

SUBMISSION TO CONGRESS

**Food & Drug Administration
Work Plan and Proposed Funding Allocations
of FDA Innovation Account**

**Required by Section 1002 of the
21st Century Cures Act (Public Law 114-255)**

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Commissioner of Food and Drugs
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/s/ Scott Gottlieb, M.D. (Signed on June 7, 2017)

**Department of Health and Human Services
Food and Drug Administration**



EXECUTIVE SUMMARY

The 21st Century Cures Act (Cures Act) was enacted into law on December 13, 2016, after a bipartisan, multi-year effort. The Cures Act primarily affects activities of the Department of Health and Human Services (HHS) and its agencies, including the Food and Drug Administration (FDA or the Agency).

Title I, section 1002 of the Cures Act, establishes an “FDA Innovation Account” (Innovation Account) for Fiscal Year (FY) 2017 – FY 2025 and authorizes \$500 million in funding, subject to annual appropriations, to be used by FDA to carry out certain provisions in Title III of the Cures Act. Section 1002 also requires FDA to develop a work plan describing the allocation of any Innovation Account funds that may be appropriated for eligible activities. Section 1002(c)(1)(A) requires:

Not later than 180 days after the date of enactment of this Act, the Commissioner shall submit to the Committee on Health, Education, Labor, and Pensions and the Committee on Appropriations of the Senate and the Committee on Energy and Commerce and the Committee on Appropriations of the House of Representatives, a work plan including the proposed allocation of funds appropriated pursuant to the authorization of appropriations under subsection (b)(3) for each of fiscal years 2017 through 2025 and the contents described in subparagraph (B).

Prior to submission of the work plan to Congress, the Cures Act requires FDA to seek recommendations from the Science Board to the FDA (FDA Science Board) on the proposed allocation of funds and contents of the work plan.

As illustrated in the following table, Congress directed that the funds authorized in the Innovation Account should be distributed in varying amounts over nine fiscal years.

Title I, Section 1002 of the Cures Act ¹

FDA Innovation Account									
Funds Authorized – Subject to Yearly Appropriation									
Fiscal Year (FY):	2017	2018	2019	2020	2021	2022	2023	2024	2025
\$ (in millions)	20	60	70	75	70	50	50	50	55

Title III of the Cures Act is specifically focused on medical product development activities regulated by FDA, with all but a few of the sections under Title III directly requiring FDA action or involvement.² Title III includes authorities FDA can use to help modernize drug, biological, and device product development and review, and to create greater efficiencies and predictability in product development and review. The Cures Act also improves FDA’s ability to hire and retain scientific, technical, and professional experts in positions that support the development, review, and regulation of medical products.

After submitting this initial work plan, in future years FDA is required to submit annual reports to Congress in FY 2018 - FY 2025 on the activities conducted using any Innovation Account funds that

¹ Details in the Tables may not add up to the totals due to rounding.

² In other Cures Act titles not focused on FDA, the Agency is required to provide consultation and serve on working groups, headed by other HHS agencies. These include, among others, consultation with the National Institutes of Health (NIH) on research on pregnant and lactating women, tick-borne diseases, animal care and research, and certain activities related to the NIH ClinicalTrials.gov data bank.

may be appropriated on an annual basis. In addition, FDA will provide a public website for tracking FDA's implementation activities related to the Cures Act, including the statutory deadlines for various provisions, as was done for previous legislative enactments.

The work plan, which incorporates recommendations of the FDA Science Board and is included as Appendix A, identifies the proposed allocation of funds for projects that fall within subtitles A – F and section 3073 identified in Title III of the Cures Act as eligible for Innovation Account funds.

BACKGROUND

A. Methodology/Process

Rather than allocate potential innovation funds across all eligible provisions, FDA leadership identified a set of principles to prioritize those projects/activities that fall within subtitles and sections identified in the Cures Act as eligible for Innovation Account funds. The principles derive from FDA's mission to protect the public health by assuring the safety, effectiveness, and security of drugs, vaccines and other biological products, and medical devices. The principles gave priority to:

- Provisions that present the greatest opportunity for FDA to foster innovation and integrate advances in biological sciences, engineering, information technology, and data science, to most directly improve the Agency's product review tools and processes.
- Provisions that address the greatest need for scientific modernization.
- Provisions that have the most immediate impact on delivery of services to patients, the medical product industry, academia, and health professionals.
- Provisions for which other funds may not be available.

Together, the Agency's medical product centers and other affected FDA offices used these criteria to identify funding needs to carry out the statutory requirements and activities within the eligible subtitles and sections. Activities that could better equip FDA to advise sponsors on, and otherwise facilitate, the efficient development of new products and to more effectively and efficiently review them were prioritized. FDA also took into consideration other available funding streams to implement the Cures Act, including medical product user fees. As a final step, the proposals were reviewed and prioritized collectively to ensure the total proposed allocations did not exceed the annual Innovation Account amounts authorized to be appropriated from FY 2017 - FY 2025.

The resulting work plan (Appendix A) provides the list of subtitles and sections for which Innovation Account funds could be allocated, if appropriated on a yearly basis, and includes a description of the necessary work and justification for the proposed allocation of funds.

The Cures Act includes provisions that have the potential to have far-reaching effects on scientific advancements in medical product development. The speed at which science is evolving is unprecedented, creating an era of biomedical discovery and innovation. For this reason, and given the significant changes in medicine, science, and other factors, including the Agency's other mission-critical work, FDA believes it is prudent for the work plan to preserve the Agency's ability in future years to take a flexible approach to implementing the Cures Act. If Innovation Account funds are appropriated on an annual basis, FDA is committed to undertaking a yearly planning and prioritization exercise to identify activities eligible for the Innovation Account funds.

The Agency proposes to allocate the authorized Innovation Account amounts to the activities that represent the best opportunity to achieve the goals of the Cures Act in conjunction with other funding sources subject to their availability. Consequently, FDA’s proposed allocation does not spread the Innovation Account funds across all eligible sections. Some eligible provisions may assist FDA in carrying out its responsibilities but do not require any specific investment in new or expanded program activities. Others complement projects and commitments under current or anticipated reauthorized user fee programs and could be funded in part through some user fee resources subject to the availability of funds. Still others dovetail with on-going work supported by budget authority. For example:

- Section 3003 exempts certain voluntary surveys from the Paperwork Reduction Act, and thus does not require implementation funds.
- Implementation of some provisions related to regenerative advanced therapies (sections 3034, 3035) is well underway and being accomplished without a request for innovation funds.
- The work plan does not include a proposed allocation of innovation funds for FDA-related activities in Subtitle E such as Antimicrobial Resistance Monitoring (section 3041) (primarily handled by the Centers for Disease Control and Prevention) or the Limited Population Pathway (section 3042), because work on these activities will be conducted using other resources subject to their availability.
- Under the Medical Device Innovation subtitle, the provisions on Classification Panels (section 3055) and Cleaning Instructions and Validation Data Requirement (section 3059) are not included in the work plan because the Agency anticipates using other resources subject to their availability.
- FDA is not requesting innovation funds to help support the Government Accountability Office (GAO) review of FDA priority review programs required by section 3014, because this effort will be incorporated in the Agency’s regular work with GAO.

Since the FDA work plan is mandated by section 1002 to cover only proposed uses of any Innovation Account funds, the above Cures Act sections are not part of the work plan allocations. However, the full list of Cures Act Title III activities eligible for Innovation Account funds is included as part of the work plan (Appendix A).

The eligible activities and proposed allocation plan are contingent upon the Innovation Account funds being appropriated each year at the levels authorized.

B. FDA Science Board

In section 1002(c)(1)(B) of the Cures Act, Congress required “recommendations from the Science Board to the Food and Drug Administration, on the proposed allocation of funds ... and on the contents of the proposed work plan.” FDA convened the FDA Science Board on May 9, 2017, with a request for the Science Board to review the proposed work plan and proposed allocation of the Innovation Account funds and to provide recommendations for FDA to consider when preparing the final work plan. The Science Board’s recommendations are summarized in Appendix B. FDA carefully considered these recommendations and took them into account when finalizing the work plan for submission to Congress.

For background, the FDA Science Board³ is a chartered Federal Advisory Committee Act (FACA) committee that provides expert advice to the FDA Commissioner and other officials. Such advice is provided when requested on specific, complex scientific and technical issues important to FDA and its mission, including those that support FDA in keeping pace with technical and scientific developments. The FDA Science Board is authorized by its charter to have up to 21 voting members knowledgeable in scientific fields relevant to FDA regulated products. Currently, there are 15 voting members. The FDA Science Board Meeting held on May 9, 2017⁴ was a public meeting conducted according to FACA.

FDA requested the Science Board to consider the following questions when reviewing the proposed work plan and preparing its recommendations:

1. Are the criteria used by FDA to prioritize the proposed allocation of funds appropriate?
2. Are the proposed activities reasonably likely to contribute to successful achievement of the Cures Act requirements?

CONCLUSION

The work plan describes activities that are intended to successfully achieve the Cures Act requirements in areas that are a high priority for any Innovation Account funds appropriated and other available resources. FDA can help chart a path for advancing medical product development and reviews and help bring innovative new therapies and products to patients and health care providers in a more timely and efficient manner.

³ Information about the FDA Science Board can be found at:

<https://www.fda.gov/advisorycommittees/committeesmeetingmaterials/scienceboardtothefoodanddrugadministration/default.htm>.

⁴ The transcript from the May 9, 2017, Meeting of the Science Board can be found at:

<https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/ScienceBoardtotheFoodandDrugAdministration/ucm556321.htm>.

Appendix A

Food and Drug Administration Work Plan for 21st Century Cures Act Innovation Account Activities and Proposed Allocations

Subtitle A – Patient-Focused Drug Development

Section 3001. Patient Experience Data

Section 3002. Patient-Focused Drug Development Guidance

Section 3004. Report on Patient Experience Drug Development

The Cures Act emphasizes the need for patient engagement and directs the Food and Drug Administration (FDA or the Agency) to include the patient’s voice in drug development and review. Section 3001 requires FDA to make public a brief statement regarding whether and how patient experience data and related information that was submitted, if any, was used in the review of a drug or biologic marketing application. Section 3002 requires FDA to issue one or more guidances for the purposes of drug development and regulatory decision making. Guidance should address such issues as acceptable methodological approaches for collecting, measuring, and analyzing patient experience data. Section 3004 directs FDA to issue reports at specified intervals assessing the use of patient experience data in regulatory decision making, especially focusing on the review of patient experience data and information on patient-focused drug development tools as part of approved applications. In implementing these provisions FDA aims to facilitate a more systematic gathering and use of patients’ perspectives on their disease/condition and available therapies to treat their disease/condition. FDA will consult with external stakeholders in developing the required guidances. The work plan proposes to use Innovation Account funds to implement certain elements of these provisions.⁵

FDA Innovation Account⁶									
Proposed Allocation – Subject to Yearly Appropriation									
Subtitle A – Patient-Focused Drug Development									
Sections 3001, 3002, 3004									
Fiscal Year (FY):	2017	2018	2019	2020	2021	2022	2023	2024	2025
\$ (in millions)	-	2.3	2.5	3.2	3.6	3.3	3.3	3.4	4.2

Subtitle B – Advancing New Drug Therapies

Section 3011. Qualification of Drug Development Tools

This section requires FDA to establish a qualification process for drug development tools (DDTs) (e.g., biomarkers, clinical outcome assessments) for proposed contexts of use. FDA must develop a new regulatory process under the Cures Act to qualify DDTs in order to facilitate timely and consistent

⁵ The Agency will strengthen its staff with clinical, statistical, psychometric, and health outcomes research expertise, incorporating these staff into review teams during drug development and application review where sponsors intend to use patient input as part of the development program. The guidance development work under section 3002 is a top priority for the HHS Secretary and for the Agency, both to fulfill the statutory mandate and meet the needs of patients. In view of the close alignment of the content of these statutory requirements and the commitments for guidance proposed under the Prescription Drug User Fee Act (PDUFA) VI, FDA anticipates relying on PDUFA VI fee funding to support the majority of this work.

⁶ Details in the Tables may not add up to the totals due to rounding.

review of DDT qualification submissions and publicly disseminate broader information about DDTs under review and following a qualification determination. Once a DDT is qualified under this new process, any sponsor may use it for its qualified context of use to support an application for approval or licensure of a drug or to support the investigational use of a drug.

Expert FDA staff and contractors will help develop evidentiary criteria needed to support qualification, develop regulatory informatics platforms, and integrate new review processes. This must occur quickly to ensure FDA can meet its obligations under this section within statutory timeframes, including developing and issuing guidance outlining procedures for the qualification process, holding public meetings, and posting public reports. Once fully implemented, this section has the potential to transform drug development and review.

Section 3012. Targeted Drugs for Rare Diseases

This section is intended to facilitate the development, review, and approval of genetically targeted drugs and variant protein targeted drugs intended to address an unmet need in one or more patient subgroups with respect to rare diseases or conditions that are serious or life-threatening. Under this authority, and consistent with applicable statutory standards related to drug and biological products, a sponsor of an application for a genetically targeted drug or a variant protein targeted drug may rely upon data and information previously submitted by the same sponsor (or by another sponsor who has given the applicant a contractual right of reference to such data and information) in another application. Expert FDA staff will support review activities associated with this section.

Section 3013. Reauthorization of Program to Encourage Treatments for Rare Pediatric Diseases

This provision extends the priority review voucher program for sponsors of approved rare pediatric diseases product applications that meet certain criteria intended to encourage the development of safe and effective products for rare pediatric diseases. The voucher can be redeemed by the sponsor to receive a priority review of a subsequent marketing application for a different product or the voucher can be transferred to another sponsor. “Rare pediatric disease” means a disease that is a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years (including neonates, infants, children, and adolescents) and the disease is a rare disease or condition, meeting the definition within section 526 of the Federal Food, Drug, and Cosmetic Act.

For FY 2018-FY 2020, expert FDA staff will develop draft and final guidance; review rare pediatric disease designation requests; improve IT and other systems; and manage the administration of the program which has seen increasing requests for designations, expected to continue to increase.

Section 3016. Grants for Studying Continuous Manufacturing

This section allows FDA to issue grants to study continuous manufacturing of drugs and biological products and similar innovative monitoring and control techniques. Continuous manufacturing is a new and exciting technology that is being used in the pharmaceutical industry instead of “batch” technology, a process that involves many stops and starts in a series of manufacturing steps. Not only can these breaks cause inefficiencies and delays, they also can increase the risk of introducing human error into the manufacturing process and defects in the finished product.

Continuous manufacturing has significant potential to improve the agility, flexibility, cost, and robustness in the development of manufacturing processes for both small-molecule drugs and

biotechnology products. In contrast to batch technology, continuous manufacturing uses an uninterrupted process, eliminating the breaks between manufacturing steps, thereby decreasing the possibility of introducing human error during the stops and starts of the batch process. For this reason, continuous manufacturing is generally thought to be more reliable and safer. In addition, more efficient production of quality drug and biological products can drive down manufacturing costs, potentially resulting in lower drug prices. Likewise, continuous manufacturing can allow manufacturers to both prevent and respond to drug shortage and recall events.

Expert FDA staff will issue grants to enhance knowledge of novel continuous manufacturing technologies, and develop well-defined scientific standards and policies for clearly articulating how the Agency will evaluate these technologies as part of regulatory submissions for new drugs, generic drugs, biotechnology products, and biosimilars.

FDA Innovation Account Proposed Allocation – Subject to Yearly Appropriation Subtitle B – Advancing New Drug Therapies Sections 3011, 3012, 3013, 3016									
Fiscal Year (FY):	2017	2018	2019	2020	2021	2022	2023	2024	2025
\$ (in millions)	5.0	14.2	13.1	11.2	11.3	9.7	9.8	10.3	10.7

Subtitle C – Modern Trial Design and Evidence Development

Section 3021. Novel Clinical Trial Designs

This section directs FDA to assist sponsors in incorporating complex adaptive and other novel trial designs into proposed clinical protocols and applications for new drugs and biological products in order to facilitate more efficient product development. To accomplish this FDA must hold a public meeting 18 months after the date of enactment of the Cures Act and issue guidance on, among other things, how to use such novel trial designs, how they can help to satisfy the substantial evidence standard, and recommended analysis methodologies.

FDA expert staff will plan and conduct the public meeting, further develop novel clinical trial designs and approaches, and draft the required guidance.

Section 3022. Real World Evidence

This section directs FDA to establish a program to evaluate the potential use of real world evidence to help support the approval of a new indication for an already approved drug or to help support or satisfy post approval study requirements. Real world evidence is defined as data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than randomized clinical trials. Real world evidence can be derived from a variety of sources relating to the delivery of healthcare and its outcomes, including electronic health records, claims and billing data, and product and disease registries. Use of such evidence has the potential to allow researchers to answer questions about treatment effects and outcomes efficiently, saving time and money while yielding answers relevant to broader populations of patients than would be possible in a specialized research environment. This could help streamline clinical development and help inform the safe and effective use of products.

Expert FDA staff with expertise in statistics, data science, meta-analysis, clinical outcomes research, and other areas will develop the framework and methodologies for evaluating the use of real world evidence, draft guidance, and hold a workshop on using real world evidence in regulatory decision making.

Section 3023. Protection of Human Research Subjects

Within three years of enactment of the Cures Act, FDA’s human subject regulations are required to be harmonized, to the extent practicable, with HHS’s Common Rule (human subject regulations applicable to certain federally conducted or supported research). These harmonization activities will be designed to, among other things, increase efficiencies of the clinical trial system, reduce ambiguity in interpretation of FDA and HHS regulations, protect vulnerable populations, and alleviate burden on clinical investigators. After the rulemaking is effective, and as a result of the harmonization, FDA will be required to conduct periodic updates and reviews of its regulations on various provisions because of certain requirements of the new Common Rule regulations. Subsequent to the rulemaking, it will be necessary to revise or create relevant guidance (currently estimated to include at least five guidance documents), forms, training, and assistance regarding the revised regulations. To accomplish this rulemaking, including contractual work and other necessary work subsequent to the effective date of the rule, FDA will use experienced staff familiar with the rulemaking and harmonization process.

Section 3024. Informed Consent Waiver or Alteration for Clinical Investigations

This provision changes the law and enables FDA to issue regulations to allow an Institutional Review Board (IRB) to waive the requirement for informed consent for certain minimal risk research if human subject protection safeguards are met. The HHS Common Rule has permitted this type of waiver for decades. The ability to waive informed consent for certain minimal risk research is important to the conduct of studies that could contribute substantially to the development of products to diagnose or treat diseases/conditions or address unmet medical needs. The waiver also would help enable the conduct of certain comparative effectiveness research in cluster randomized trials, as well as other types of analyses of large identifiable data sets, including some patient centered data.

To implement this provision FDA will need to issue proposed and final rules to revise FDA’s regulations; and issue guidance. FDA will use highly experienced expert FDA staff with regulation and guidance development expertise to lead these efforts.

FDA Innovation Account Proposed Allocation – Subject to Yearly Appropriation Subtitle C – Modern Trial Design and Evidence Development Sections 3021, 3022, 3023, 3024									
Fiscal Year (FY):	2017	2018	2019	2020	2021	2022	2023	2024	2025
\$ (in millions)	1.9	4.6	8.2	10.8	8.0	6.0	6.1	5.9	6.3

Subtitle D –Patient Access to Therapies and Information

Section 3031. Summary Level Review

This section allows FDA to rely on qualified data summaries to support approval of a supplemental application for a qualified use of a drug. Data summaries may be used if the drug has existing safety data that is available and acceptable to FDA as part of the supplemental application and if the full data used to develop the qualified data summaries are submitted in the application. This may save

considerable time and reviewer resources because Agency reviewers may not need to reexamine the primary raw datasets or conduct additional analyses of the data. The initial focus of FDA's implementation of this provision will be on supplemental applications for cancer drugs.

Expert FDA staff in the Oncology Center of Excellence will develop policies and procedures for implementation of summary level review for appropriate oncology applications for drugs and biologics products.

Section 3033. Accelerated Approval for Regenerative Advanced Therapies

This section allows FDA to build on existing expedited programs available to regenerative medicine products by establishing a new program to foster their development and approval through the new Regenerative Medicine Advanced Therapy (RMAT) Designation. Upon RMAT designation, sponsors of such products are eligible for increased and earlier interactions with FDA to help facilitate an efficient development program, including discussion of which approval pathways would be appropriate and the size of clinical trials. In order to support effective development and review of these products, the Center for Biologics Evaluation and Research (CBER) will provide continual regenerative medicine advanced therapies training for all Center staff who may work on these products. Robust training is crucial to ensure that FDA reviewers are well versed in the latest practices in this rapidly evolving field of medicine.

Section 3036. Standards for Regenerative Medicine and Regenerative Advanced Therapies

This section requires the establishment of standards and consensus definitions to support the development and review of regenerative medicine therapies, including with respect to the manufacturing processes and controls of such products.

In order to meet the requirements of the Cures Act, CBER will use Innovation Account funds to facilitate a public process with the National Institute of Standards and Technology and other stakeholders to coordinate and prioritize the development of standards and consensus definitions of terms. Such standards and terms will help foster the development, evaluation, and review of regenerative medicine therapies, including with respect to the manufacturing processes and controls for such products. Innovation funds will support expert FDA staff engaged in this work, as well as help facilitate long-term engagement with stakeholders on regenerative medicine standards development and consensus definitions through the creation of a public-private partnership.

Section 3038. Combination Product Innovation

This section updates and modernizes FDA's regulation of combination products. It requires FDA to provide clear rationales for combination product designations, ensure timely inter-center coordination and work with sponsors to help establish clear premarket and postmarket expectations. Under this legislation, a sponsor can request engagement with FDA including a combination product agreement meeting to discuss, among other things, standards and requirements for market authorization. FDA must issue guidance to help facilitate such meetings.

The legislation authorizes combination product sponsors, in certain circumstances, to rely on FDA's prior findings of safety or effectiveness or substantial equivalence. It also mandates that FDA develop, publish, and maintain a listing of efficiencies for complying with current good manufacturing requirements for combination products. Additionally, the legislation enhances existing oversight

functions for the program within FDA and adds additional elements for FDA’s annual reports to Congress about the program.

FDA expert staff will conduct assessments of existing policies, procedures, and information technology systems and make necessary modifications; establish new tracking systems; and support program implementation. Staff also must develop and revise guidances, rules, notices, SOPs, training, and other tools necessary to implement the section.

These changes will facilitate efficient, consistent, and predictable combination product designation and regulation.

FDA Innovation Account Proposed Allocation – Subject to Yearly Appropriation Subtitle D – Patient Access to Therapies and Information Sections 3031, 3033, 3036, 3038									
Fiscal Year (FY):	2017	2018	2019	2020	2021	2022	2023	2024	2025
\$ (in millions)	7.8	23.9	26.8	29.5	27.9	16.6	17.0	17.0	18.7

Subtitle F – Medical Device Innovation

Section 3051. Breakthrough Devices

This section writes into law and expands FDA’s Expedited Access Pathway program, which allows for expedited development and review of devices that represent breakthrough technologies for life threatening or irreversibly debilitating diseases/conditions. By statute, the program has been expanded now to include devices subject to 510(k) submissions. The Breakthrough Devices program requires frequent and extensive interactions between device companies and FDA staff during the device development phase, as well as priority review for breakthrough medical devices.

FDA estimates that this program will grow at a rate as high as 20 percent per year over the next 10 years. FDA expert staff will accommodate the increased workload and will need to acquire the IT systems needed to fully implement the program. The program will accelerate patient access to these lifesaving therapies.

Section 3052. Humanitarian Device Exemption

A Humanitarian Use Device (HUD) is a device intended to benefit patients by treating or diagnosing a rare disease or condition. Before the passage of the Cures Act, “rare” was defined as fewer than 4,000 individuals in the United States. Section 3052 raises the eligibility cap to not more than 8,000 individuals in the United States. A HUD may be marketed after approval of a Humanitarian Device Exemption application which requires a showing of safety and probable benefit (rather than safety and effectiveness). FDA must issue guidance that defines the criteria for establishing “probable benefit.”

FDA expert staff will accommodate the increased workload, and will need to acquire the IT systems needed to implement and track the impact of this change on the development of devices for rare diseases/conditions. This change will expand patient access to needed devices, and is expected to encourage development of more devices for rare diseases/conditions.

Section 3053. Recognition of Standards

This provision requires FDA to make a determination on requests for recognition of all or part of standards established by nationally or internationally recognized standards organizations for the purposes of conducting device reviews, within 60 days. FDA's rationale for these decisions must be made public, as appropriate, and relevant FDA employees must be trained in use of recognized standards in premarket device review.

FDA expert staff will coordinate review of submitted standards across review divisions, and respond to external information requests regarding the recognition of new standards. FDA will also expand its participation in national and international standard setting organizations across all device areas (e.g., cyber security, robotics, software, and additive manufacturing). This standards recognition work will require operating funds to support travel for FDA participants. Greater use of nationally and internationally recognized standards will promote more efficient and consistent device review, and will reduce the burden on manufacturers from inconsistent standards in use by different international regulatory authorities.

Section 3056. Institutional Review Board Flexibility

This section eliminates the requirement that device trial sponsors always use a local Institutional Review Board (IRB). This change will provide flexibility and promote efficiencies in the clinical trial system. This also will help to reduce burden on investigators. Several key guidance documents will be developed related to the use of centralized IRBs.

Section 3058. Least Burdensome Device Review

This provision requires FDA to train relevant employees on application of the "least burdensome" principle in device review, audit the training, and periodically assess implementation of the "least burdensome" principles.

FDA will use both expert staff and contractors to conduct these audits. More consistent and meaningful application of the "least burdensome" principle in device review will improve review efficiency and consistency, and will reduce the regulatory burdens on manufacturers.

Section 3060. Clarifying Medical Device Software

This provision exempts specific categories of medical software from FDA regulation based on their low levels of risk to patients. However, the provision provides a process by which exempted software will not be excluded from FDA's jurisdiction based on a finding from the HHS Secretary that such software function would be reasonably likely to have serious adverse health consequences. FDA expert staff will implement a system for surveillance of the exempted products or functions. Surveillance capabilities would benefit the public by ensuring that exempted software products or functions do not pose safety concerns or contribute to serious adverse health consequences.

FDA Innovation Account Proposed Allocation – Subject to Yearly Appropriation Subtitle F – Medical Device Innovations Sections 3051, 3052, 3053, 3056, 3058, 3060									
Fiscal Year (FY):	2017	2018	2019	2020	2021	2022	2023	2024	2025
\$ (in millions)	5.3	12.3	15.6	16.1	14.9	11.0	10.9	10.7	12.2

Subtitle G - Improving Scientific Expertise and Outreach at FDA

Section 3073. Intercenter Institutes

This section requires FDA to establish one or more intercenter institute(s) to help develop and implement processes for coordination of activities in major disease areas between the drug, biologics, and device centers.

FDA has established the Oncology Center of Excellence (OCE) to create a unified policy approach and clinical review for all drugs, biologics, and devices used in medical oncology. It will leverage the combined talents and skills of all FDA regulatory scientists and reviewers who work in medical oncology product review. OCE will also serve as a single point of contact for external stakeholders for FDA’s work in cancer, including professional societies and patient advocacy groups.

FDA medical and professional staff will coordinate review of oncology product applications across the medical product centers, policy development, and collaboration with external stakeholders. This Center of Excellence will help expedite the development of oncology and hematology medical products and support an integrated approach in the clinical evaluation of drugs, biologics, and devices for the treatment of cancer.

FDA Innovation Account Proposed Allocation – Subject to Yearly Appropriation Subtitle G – Improving Scientific Expertise and Outreach at FDA Section 3073									
Fiscal Year (FY):	2017	2018	2019	2020	2021	2022	2023	2024	2025
\$ (in millions)	-	2.8	3.7	4.1	4.3	3.4	2.9	2.8	3.0

Complete List of Cures Act Title III Activities Eligible for FDA Innovation Account Funds	
Subtitle A - Patient Focused Drug Development	
Sec. 3001	Patient experience data.
Sec. 3002	Patient-focused drug development guidance.
Sec. 3003	Streamlining patient input.
Sec. 3004	Report on patient experience drug development.
Subtitle B - Advancing New Drug Therapies	
Sec. 3011	Qualification of drug development tools.
Sec. 3012	Targeted drugs for rare diseases.
Sec. 3013	Reauthorization of program to encourage treatments for rare pediatric diseases.
Sec. 3014	GAO study of priority review voucher programs.
Sec. 3015	Amendments to the Orphan Drug grants.
Sec. 3016	Grants for studying continuous drug manufacturing.
Subtitle C - Modern Trial Design and Evidence Development	
Sec. 3021	Novel clinical trial designs.
Sec. 3022	Real world evidence.
Sec. 3023	Protection of human research subjects.
Sec. 3024	Informed consent waiver or alteration for clinical investigations.
Subtitle D - Patient Access to Therapies and Information	
Sec. 3031	Summary level review.
Sec. 3032	Expanded access policy.
Sec. 3033	Accelerated approval for regenerative advanced therapies.
Sec. 3034	Guidance regarding devices used in the recovery, isolation, or delivery of regenerative advanced therapies.
Sec. 3035	Report on regenerative advanced therapies.
Sec. 3036	Standards for regenerative medicine and regenerative advanced therapies.
Sec. 3037	Health care economic information.
Sec. 3038	Combination product innovation.
Subtitle E - Antimicrobial Innovation and Stewardship	
Sec. 3041	Antimicrobial resistance monitoring.
Sec. 3042	Limited population pathway.
Sec. 3043	Prescribing authority.
Sec. 3044	Susceptibility test interpretive criteria for microorganisms; antimicrobial susceptibility testing devices.
Subtitle F - Medical Device Innovations	
Sec. 3051	Breakthrough devices.
Sec. 3052	Humanitarian device exemption.
Sec. 3053	Recognition of standards.
Sec. 3054	Certain class I and class II devices.
Sec. 3055	Classification panels.
Sec. 3056	Institutional review board flexibility.
Sec. 3057	CLIA waiver improvements.
Sec. 3058	Least burdensome device review.
Sec. 3059	Cleaning instructions and validation data requirement.
Sec. 3060	Clarifying medical software regulation.
Subtitle G - Improving Scientific Expertise and Outreach at FDA	
Sec. 3073	Establishment of Food and Drug Administration Intercenter Institutes.

Appendix B

Summary of Science Board Recommendations

At the beginning of the FDA Science Board meeting on May 9, 2017, the Food and Drug Administration (FDA or the Agency) presented an overview of the 21st Century Cures Act (Cures Act) which covered key provisions and planned implementation activities. FDA gave specialized, detailed presentations on key sections of the Cures Act such as those involving patient engagement, drug development tools, and regenerative medicine. The Agency also explained that section 1002 of the Cures Act requires FDA to seek recommendations from the Science Board on the proposed allocation of funds and content of the work plan. In framing the Science Board's charge, the Agency requested that the Science Board Members consider the following questions:

1. Are the criteria used by FDA to prioritize the proposed allocation of funds are appropriate?
2. Are the proposed activities are reasonably likely to contribute to the successful achievement of the Cures Act requirements?

The Science Board Chair reiterated the charge to the Members and led them through a discussion of each of the provisions identified in the proposed work plan and the proposed allocation of innovation funds. For each such provision, the Science Board Members reviewed the Agency's description of activities and had the opportunity to ask questions or make comments. FDA subject matter experts were available to answer any questions or address any Member's concerns. In addition to its consideration of the proposed work plan and funding allocations, the Science Board also discussed more general issues concerning FDA's scientific and regulatory public health responsibilities. A summary of the recommendations made on the specific provisions of the proposed work plan and allocation of Innovation Account funds is provided below.

As captured in the transcript of the meeting,⁷ the Science Board Members complimented FDA on its efforts to develop the work plan in such a short timeframe and with an appropriate level of detail that allowed them to conduct their review. When asked by the Science Board Chair whether the criteria FDA used to prioritize the proposed allocation of funds were appropriate and if the proposed activities FDA included in the work plan are reasonably likely to contribute to successful achievement of the Cures Act requirements, the Science Board Members unanimously agreed that both of these charges were met.

General Recommendations:

- The criteria FDA used to prioritize the activities eligible for innovation funds should mention that these are consistent with the Agency's public health mission.
- It will be important, in order to generate new knowledge through collaborative mechanisms, for FDA to keep stakeholders and the public apprised of its strategy for timely implementation, and progress as it is made.

⁷ [May 9, 2017, Meeting of the Science Board to the FDA transcript available at: https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/ScienceBoardtotheFoodandDrugAdministration/ucm556321.htm](https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/ScienceBoardtotheFoodandDrugAdministration/ucm556321.htm)

Recommendations Regarding Specific Provisions:

- Sections 3001-3004: Patient Focused Drug Development

Several Science Board Members expressed interest in FDA's proposed activities in these areas, stressing the importance of patient insights and other collaborative models in generating new knowledge. They also mentioned the challenges in translating qualitative assessments into quantitative data for use in regulatory decision making. They acknowledged that the activities for these sections describe the issuance of a number of guidance documents and how important it will be for the Agency to incorporate outside perspectives into the guidance development process.

- Section 3024 – Informed Consent Waiver or Alteration for Clinical Investigators

Several Science Board Members asked questions about the intent of this section. As a result, the Chair recommended that FDA edit this section in the work plan to clarify the effect of the provision.

- Section 3051 – Breakthrough Devices

It was unclear to at least one Science Board Member that FDA has an existing Expedited Access Pathway Program in place for medical devices and that this provision expands upon that program.

- Section 3052 – Humanitarian Device Exemption

The existing authorities and regulations surrounding humanitarian device exemptions were not clear to several Science Board Members. For this reason, the Chair recommended that FDA edit this section in the work plan to clarify the effect of the provision.