperability of electronic patient data by imposing penalties on HIT vendors that HHS identifies as blocking information (and therefore interoperability). Table 5 outlines these provisions.

Goal	Provision	Implementation next steps
Clarify regulation of medical software	Identifies specific medical software categories that will not be regulated as a medical device unless there is found to be a safety concern— these include software used for administrative tasks or to support a healthy lifestyle, electronic patient records, medical device data systems (MDDS), and certain clinical decision support tools	Requires HHS Secretary to consult with agencies and publish a report by December 2019, and every two years after, that includes stakeholder input on any health risks and benefits associated with the medical software
Advance interoperability initiatives	Expedites interoperability among EHR systems by developing a voluntary model framework and common agreement for health providers Creates a streamlined HIT Advisory Committee at HHS (by combining existing policy and standards committees) to address issues related to interoperability, privacy, and security. New committee will engage stakeholders to identify priorities for interoperability standards adoption OIG is tasked with investigating claims of information blocking among health IT vendors	 Requires HHS to defer to HIT standards developed in the private sector when developing the voluntary model framework Requires HHS to develop a strategy on reducing administrative and regulatory burdens related to EHRs (documentation, etc.) within one year Authorizes OIG to impose penalties not to exceed \$1 million per violation; also, vendors face loss of certifications. Examples of violations include implementing systems in ways that are likely to restrict the: Access, exchange, or use of electronic health information when exporting complete information sets or transitioning between HIT systems; and Implementation of HIT in nonstandard ways that are likely to substantially increase the complexity or burden of accessing, exchanging, or using electronic health information

Table 5. Provisions related to the regulation of medical software and HIT

Source: 114-225 Public Law 114-255

Reactions and potential challenges to Cures provisions to regulate medical software and HIT

Advance the conversation on regulating medical

software. The Cures Act specifies which types of software the FDA will exclude from regulation as a medical device, but raises the question of how the FDA will regulate software that will be designated as a medical device. The FDA will continue to regulate digital and mobile health software that supports active patient monitoring or clinician-decision support tools that collect data from a patient, or on which physicians solely rely for decision making as a medical device.²⁶ The FDA has released some guidance on how Software as a Medical Device (SaMD) should be regulated,²⁷ although questions remain about how to classify the risk level for various types of software, and how to evaluate benefit/risk.

Shifting priorities may detract from some HIT

provisions. At this year's Healthcare Information and Management Systems Society (HIMSS) conference, some stakeholders expressed concern that competing priorities in the health care agenda may slow the implementation of portions of the Cures Act that aim to solve some of the nation's HIT challenges.²⁸

What considerations should be top-of-mind for life sciences companies?

Engage in the dialogue on medical software

regulation. Many innovators are designing digital health technologies in combination with drugs, biologics, or devices—adding complexity to the regulatory process. Life sciences companies developing these types of products should consider engaging in a dialogue with the FDA to develop a framework for the regulation of medical software not excluded by the law.

Deepen health system partnerships and

collaborations. To thrive in a market that demands demonstrable value, life sciences companies may be wise to embrace a new operating model based on end-to-end evidence management. Health care system fragmentation produces an incomplete picture of the patient as related to RWE and patient experience data. Linking various data sources together (e.g., claims + EHR + patient reported outcomes) could bring the patient picture into focus; however, the current data vendor landscape can make this difficult. Deloitte's 2017 RWE Benchmark Study showed that companies perceive the biggest challenge to accessing RWE to be gaining access to external data.

Modernizing the SaMD regulatory process

Deloitte's forthcoming paper, Modernizing the Regulatory Process: Bringing the FDA into the Digital Age, examines how the medical device world is changing, including considerations for regulating software, solutions for making the process more agile, and ways to avoid a one-size-fits-all approach for devices. In February 2017, Deloitte held a workshop where multiple stakeholders including medical device companies, startups, venture capitalists, researchers, regulators, patient advocacy groups, and technology companies assembled to explore and contribute to developing recommendations around the development of a new regulatory paradigm for SaMD. Outcomes included reaching consensus on some starting principles:

- The role of the regulator should include co-creation and acceleration of innovation; value is a key design principle to ensure regulators are bolstering the process
- Key parameters of information sharing need to be identified, including what kind of data will be shared and with whom, what incentives may encourage data

sharing, and how to maintain company confidentiality and data security

- Interoperability, communication, accessibility, and transparency between groups is critical as the device moves through the stages of the regulatory paradigm
- The inclusion of update/modification plans are critical for designing and maintaining a dynamic and adaptive process
- Defining how public safety and health are measured will provide greater transparency to enterprises and organizations going through the process
- Using a Transportation Security Administration (TSA) "pre-check" metaphor to allow for expedited processes for enterprises with cultures of organizational excellence, the group thought a "trusted flyers" program option should include tiers of "maturity" or gradation to categorize organizations

Companies may want to adopt new strategies and capabilities to support external partnerships and collaborations with health systems, patient advocacy groups, and other data aggregators to access this data. In addition, companies could consider developing the ability to integrate data sets, understand and apply the appropriate resources for analytics, and work through external partnerships to resolve tactical issues around data quality.²⁹

Establishing a pathway for regenerative medicine

Before the passage of the Cures Act, regenerative medicine products had two pathways to approval: select products could be made available at clinics without premarket review while all other products were treated like drugs and required a full biologics licensing application. That regulatory dynamic led to the availability of several products that were not FDA approved. The Cures Act updates the regulatory pathway for regenerative medicine products, bringing more of them under FDA oversight and creating flexibility for more complex products. The law seeks to regulate regenerative medicine products that may have previously been precluded from premarket review by classifying such products as moderate risk (unless deemed otherwise). And, for those products that would have required full biologic licensing, there is the option of an accelerated pathway. Specific provisions are outlined in Table 6.

Reactions and potential challenges to Cures provisions to establish a pathway for regenerative medicine

Ensure adequate patient safety protections in regenerative medicine product use. While additional regulatory clarity around regenerative medicines is generally seen as positive, some stakeholders think work remains in regulating this specific product class. The California Institute for Regenerative Medicine has expressed concern about how effective the FDA will be, given the resources required for regulating products at the clinic level.³⁰ Some consumer advocates are also concerned that products will be marketed without demonstrated evidence of clinical benefit.³¹ Some therapies, such as CAR-T, have started to demonstrate clinical benefit, but have also shown very serious side effects (cytokine release syndrome and tumor lysis syndromes). The long-term impacts for gene-therapy based treatments are also unknown. The dialogue on how to best regulate this class of products and manage between benefit/risk tradeoffs is likely to continue.

Goal	Provision	Implementation next steps
Establish approval pathway for regenerative medicine	Allows FDA to grant accelerated approval for regenerative therapeutic products and provides a rationale for accelerating approval while maintaining standards of evidence and regulatory authority	FDA to issue guidance on the review of regenerative therapies as classification of regenerative devices as higher risk (Class III) within one year
Define the scope of regenerative medicine	Establishes that devices used with a regenerative therapeutic product will be considered moderate risk devices, unless the Secretary of HHS determines that device or intended use requires higher risk classification Defines "regenerative medicine and advanced therapies"—includes cell therapy, gene therapy, gene-modified cell therapy, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products	No further guidance required

Table 6. Provisions related to regenerative medicine

What considerations should be top-of-mind for life sciences companies?

Engage in a dialogue with the FDA on how to advance regenerative medicine products. While the Cures Act specifies regulatory paths for regenerative medicine, it is unclear what evidence the FDA will require to support those specific pathways. The agency has one year to issue guidance on how it will classify and evaluate regenerative medicine devices. In the meantime, companies pursuing these technologies may be uncertain about how best to proceed, and what evidence the FDA will require under the accelerated pathway. These companies should consider proactively engaging the agency in a dialogue to determine how to advance regenerative medicine therapies.

21st Century Cures and the evolving R&D and regulatory landscape

Even as the life sciences industry waits for regulations and other guidance to implement the Cures Act, the administration is emphasizing fewer and less complex regulations in general, including the FDA approval process. Early in 2017, the administration released an Executive Order titled "Reducing Regulation and Controlling Regulatory Costs" which calls for executive departments or agencies to pull back at least two existing regulations for every new one they issue. The order requires that for every dollar of additional cost imposed on US society by regulations, there must be an equivalent reduction elsewhere. It is unclear how this executive order could potentially impact the implementation of the Cures Act.

In late February, the administration released an order directing each federal agency to set up a regulatory reform task force to review existing regulations and identify rules to repeal or modify—a move it said will boost the economy by removing burdensome and costly regulations for business. New approaches and advanced technologies may make it possible to pursue a regulatory reform agenda that does not sacrifice protections. For drug and device approvals, this could mean opportunities to apply technologies like data analytics and enable the industry and the FDA to make meaningful headway in streamlining the development and approval processes while maintaining public health protections.^{32,33}

The industry relies on a robust and continually adaptive regulatory and guidance process from the FDA—without it, they face a lack of clarity and uncertainty. Some life science stakeholders have noted that the FDA has done much to streamline the regulatory process in recent years, and that the industry depends on its review and approval process to help ensure safe, effective products move through the pipeline.³⁴ Yet while the FDA has worked to transform the development and approval process, progress in the discovery and testing stages of drug development will likely need to keep pace to enable innovative treatments and cures.

Critics of the Cures Act, however, argue that provisions to speed-up the development and approval of drugs and devices will lower FDA's regulatory bar for ensuring that safe and effective products go to market. Consumer advocacy groups such as Public Citizen and leading health care experts such as the former FDA Commissioner David Kessler are concerned that the Cures Act could lead to approving products that are less safe or effective than existing criteria permits.³⁵ However, it may be possible to achieve cost reductions without removing protections, if policymakers focus on smarter regulation. The 21st Century Cures Act offers opportunities to speed-up processes that cause delays (and, therefore, increase costs), by taking advantage of new technologies and data sources, and providing clarity and guidance to life sciences companies to assist with compliance efforts.



Looking ahead: The path to getting innovative therapies to patients

The discovery, development, approval, and delivery journey for life sciences companies has never been static or straightforward. The shift towards prioritizing new kinds of data, adopting a more patient-centered focus, and incorporating the value paradigm of patients, providers, and payers, will likely continue to shape the strategic choices life sciences companies make. The 21st Century Cures Act's focus on accelerating approvals in ways that are applicable beyond oncology, as well as expected clarity around combination products and medical software, may prompt some companies to rethink and change their portfolios and therapeutic area strategies. Companies may also step-up engagement with regulators, payers, and prescribing clinicians to help them refine strategies and decision making around their product development plans.

Our research and discussions with life sciences industry stakeholders corroborate the growing importance of meaningful partnerships and dialogues; the increasing integration of RWE, novel clinical approaches, and patient experience data in drug development and approval; and potentially improving clarity around medical software, POC diagnostics, and combination products—offerings that do not fit traditional categorizations or pathways. In many ways, the drug and device development and approval process of yesterday is over: life sciences companies can risk being out-of-date if they are not taking advantage of the newer breakthrough, priority, or accelerated pathways. While this paper has focused primarily on implications for life sciences companies (see Table 7), other health care stakeholders should consider how Cures-driven changes in drug and device development, approval, and delivery that Cures brings will impact them:

- Hospitals and health systems that participate in research will likely need to consider the interoperability expectations and requirements that the Cures Act will roll out, as well as implications around data transparency and evolving privacy and security protections. How prescribing clinicians define the value equation around different populations and medical conditions will likely continue to be important to life sciences companies as they prepare to go to market.
- Health plans should consider identifying effective strategies for communicating with life sciences companies when making formulary decisions. In addition, health plans interested in pursuing valuebased contracts should determine appropriate measures of value, strategies to integrate data with the contracting life sciences company, and ways to control non-drug factors that can influence outcomes. CMS, as the largest payer in the US health care system, also plays a major role in getting innovative therapies to patients on the delivery side. After the FDA approves drugs, devices, and diagnostics, companies must work to get their products covered and paid for, which typically starts with CMS. Some stakeholders have noted that getting additional clarity and guidance from CMS around coding processes and coverage will be important to this discussion.

• For federal agencies, there are many provisions in the Cures Act that call for coordination with each other and create processes and workgroups to strengthen collaborations with the private sector. Agencies will need to think through how to appropriately allocate resources to implement future reporting and guidance. For the FDA, the Cures Act calls for the agency to issue guidance in the next 12 to 24 months related to modernizing the approach to clinical trial design and data analysis, and incorporating tools to shorten the drug development process. The agency is also tasked with creating a framework in partnership with industry stakeholders around RWE, and issuing guidance on the review of regenerative therapies as classification of regenerative devices as higher risk (Class III). In addition, the Act requires the FDA to issue guidance on the breakthrough pathway for medical devices, and final guidance by the end of 2020 on the process for managing drug-device combination product pre-submission interactions.

Few stakeholders would likely argue that the time it takes to develop a new therapy and get it to market is quick enough for patients and families waiting for innovative treatments that cure disease or turn lifethreatening diseases into manageable conditions. Life sciences companies and the FDA are working to overcome barriers and evolve their programs through integrating recent advances in technology and analytics. It is critical that key stakeholders—life sciences companies, providers, health plans, the FDA, and of course, patients—continue to collaborate towards delivering better care and innovative therapies.

It is critical that key stakeholders continue to collaborate towards delivering better care and innovative therapies.



Table 7. Implications for biopharma and medical device companies

Goal of Cures	Implications for biopharma	Implications for medtech
Faster drug approvals		
Enable faster drug approvals by modernizing the approach to clinical trials—incorporating new sources of evidence and new tools to shorten the drug development process	Engage in proactive conversations with the FDA early on in development to understand which innovative tools or sources of evidence might apply to their program and expedite development Expand capabilities required to access, collect, and analyze RWD Leverage incentives to develop drugs for specific populations, including pediatric rare disease and antimicrobials Continuing to work with the FDA, patient advocacy groups, and provider groups to delineate pathways for patient and caregiver involvement	No direct impacts from Cures. Medtech companies should, however, continue to work with the FDA to understand how to incorporate patient-centered approaches and RWE into product development plans
Health care economic information communications		
Provide clarity on certain HCEI communications between biopharma and health care stakeholders	Expand the dialogue on economic evidence with health care stakeholders and explore value-based contracting	No direct impacts from Cures. Medtech companies should, however, continue to work with stakeholders to determine how to best structure value-based contracts within current regulatory constraints
	Regenerative medicine	
Establish approval pathway for regenerative medicine	Engage in a dialogue with the FDA on how to advance regenerative medicine products while guidance on approval pathways are being developed	

Table 7. Implications for biopharma and medical device companies

Goal of Cures	Implications for biopharma	Implications for medtech	
Medical device innovation			
Clarify and improve existing approval process, create regulatory flexibility for devices that treat life- threatening conditions or impact small populations	No direct impacts from Cures	Encourage greater investment in medical technology innovation and consider partnerships with companies that are developing life-changing innovations Generate data to support regulatory approval but also market access—consider investing early in evidence that supports coverage and reimbursement as well as regulatory approval Invest in RWE capabilities to incorporate new sources of data into the device development and approval process	
Improve access to POC diagnostics	Biopharma companies should consider how POC diagnostics could be used to increase patient engagement and drive utilization of products, especially for chronic disease	Take advantage of opportunities to advance POC diagnostics that can expedite diagnosis in lower cost care-delivery settings and get treatments to patients faster	
	Combination products		
Improve regulation of combination products and increase opportunity for sponsor engagement in dispute resolution	Take advantage of the opportunity to advance combination products through increased dialogue with FDA, leveraging evidence that supports a product's primary mode of action		
Regulation of medical software			
Clarify regulation of medical software	Engage in ongoing dialogue with the FDA to develop the framework for the regulation of software that will be regulated as a medical device, particularly devices that might be used to drive greater patient engagement		
Advance interoperability initiatives	Deepen partnerships and collaborations with health systems to access RWE		

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Acknowledgements

We also wish to thank Greg Reh, Mary Cummins, Ralph Marcello, Neil Lesser, Dan Ressler, Brett Davis, Glenn Snyder, Jennifer Malatesta, Amit Agarwal, Jeff Morgan, Chris Cormack, Jessica Nadler, Andrew Ryscavage, Mohinder Sutrave, Lauren Wallace, and the many others who contributed their ideas and insights to this project.

To download a copy of this report, please visit https://www2.deloitte.com/us/21st-century-cures.

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Endnotes

- ¹ FDA, Targeted Drug Development: Why are many diseases lagging behind? 2015
- ² Science News Staff, "NIH, DOE Office of Science face deep cuts in Trump's first budget," March 16, 2017
- ³ FDA, White Paper: FDA and accelerating the development of the new pharmaceutical therapies, 2015
- ⁴ Derrick Gingery and Ferdous Al-Faruque, "A burning FDA hiring freeze question: What about user fee-supported staff?" Pink Sheet, January 24, 2017
- ⁵ Leah Isakov, Andrew W. Lo, Vahid Montazehodjat, "Is the FDA too conservative or too aggressive? A Bayesian decision analysis of clinical trial design," August 11, 2015
- ⁶ Michael Hiltzik, Column: "The 21st Century Cures Act," LA Times, December 5, 2016
- ⁷ Zachary Brennan, "Studies raise new concerns over FDA expedited approval designations, supplemental indications," Regulatory Affairs Professional Society, September 24, 2015
- ⁸ Corinna Sorenson et al, "Advancing value assessment in the United States: A multistakeholder perspective," Elsevier, 2017
- ⁹ Deloitte Center for Health Solutions, "Getting real with real world evidence: 2017 RWE benchmark study," 2017
- ¹⁰ Deirdre Coleman, "Real world revolution," Eye for Pharma, January 19, 2017
- ¹¹ The Pew Charitable Trusts, Limited Population Approval Pathway: Background, 2014
- ¹² Public Law 105-115
- ¹³ FDA, Drug and Device Manufacturer Communications with Payers, Formulary Committees, and Similar Entities Questions and Answers, Guidance for Industry and Review Staff, January 2017
- ¹⁴ Gary Twachtman, "Medication adherence: a positive story you are not hearing," In Vivo, November 20, 2013.
- ¹⁵ Deborah Mazer and Gregory Curfman, 21st Century Cures act lowers confidence in FDA approved drugs and devices, Health Affairs blog, February 14, 2017
- ¹⁶ Innovation Counsellors LLC, "A future at risk: Economic performance, entrepreneurship, and venture capital in the US medical technology sector," October 2016
- ¹⁷ Innovation Counsellors LLC, "A future at risk: Economic performance, entrepreneurship, and venture capital in the US medical technology sector," October 2016
- ¹⁸ GlobalData, "Point of Care Diagnostics Market Will Rise to Almost \$3 Billion by 2021," Medical Design Technology Magazine, March 21, 2016
- ¹⁹ FDA, "Use of real world evidence to support regulatory decision-making for medical devices: Draft guidance for industry and FDA staff," July 27, 2016
- ²⁰ FDA, National Evaluation System for health Technology, January 31, 3017
- ²¹ FDA, FY 2015: Performance report to Congress for the Office of Combination Products, 2016
- ²² Robert Church, Heidi Forster Gertner, Yarmela Pavlovic, Randy Prebula, "A 'cure' for combination products: 21st Century Cures Act mandates greater transparency of combination product designations," January 25, 2017
- ²³ Ibid
- ²⁴ Ibid
- ²⁵ Global Market Insights, "Digital health market size by technology," November 2016
- ²⁶ Akin Gump Strauss Hauer & Feld LLP, "The 21st Century Cures medical software provisions: additional clarity for digital health, but also more questions," January 3, 2017
- $^{\rm 27}\,$ FDA, "Software as a medical device," August 5, 2016
- ²⁸ Rachel Z. Arndt and Joseph Conn, "Questions and uncertainty cloud normally sunny HIMSS," February 25, 2017
- ²⁹ Terry Hisey, Brett J. Davis, "Pharma's big push for value," Pharmaceutical Executive, May 5, 2016
- ³⁰ Kelly Sevick, "Under 21st Century Cures legislation, stem cell advocates expect regulatory shortcuts," December 12, 2016
- ³¹ Andrew Joseph, "After criticism from scientists, Congress eases its pursuit of faster stem cell therapies," November 30, 2016
- ³² Deloitte Center for Government Insights, "How to implement President Trump's 'One in, Two Out' Regulation Initiative," 2017
- ³³ John Carroll, EndPoints News, EndPoints, February 28, 2017
- ³⁴ Deborah Mazer and Gregory Curfman, "21st Century Cures act lowers confidence in FDA approved drugs and devices," Health Affairs blog, February 14, 2017
- ³⁵ Laura McGinley, "Trump calls the FDA slow and burdensome, but its faster than ever," Washington Post, March 2, 2017



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