ReedSmith

The business of relationships.

Life Sciences Health Industry Group

Client Briefing

21st Century Cures Act: Key Provisions of Interest to Drug/Device Clients

Written by: Celeste A. Letourneau, Lisa M. Baird, Kevin M. Madagan, Nicole J. Aiken-Shaban, Matthew D. Jacobson, Vicki J. Morris and Yetunde D. Oni

December 2016

Contents

On December 13, 2016, President Obama signed into law the 21st Century Cures Act (Cures Act). It is hoped that provisions in the new bill, and the $6.3 billion it provides for medical research over the next decade, will spur innovation and new progress in medical treatments for the patients who need them.

This Client Briefing summarizes and analyzes the provisions in the Cures Act related to drug, device, and biologic development and approval. A companion Client Briefing focuses on provisions of the Cures Act that have not received as much attention but are equally significant, those affecting the Medicare and Medicaid programs. In addition, our recent blog post addresses the Cures Act provisions regarding mental health and substance abuse, and funding for combating opioid abuse.

SUBTITLE A—PATIENT-FOCUSED DRUG DEVELOPMENT

Patient Experience Data (Section 3001)

The Cures Act requires FDA to disclose patient experience data and related information reviewed as part of an approved new drug application (NDA) or biologics license application (BLA). Such "real-world evidence" may include data collected by patients, caregivers, advocacy groups, or manufacturers about patients' experiences with a disease or condition, and treatment preferences, information on patient-focused drug development tools, or other information the FDA determines to be relevant.

This provision and the related provisions below take effect 180 days after enactment.

Patient-focused Drug Development Guidance (Section 3002)

The Cures Act requires FDA to issue draft and final guidance documents within the next five years about the collection and use of real-world evidence. In particular, these guidance documents will address:

- Methodologies for the collection of patient experience data for use in regulatory decision-making
- Methodologies to collect information about patient preferences regarding burden of disease, burden of treatment, and the benefits and risks in the management of the patient's disease
- Developing methodologies to "measure impacts to patients that will help facilitate collection of patient experience data in clinical trials"
- Methodologies for collecting and analyzing clinical outcome assessments for use in regulatory decision-making
- How proposed draft guidances can be proposed to the Agency (in other words, a guidance on proposing guidances)
- The format and content required for submitting patient experience data
- How the Agency will respond to patient experience data, including patient experience data submitted separate from a regulatory application
- How the Agency will use relevant patient experience data, including with respect to risk-benefit assessments

The FDA already has started this work. In July 2016, the Agency issued a draft guidance, *Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices*. And on December 8, 2016, FDA officials published "Real World Evidence – What Is It and What Can It Tell Us?" in the *New England Journal of Medicine*.

Report on patient experience drug development (Section 3004)

The Cures Act directs the FDA to publish reports on FDA.gov roughly every five years (by June 1, 2021, 2026 and 2031) that assess the use of patient experience data in regulatory decision-making.

SUBTITLE B—ADVANCING NEW DRUG THERAPIES

Biomarkers, Clinical Outcome Assessments, and New Drug Development Tools (Section 3011)

The Cures Act underscores the importance of drug development tools like biomarkers and other methods or materials that may help drug development and regulatory review, and prevent failure rates in drug development. A drug development tool (DDT) is defined as: "a biomarker; a clinical outcome assessment; and any other method, material, or measure that the Secretary determines aids drug development and regulatory review." The Cures Act directs FDA to establish a process for the qualification of DDTs for the proposed circumstances under which the tools will be used in drug development and

regulatory review - i.e., for its proposed context of use. The Cures Act describes the process for qualification submissions for review, including refusal or acceptance on scientific merit, and the use of external experts for review. It also allows for prioritization of the review of a full qualification package, based on severity and rarity of the condition targeted by the DDT, and the proposed context of use within the public health priority framework. Once qualified, a DDT may be used to either support or obtain approval or licensure of a drug or biological, and it may also be used to support the investigational use of a drug or biological product. After qualification and based on new information, FDA may rescind or modify the qualification. FDA is required to have meetings with stakeholders to address its revised decision before the effective change of revision or modification.

FDA has already issued a procedural guidance on this topic in its *Guidance for Industry Qualification Process for Drug Development Tools (January, 2014),* and runs a DDT qualification program at the Centers of Drug Evaluation and Research (CDER). The Cures Act requires FDA to provide further guidance (draft) on the implementation of the qualification process within three years and finalization within six months of the close of comments for the draft guidance. FDA's new DDT qualification guidance must, among other things, provide a conceptual framework describing the appropriate standards and scientific approaches to support the development of biomarkers with previously established taxonomy classification. Note that the taxonomy classification of the biomarkers will be established through a collaborative process with biomedical research consortia and other interested parties. Finally, FDA's DDT guidance will establish the requirements for the qualification process, and timeframes for the review of the qualification submission, as well as the process by which FDA may consult external experts.

The Cures Act also requires FDA to update its website on at least a biannual basis with:

- Information relating to each DDT qualification submission (including review process stage, whether external scientific experts were used during the review process, and any data or evidence submitted by the requestor)
- Formal written determinations in response to each submission
- Rescission or modifications determinations for each submission
- Conclusions or recommendations for determinations to qualify DDTs
- A comprehensive list of all DDTs qualified with the surrogate endpoints that served as the basis of approval or licensure

Although FDA already recognizes biomarkers as evidenced by the prior procedural guidance document and DDT program at CDER, the new framework mandated by the Cures Act for qualifying biomarkers is a welcome development in the industry because the standardized framework will help accelerate the pace of clinical trials. There may, however, be a need for additional funding to ensure that biomarkers are linked to patient outcomes. The funding currently allowed for in the Cures Act is modest and subject to annual appropriations.

Unmet Medical Need, Orphan Drugs, and Priority Review Vouchers (Section 3012 – 3015)

The Cures Act clarifies FDA's authority to establish processes for development, review and approval of genetically targeted drugs and variant protein targeted drugs to address unmet medical needs in patient subgroups, including mutation of genes in rare diseases, or serious or life-threatening conditions. In order to expedite development of this category of drugs, FDA may allow the sponsor of an application for a genetically targeted drug or variant protein targeted drug to rely on data and information previously developed by the same sponsor (or data for which the sponsor has contractual right of reference). The sponsor may also rely on data and information submitted for previously approved applications. The sponsor may rely on such previously submitted data or information if the new drug being developed incorporates or uses the same or similar genetically targeted technology as that of the previously approved drug application. Although this provision of the Cures Act accelerates the process of drug development process for these drugs, it does not alter the existing approval standards for the drugs.

Further, the Cures Act reauthorizes the pediatric rare disease priority review voucher program (the "Program") to encourage treatments of rare pediatric diseases. The Program, which is set to expire December 31, 2016, is designed to allow recipients of the vouchers to receive expedited review of new drug products developed for rare diseases or conditions. Despite concerns and criticisms from the public on the effectiveness and impact of the Program, the Cures Act extends and reauthorizes the Program for another four years - until September 30, 2020. However, priority review voucher awards may still be awarded after September 30, 2020, if the drug was designated as a drug for a rare pediatric disease before September 30, 2020, and if it is approved under section 505 of the Food, Drug, and Cosmetic Act

("FDCA") or section 351 of the Public Health Services Act ("PHSA") before September 30, 2022.

The Cures Act hopes to address these issues of effectiveness and impact of the Program by requiring the comptroller general to study the impact of the Program on the development of drugs relating to:

- Neglected tropical diseases under section 524 of the FDCA
- Rare pediatric diseases under section 529 of the FDCA
- Medical countermeasure (i.e., FDA-regulated products that may be used in the event of a potential public health emergency stemming from a terrorist, a naturally occurring emerging disease, or a natural disaster) under section 565A of the FDCA

The comptroller general is required to submit the reports on these studies to Congress before January 31, 2020. Among other things, the reports will contain analyses on whether the Program addressed the unmet needs for the targeted diseases.

Importantly, the Cures Act also expands the scope of grants and contracts available to drug manufacturers for orphan drug development. Currently, section 5 of the Orphan Drug Act allows the Secretary to make grants and enter into contracts to assist in defraying the costs of "qualified testing" expenses incurred in connection with a rare disease or condition. The Cures Act expands the meaning of the term "qualified testing" to include not only human and preclinical testing, but also any observational studies conducted to assist in understanding the natural history of the rare disease or condition. The grant may also cover studies designed to develop a drug development tool related to the rare disease or condition, or studies designed to understand the full spectrum of the disease manifestations, including those describing genotypic and phenotypic variability in subpopulations affected by a rare disease. This is important because drug developers can now get funding for early stages of drug development when they previously could not.

Continuous Drug Manufacturing Grants (Section 3016)

Continuous manufacturing allows for faster production and more reliable products through an uninterrupted process—as opposed to the traditional batch-by-batch approach that many drug manufacturers have been using for decades.

Last year, the FDA encouraged drug manufacturers to consider the transition from batch to continuous manufacturing. The Cures Act advances this initiative by allowing the Secretary of Health and Human Services ("HHS") to award grants to academia and nonprofit organizations to study continuous manufacturing and biological products. While this focus on continuous manufacturing may divert resources from other technological drug manufacturing advancements, such as additive manufacturing (3D printing), these grants may spur broader innovation as they reflect movement away from traditional manufacturing techniques. Moreover, the Cures Act's call for grants to study biologic products would seemingly support grants related to bioprinting.

SUBTITLE C—MODERN TRIAL DESIGN AND EVIDENCE DEVELOPMENT

Novel and Adaptive Clinical Trial Designs (Section 3021)

The Cures Act requires FDA to help sponsors use complex adaptive and novel trial designs in their proposed protocols and applications for drugs. Expanding on FDA's 2010 draft guidance on this topic, the Cures Act requires FDA to issue guidance that will describe how complex adaptive and novel trial designs may help satisfy the substantial evidence standard required in new drug applications, and how sponsors may obtain feedback on technical issues relating to modeling and simulations.

Before issuing the guidance, FDA must consult with various stakeholders at a public meeting to be held by June 13, 2018. FDA must publish a draft guidance within 18 months of this meeting, and a final guidance within one year of the close of the comments period of the draft guidance.

Real World Evidence (Section 3022)

The Cures Act requires FDA to evaluate and advise the industry about the potential uses of real world evidence – defined as "data regarding the usage, or potential benefits or risks, of a drug derived from sources other than randomized clinical trials" – to support the approval of a new indication for an approved drug, and to support or satisfy post-approval study requirements.

This is a significant development. Supporters of incorporating "real world" evidence into product evaluations believe the Cures Act will make the drug approval process less costly and time consuming for sponsors, while also expediting patients' access to potentially life-saving therapies. Critics have voiced concerns that the use of real-world evidence may adversely affect patient safety. Regardless of your position, the call for real world evidence will undoubtedly make it easier to focus drug development efforts on subpopulations with higher risk-benefit ratios. Further, the use of real world

evidence will reduce the burden of data collection during clinical trials, because relevant data should be readily available (or increasingly readily available) through electronic health records in provider settings and pharmacies, and other laboratory information systems.

To get things underway, the Cures Act requires FDA to establish, no later than December 13, 2018, a draft framework that will, among other things, describe the sources of real world evidence, gaps in data collection activities, standards and methodologies for collection of the real world evidence, and priority areas.

FDA then has until December 13, 2021, to issue a draft guidance describing the circumstances under which sponsors and FDA may collect, analyze, and rely on real world evidence.

The Common Rule vs. FDA Human Subject Regulations (Section 3023)

The Cures Act attempts to simplify and streamline the process by which researchers comply with applicable regulations for the protection of human subjects in research. It does this by directing the Secretary of HHS to harmonize the differences between the HHS Human Subject Regulations (otherwise known as the "Common Rule") and the FDA Human Subject Regulations. The Secretary must ensure that any human subject research that is subject to the HHS Regulations and to the FDA Human Subject Regulations may:

- Use joint or shared review; or
- Rely on the review of an independent institutional review board or an institutional review board of an entity other than the sponsor of the research

This harmonization effort must be completed by December 13, 2019, and a progress report submitted to Congress a year before this deadline (i.e., by December 13, 2018).

Stakeholders involved in human subject research should pay close attention to this harmonization process as it may broaden the scope of the data that can be used for research – especially in situations where a category of data was explicitly exempted under the common rule, but not necessarily exempted under FDA's human subject rules.

Informed Consent Waivers (Section 3024)

The Cures Act grants FDA the flexibility to alter the informed consent clinical trials requirement using the minimal risk provision, similar to the use of the provision under Common Rule. The Cures Act specifies that informed consent may be waived or altered for a proposed clinical testing involving an investigational drug or device, if the proposed clinical testing poses no more than minimal risk to the human subjects and includes appropriate safeguards to protect the rights, safety, and welfare of either the human subject or the investigator.

The Cures Act does not define minimal risk but, in 45 C.F.R. § 46.102, HHS defines "minimal risk" as "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." Minimal risk may be a difficult standard to establish in reality. If FDA adopts HHS' definition, it may expand the scope of clinical trials that may be conducted because, other things being equal, informed consent will not be required if the study does not pose a risk greater than that encountered in daily life. This should streamline recruitment, and hopefully expand the participant pool, for certain clinical trials.

SUBTITLE D—PATIENT ACCESS TO THERAPIES AND INFORMATION

Summary Review (Qualified Data Summaries) (Section 3031)

In an effort to streamline data review of supplemental applications, the Cures Act allows FDA to rely on "qualified data summaries" – defined as summaries of clinical data demonstrating safety and effectiveness – to support approval of supplemental NDA or BLA applications for qualified indications (i.e., indications considered by FDA to be appropriate for summary level review). All data used to develop the qualified data summary must still be submitted to FDA as part of the supplemental application.

Permitting FDA to rely upon qualified data summaries should promote evidence development tools and ease the burden on both sponsors and FDA during the supplemental application process.

The Cures Act also requires FDA to post initially and update annually information on:

- The number of applications reviewed using qualified data summaries
- The average time for review of such supplement applications using qualified data summaries
- The average time for review of supplemental applications not using qualified data summaries
- The average time of review of a supplemental application where FDA used both the qualified data summary and the full data set in its review

This information will likely be informative to potential (and actual) applicants, and will set expectations with average application processing timelines.

Expanded Access Program Transparency (Section 3032)

In a move to increase transparency related to expanded access programs, the Cures Act amends the FDCA to require a manufacturer or distributor of investigational drugs to make publicly available (i.e., on the Internet) its policy for requests for compassionate use of its products through expanded access programs. Compassionate use, also referred to as expanded access, is the use of an investigational medical product (i.e., one that has not been approved by FDA) outside of a clinical trial.

The manufacturer or distributor policy must contain:

- Contact information for expanded access requests
- A description of the procedures for making requests, including processing time
- Criteria used to evaluate compassionate use requests
- A hyperlink to the expanded access program listing on a public data base, such as www.clinicaltrials.gov

FDA does not view posting of any such policy as a guaranty of access to investigational drugs under the applicable policy.

The new requirement applies to investigational drugs, beginning February 11, 2017, or thereafter, at the first initiation of a Phase II or Phase III study of such investigational drug.

Drug manufacturers should develop and/or review their compassionate use policy and carefully consider the criteria for review to ensure it meets these new requirements of this section.

Regenerative Medicine (Section 3033 – 3036)

The Cures Act requires FDA to issue a draft guidance by December 13, 2017, to address, among other things, how the Agency will regulate combination devices and regenerative devices, such as cell or tissue products. The draft guidance must be finalized within a year after the comments period closes. Currently, FDA has been relatively silent on how it will handle bioprinting—the 3D printing of human tissues by depositing cells layer-by-layer to grow organs. While the FDA issued a draft guidance in May 2016 on technical considerations for 3D printing of medical devices, the guidance did not include bioprinting or combination products (part bioprinting or 3D printed products).

The Cures Act provides that the FDA notify Congress yearly of the applications received for these regenerative devices/therapies and the percentage approved/cleared.

Two years after the enactment of the Act, NIST, in conjunction with manufacturers, clinicians, and industry organizations, among others, should develop standards for regenerative medicine and regenerative advanced therapies, including standards related to the manufacturing process. The Act defines "regenerative medicine and advance therapies" to include human cell and tissue products, among other things. As with the guidance that the FDA is required to create pursuant to the Act, these standards will help bioprinting manufacturers understand what requirements they will need to abide by in 3D printing products using cells, including 3D printing organs and body parts. While the use of bioprinted products may still be a ways off, developing standards and regulations now will help the technology advance and become more of a reality.

Health Care Economic Information (Section 3037)

Since its enactment in 1997, section 114 of the Food and Drug Administration Modernization Act (FDAMA) created a safety harbor that permitted drug manufacturers to respond to requests for, and provide, health care economic information that was not in the product labeling to "formulary committees and similar entities." For the safe harbor to apply, three criteria had to be met: (i) the information had to be provided to a formulary committee, or other similar entity, in the course of selecting drugs for managed care or other similar organizations; (ii) the information had to be directly related to an approved indication; and (iii) the information had to be based on competent and reliable scientific evidence. Despite a lack of clear guidance from FDA, it is generally understood that promotion of health care economic information resulting in an implied or direct clinical claim inconsistent with the product labeling could result in the labeling being viewed by the Agency as false and misleading, and thus misbranding the drug. Section 3037 of the Cures Act modifies all three criteria for the safe harbor. It expands the audience to include payors in addition to formulary committees or other similar titles, but it adds the requirement that all of these entities must have the "knowledge and expertise in the area of health care economic analysis," and must be "carrying out [ ] responsibilities for the selection of drugs for coverage or reimbursement." It also loosens the relationship of the information to the approved indication from "directly related" to "relates" to an approved indication. While it retains the lesser evidentiary standard of competent and reliable scientific evidence, the FDAMA 114 safe harbor will now require a "conspicuous and prominent statement

describing any material differences" between the health care economic information and the product's approved labeling. Last, the Cures Act expands the scope of health care economic information that is eligible for the safe harbor from the prior definition of an analysis to the more expansive "clinical data, inputs, clinical or other assumptions, methods, results, and other components" of the analysis. The definition also specifies that health economic information could be based on the economic consequences of the separate or aggregated clinical consequences of the represented health outcomes. Finally, the Cures Act's definition of health economic information describes the outer bounds of the extent to which health economic information may be inconsistent with a drug's FDA-approved labeling, that is, any analysis that only relates to an unapproved indication is excluded.

These revisions will allow manufacturers to more easily address requests for health care economic information that reflects actual clinical practice, rather than those situations studied in the clinical trials used to bring the product to market.

While the above-described changes to the safe harbor help to modernize manufacturers' ability to share health care economics information, remaining ambiguities in the statute (e.g., a lack of guidance on what constitutes a "material difference") may influence manufacturers to avoid relying on the revised safe harbor until FDA's interpretation of these provisions becomes clear.

Combination Products (Section 3038)

The Cures Act takes significant steps to streamline the approval process for combination products, which currently present particular regulatory approval problems.

Combination products include some of the most innovative and cutting-edge health care products, and combine, in some conjugation or other, drugs, devices and biologics, whether entirely or partially 3D-printed. Currently, a product that combines new treatment with a new device must pass through two processes in order to obtain FDA approval.

The Cures Act requires FDA to establish a primary Agency center to regulate combination products. As currently regulated, these products will be subject to premarket review under a single application based on the "primary mode of action" of the combination product. As an example, a combination product with a primary mode of action of a device will be reviewed by the Center for Devices and Radiological Health (CDRH). Importantly, manufacturers now have the ability to challenge FDA's determination of the primary mode of action. Within four years, FDA will issue a final guidance describing the process of managing interactions with manufacturers developing combination products, best practices for Agency feedback on those products, and information on meetings between manufacturers and FDA.

Importantly, the Cures Act requires FDA to meet with sponsors early in the development process to determine how best to review a combination product, which will set expectations for both parties. This additional regulatory clarity hopefully will encourage innovation of combination products, and will streamline the approval process.

SUBTITLE F—MEDICAL DEVICE INNOVATIONS

The Cures Act is intended to hasten and improve the process for approving innovative medical devices and to address other device innovation-related hurtles, including institutional review board (IRB) flexibility, clinical laboratory waivers, and clarifications to medical software regulation.

"Breakthrough" Medical Device Pathway (Section 3051)

Building on existing priority review device pathways, the Cures Act promotes and provides efficient and flexible approaches to expedite the development of, and prioritize the FDA's review of, devices that represent breakthrough technologies. To do so, the Cures Act requires FDA to establish a program to expedite the development of, and provide for the priority review for, devices that:

- Provide for more effective treatment or diagnosis of life-threatening or irreversible debilitating human disease or conditions; *and*
- Represent breakthrough technologies for which no approved or cleared alternatives exist that offer significant advantages over existing approved or cleared alternatives; *or*
- The availability of which is in the best interest of the patients

To obtain designation as a breakthrough device, the device sponsor may request that designation any time prior to the submission of an application for premarket approval under 515(c), a premarket notification under section 510(k), or a petition under section 513(f)(2) (de novo). FDA then has 60 days to determine whether the device meets the above-mentioned criteria of a breakthrough device and, if so, designate the device for expedited development and priority review.

By December 13, 2017, FDA is required to provide further guidance regarding the process by which a person may seek a designation as a breakthrough

device, a template for requests for breakthrough device designation, and information about the criteria that will be used in evaluating a request for designation and in assigning and training a team of staff to review devices designated for expedited development and priority review.

Humanitarian Device Exemptions (Section 3052)

For device manufacturers and sponsors seeking approval under the humanitarian device exemption (HDE) (21 U.S.C. 360j), the Cures Act expands a key limitation of the exemption to devices that treat diseases and conditions that affect up to 8,000 individuals in the United States. The new limit doubles the former cap of 4,000 individuals, thereby expanding the opportunity to attain approval under this exemption.

Device manufacturers and sponsors should also be on the lookout for FDA guidance that defines the criteria establishing "probable benefit" as that term is used in FDCA section 520(m)(2)(c). FDA is now required to issue guidance on this narrow topic no later than June 13, 2018.

National and International Recognized Standards (Section 3053)

The Cures Act establishes a streamlined process at FDA for the submission, review, and recognition of standards established by a nationally or internationally recognized standard organization for purposes of medical device review. Specifically, it forces FDA to allow anyone to submit a request for recognition of all or part of an appropriate standard established by a nationally or internationally recognized standard organization. Upon receipt, FDA will have 60 days to determine whether to accept and allow the standard to be used for purposes of meeting a premarket submission requirement or other applicable requirement under the FDCA. FDA's publicly available determination must explain the scientific, technical, regulatory, or other rationale for the Agency's decision.

Exempt Medical Devices (Section 3054)

The FDA must, by April 2017 (and then at least once every five years thereafter), identify and publish a list of all Class I device types that it considers exempt from the FDCA's premarket notification requirements. (This FDA publication will not include a notice and comment period.)

On or before March 2017, FDA must publish a proposed list of all types of Class II devices that it considers exempt. This will be followed by a 60-day notice and comment period. The Cures Act then requires FDA to publish a final list by July 17, 2017.

Device Classification Panels (Section 3055)

The Cures Act improves FDA's medical device classification panel review process by allowing a sponsor representative to address a panel (either alone or in collaboration with other sponsor representatives) to correct misstatements of fact and provide clarifying information. Notably, however, this sponsor right to address a panel is subject to the discretion of the panel chairperson.

The Cures Act further improves the panel review process by requiring device-specific panels to contain at least two experts on the applicable disease or condition, and at least one expert on the device technology.

Institutional Review Boards (Section 3056)

The Cures Act aligns FDA's approach to the role of IRBs in device trials to its approach taken for drug trials by eliminating the need for a sponsor of a medical device clinical trial to use a local IRB.

Allowing the use of centralized IRB models may improve the efficiency of a sponsor's IRB review process, and reduce expenses and duplication of effort in the conduct of multicenter device clinical trials. For sponsors new to the use of centralized IRB review, FDA's current *Guidance for Industry, Using a Centralized IRB Review Process in Multicenter Clinical Trials* (March 2006), provides recommendations on the role and structure of a centralized IRB.

CLIA Waivers (Section 3057)

Sponsors may submit an application for a Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver if they think the FDA has mistakenly categorized their device (e.g., as moderately complex). Currently, to qualify for a CLIA Waiver, FDA recommends that sponsors demonstrate that their device is accurate by running prospective clinical studies conducted at the intended use sites.

The Cures Act requires FDA to revise its existing *Recommendations for CLIA Waiver Applications for Manufacturers of In Vitro Diagnostic Devices* (Jan. 2008), to replace the current accuracy requirement with a demonstration of accuracy through comparable performance between waived and moderate-complexity laboratory users. Notably, this revision will make it easier to show that certain devices are "accurate" and can be exempted from routine inspections and other more onerous requirements under CLIA. Ultimately, the easier path to showing the "accuracy" of these devices will expand patient access to point-of-care diagnostics.

FDA will issue draft guidance on these proposed revisions by December 13, 2017, and, no later than

one year after the comment period closes, FDA will finalize its guidance on these revisions.

Reusable Medical Devices (Section 3059)

The Cures Act requires FDA to identify (and by April 19, 2017, publish a list of) reusable device types for which premarket notices "are required" to include validated instructions for use and validation data regarding cleaning, disinfection, and sterilization. The Cures Act allows FDA to revise this list as the Agency "deems appropriate" with a notice in the *Federal Register*.

Notably, this will not change current FDA practice. It merely codifies what FDA started doing in March 2015, when the Agency issued a final guidance for reprocessed medical devices – *see* Final Guidance for Industry and FDA Staff: Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling (March 2015). Appendix E of the 2015 final guidance identifies and lists a subset of medical devices that FDA believes pose a "greater likelihood of microbial transmission and represent a high risk of infection (subclinical or clinical) if they are not adequately reprocessed." According to the guidance, all 510(k) submissions for the device types listed in Appendix E should include protocols and complete test reports of the validation of the reprocessing instructions so that FDA has the information it needs to evaluate substantial equivalence.

Medical Device Modifications – Guidance (Section 3059)

Hidden in section 3059 of the Cures Act is a requirement that FDA issue a final guidance regarding when a premarket notification is required to be submitted for a modification or change to a legally marketed device. The Cures Act requires FDA to issue this final guidance "not later than 1 year after the date on which the comment period closes for the draft guidance" on this subject.

Medical Device Software (Section 3060)

The Cures Act codifies current FDA enforcement discretion policies by identifying five specific categories of medical software that, given certain conditions, will not be regulated as a medical device based on their low level of risk to patients.

- *Administrative Support Software.* Medical software intended for "administrative support of a health care facility."
- *General Wellness/Lifestyle Software*: Medical software intended for "maintaining or encouraging a healthy lifestyle" that is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition.
- *Electronic Health Records:* Medical software intended to serve as electronic patient records, including patient-provided information, to the extent that such records are intended to transfer, store, convert formats, or display the equivalent of a paper medical chart. To qualify for this exception, the records must have been created, stored, transferred, or reviewed by health care professionals and be a certified Health Information Technology – meaning the software has been successfully tested and certified by the Office of the National Coordinator for Health Information Technology (ONC) Health IT Certification Program.
- *Medical Device Data Systems (MDDS):* Medical software intended for transferring, storing, converting formats, or displaying clinical laboratory tests or other device data and results. Notably, under this exemption, the MDDS may communicate "general information about such findings, and general background information about such laboratory test or other device."
- *Clinical Decision Support (CDS) Software:* Medical devices software designed to analyze clinical and nonclinical data to help support or guide clinical diagnosis and treatment decisions. This exemption does not apply to CDS software that uses medical imaging or signals obtained from *in vitro* diagnostic (IVD) devices. FDA will need to issue guidance to clarify the boundaries of this CDS exemption.

These exemptions do not apply to medical device software that FDA, after a public notice and comment period, finds to be one that is reasonably likely to have serious adverse health consequences.

SUBTITLE G—IMPROVING SCIENTIFIC EXPERTISE AND OUTREACH AT FDA

Adverse Event Reporting System (Section 3075)

The Cures Act changes the requirement for bi-weekly screening of the Adverse Event Reporting System database by FDA to the more general term "screenings."

It also requires FDA to post on its Internet website guidelines that detail best practices for drug safety surveillance using the Adverse Event Reporting System, as well as criteria for public posting of adverse event signals.

The Cures Act also revises the FDCA Risk Evaluation and Mitigation Strategy (REMS) section to reduce the frequency at which FDA, through the Drug Safety and Risk Management Advisory Committee (or successor committee), is required to seek input from health care providers on how elements for safe use of a drug may be standardized in section 505-1(f)(5) of the FDCA.

FDA now only needs to get periodic input from these health care providers, as opposed to the previous requirement for annual input.

Authors

Celeste A. Letourneau
Partner, Reed Smith LLP
Washington, D.C.
+1 202 414 9260
cletourneau@reedsmith.com

Lisa M. Baird
Counsel, Reed Smith LLP
Los Angeles
+1 213 457 8036
lbaird@reedsmith.com

Kevin M. Madagan
Counsel, Reed Smith LLP
Washington, D.C.
+1 202 414 9236
kmadagan@reedsmith.com

Nicole J. Aiken-Shaban
Associate, Reed Smith LLP
Philadelphia
+1 215 851 8173
naiken-shaban@reedsmith.com

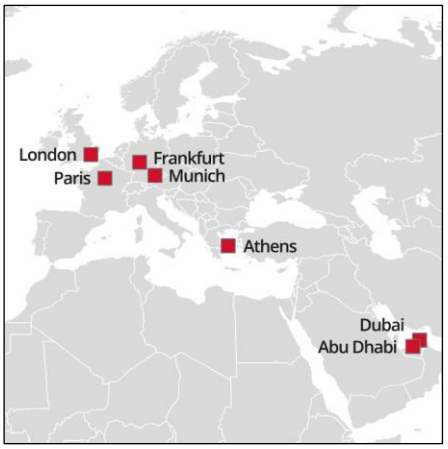
Matthew D. Jacobson
Associate, Reed Smith LLP
Washington, D.C.
+1 202 414 9292
mjacobson@reedsmith.com

Vicki J. Morris
Associate, Reed Smith LLP
Philadelphia
+1 215 241 7974
vmorris@reedsmith.com

Yetunde D. Oni
Associate, Reed Smith LLP
Washington, D.C.
+1 202 414 9472
yoni@reedsmith.com

Reed Smith is a global relationship law firm with more than 1,700 lawyers in 26 offices throughout the United States, Europe, Asia and the Middle East.

Founded in 1877, the firm represents leading international businesses, from Fortune 100 corporations to mid-market and emerging enterprises. Its lawyers provide litigation and other dispute-resolution services in multi-jurisdictional and high-stakes matters, deliver regulatory counsel, and execute the full range of strategic domestic and cross-border transactions. Reed Smith is a preeminent advisor to industries including financial services, life sciences, health care, advertising, entertainment and media, shipping and transport, energy and natural resources, real estate, manufacturing and technology, and education.



ABU DHABI
ATHENS
BEIJING
CENTURY CITY
CHICAGO
DUBAI
FRANKFURT
HONG KONG
HOUSTON
KAZAKHSTAN
LONDON
LOS ANGELES
MUNICH
NEW YORK
PARIS
PHILADELPHIA
PITTSBURGH
PRINCETON
RICHMOND
SAN FRANCISCO
SHANGHAI
SILICON VALLEY
SINGAPORE
TYSONS
WASHINGTON, D.C.
WILMINGTON

reedsmith.com