

## Highlights: Biomedical Research and Regulatory Provisions in H.R. 34, the 21<sup>st</sup> Century Cures Act

In December, the U.S. Congress overwhelmingly passed the 21<sup>st</sup> Century Cures Act (H.R. 34), an end-of-year healthcare package of bills with many mental health, substance use, and criminal justice provisions. The bill also makes significant investments in our nation’s research apparatus spanning discovery, development, and delivery. **Key provisions in the legislation affecting biomedical research and regulations are highlighted below:**

- **Establishes a 10-year National Institutes of Health (NIH) Innovation Account.** Supports NIH innovation projects by providing a total of \$4.8 billion over 10 years earmarked for the following projects:
  - ✓ \$1.5 billion for the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative;
  - ✓ \$1.5 billion for the Precision Medicine Initiative;
  - ✓ \$1.8 billion for cancer “moonshot” research; and
  - ✓ \$30 million for NIH and the Food and Drug Administration (FDA) to jointly conduct activities related to regenerative therapies.

The Director of NIH is also required to submit a work plan, including the proposed allocation of funds authorized for the NIH innovation projects, along with a description and justification for each project. Thereafter, the Director is required to submit an annual report to the relevant Committees of jurisdiction in the Congress on project progress. Overall, the funds may help researchers at the nation’s universities and medical centers receive increased grant funding centered on cancer, neuroscience, and genetic medicine. *(Section 1001)*

- **Provides \$500 million over 10 years for FDA innovation projects.** Authorizes the FDA to dedicate funds for fiscal years 2018 through 2026 for innovation projects. Directs the Commissioner of FDA to gather recommendations from the FDA Science Board to assist with making determinations on projects to pursue. These recommendations shall be submitted to relevant Committees of jurisdiction in the Congress no later than 180 days following passage of H.R. 34. *(Section 1002)*
- **Provides for a “eureka prize competition” as part of NIH’s exiting prize authority.** Requires NIH to support innovation competitions that advance biomedical science and improve health outcomes of serious diseases. Directs NIH to track the innovations funded by this prize competition. *(Section 2002)*
- **Advances the President’s Precision Medicine Initiative.** Supports the broad goals of this initiative by authorizing \$1.5 billion over 10 years. Augments current efforts to address disease prevention, diagnosis, and treatment. The initiative may include developing a network of scientists to assist in carrying out the initiative; developing new approaches for addressing scientific, medical, public health, and regulatory science issues; applying genomic technologies to provide data on the molecular basis of disease; and collecting information voluntarily provided by a diverse cohort of individuals that can be used to better understand health and disease.

There is considerable interest at NIH in ensuring patients with mental health and substance use disorders are included in this Initiative; the APA Administration is discussing with NIH how the APA Registry can be developed so that it can meaningfully contribute such patients to the Initiative. *(Sections 2011, 2036)*

- **Institutes privacy protections for human research subjects.** Requires the Secretary of HHS to issue certificates of confidentiality to researchers that receive federal funding and prohibits researchers who receive such certificates from disclosing the name of participants or any other identifiable data gathered during research. Prohibits researchers with such certificates from being compelled to disclose identifiable information about participants gathered through research. Additionally, permits the Secretary of HHS to exempt individual biomedical research data from being disclosed if the data is identifiable, or could be used for identification. The Secretary is required to provide written basis for each disclosure exemption. Further, provides FDA flexibility to waive or alter informed consent requirements for clinical trials with minimal risk. *(Section 2012, 2013, 3023, 3024)*
- **Invests in the next generation of researchers.** Creates a “Next Generation of Researchers” initiative to be housed in the Office of the Director of NIH’s office. The purpose of the initiative is to coordinate, develop, modify, and prioritize policies and programs to improve opportunities for new researchers. NIH’s existing loan repayment program is also replaced with a new program for intramural researchers and extramural researchers, allowing the Director of NIH to better target loan repayment programs to meet workforce or scientific needs. The maximum yearly loan repayment amount is increased from \$35,000 to \$50,000. *(Sections 2021, 2022)*
- **Reduces administrative burdens for researchers.** Directs the Secretary of Health and Human Services (HHS) to review regulations and policies related to disclosure of financial conflicts of interest; harmonize existing policies to reduce administrative burden; and consider ensuring that financial interest disclosure requirements are appropriate for awards that will directly fund research. Requires NIH to reduce administrative burdens related to monitoring sub-recipients of grants by primary awardees of funding. Along with the Secretaries of Agriculture and HHS, the Director of NIH is required to review animal regulations and policies to similarly reduce administrative burdens on investigators. Requires the Office of Management and Budget to establish an advisory committee called the “Research Policy Board” to provide information on effects of regulations related to federal research requirements and make recommendations on how to harmonize regulations to minimize administrative burden. The Board has two years to submit a report with recommendations. *(Section 2034)*
- **Modifies the National Center for Advancing Translational Sciences.** Removes the NIH’s National Center for Advancing Translational Science (NCATS) phase IIB clinical trial funding restriction. Proponents believe it will allow NCATS to fund key research that might not otherwise be performed by manufacturers themselves. These provisions give NCATS the ability to conduct two types of research of interest to their Director: “experimental medicine” clinical trials (e.g., rapid trials in patients with specific targets of interest, to identify early efficacy signals using proxy markers); and mining large clinical databases to identify “repurposing targets.”

In very preliminary discussions, there was interest from NCATS in the APA Registry’s ability to support both types of research. APA Administration will continue to work with NCATS to ensure the APA Registry can be used for such studies. *(Section 2037)*

- **Enhances both the rigor and reproducibility of scientific research.** Directs a working group to make recommendations to the Director of NIH within 18 months of the bill’s enactment. No later than two years after enactment, the Director is required to submit a report to the Secretary of HHS and the Congress on proposed recommendations and policy changes to be implemented to enhance rigor and reproducibility in scientific research funded by NIH.

APA Administration will carefully evaluate the NIH Working Group’s recommendations. There may be implications for different parts of the APA (e.g., new requirements for publishing and data-sharing that could affect journals and other publications). *(Section 2039)*

- **Makes technical modifications to the clinical trials database.** Updates the clinical trial registry data bank requirements to require the Director of the NIH to publicly post information from device clinical trials prior to clearance or approval of the device if the manufacturer makes such a request. The Director shall inform manufacturers of the option to request such information. In addition, clarifies whether combination products are considered drug clinical trials or device clinical trials with respect to the clinical trials data bank. *(Section 2051)*
- **Makes updates to compliance activities and policies to improve data reporting.** Directs the Secretary of HHS, through the Director of NIH and Commissioner of FDA, to submit a report describing education and outreach, guidance, and enforcement to encourage compliance with the clinical trial registry data bank. Additionally, requires a report on the total number of clinical trials with complete data bank registration information; the total number of clinical trials registered during the period for which the report is being prepared; and activities undertaken to educate about data bank registration and submission requirements. In addition, updates reporting requirements by requiring the Director of NIH to consider whether entities have complied with reporting of valid analyses in the awarding of any future grants for certain clinical trials. Directs the Secretary of HHS to consult with relevant federal agencies (e.g., FDA, ONC, NIH) and other stakeholders (e.g., patients, researchers, physicians, industry) to receive recommendations regarding enhancements to the clinical trial registry data bank.

Two aspects of these provisions will need to be kept in mind: ensuring any trials conducted on the APA Registry are registered in ClinicalTrials.gov; and ensuring the results of any trial conducted on the APA Registry are submitted to ClinicalTrials.gov. *(Sections 2052, 2053, 2054)*

- **Improve the National Neurological Conditions Surveillance System.** Requires the Director of the Centers for Disease Control and Prevention (CDC), in coordination with other agencies as the Secretary determines, to enhance and expand infrastructure and activities to track the epidemiology of neurological diseases; and incorporate information obtained into an integrated surveillance system, which may consist of or include a registry, to be known as the National Neurological Conditions Surveillance System. In addition, the Secretary shall ensure that the System is designed in a manner that facilitates further research on neurological diseases. *(Section 2061)*
- **Makes modifications to accessing, sharing, and using health data for research purposes.** Directs the Secretary of HHS to issue guidance clarifying that certain researchers may remotely access protected health information (PHI) if there are security and privacy safeguards in place. Also directs the Secretary to issue guidance clarifying the circumstances under which authorization for the use or disclosure of PHI for future research purposes contains sufficient information – purposes such that it would be reasonable for the individual to expect that PHI could be used or disclosed for future research. Establishes a working group to report on the uses and disclosures of PHI for research purposes. Members of the working group shall include the NIH, CDC, FDA, OCR, members of the research community, and patients. The working group will produce a report containing recommendations. *(Section 2063)*
- **Requires the development of patient-focused drug development guidance.** Requires FDA to issue guidance on how to collect patient experience data and determine how to utilize this information in regulatory decision making.

Some have expressed concern that this could lead drug companies to increase their efforts to encourage off-label prescribing with the goal of gaining new indications without conducting more rigorous clinical studies. From APA's recent discussions with experts at NIH, the APA Registry's plans for privacy/informed consent appear to be in keeping with both these provisions as well as what is anticipated in the final rules updating 42 CFR ("Common Rule") due out in the next month. *(Section 3002)*

- **Establishes a review pathway at FDA for biomarkers and other drug development tools that can be used to help shorten drug development time and reduce failure rates in drug development.** FDA would be required to make publicly available, on at least a biannual basis, the following: All qualified drug development tools, including all surrogate endpoints which were the basis of approval or licensure (as applicable) of a drug or biological product; information on each qualification submission under the qualification process; whether external scientific experts were utilized in the development of a qualification plan or the review of a full qualification package; formal written determinations in response to such qualification submissions; and summary reviews that document conclusions and recommendations for determinations to qualify drug development tools.

Some have raised concerns that this provision seeks to legislate in an area of science more appropriately left to FDA. Critics have said it pressures the FDA to rely more on surrogate end points instead of positive medical outcomes. *(Section 3011)*

- **Requires FDA to evaluate the use of real-world evidence to help support the approval of a new indication for a previously approved drug and to help support or satisfy post-approval study requirements.** This section requires FDA to evaluate the use of “real-world evidence” when it decides whether to approve a new indication for a drug or device that is already on the market. FDA is given two years to conduct this evaluation and issue guidance on what constitutes “real world evidence.”

One important issue that will require further consideration is whether “real-world evidence” is required to come from controlled clinical trials that involve randomization, or alternatively whether observational studies that do not involve randomization will be acceptable. Non-randomized studies are simpler to perform but may be subject to bias and confounding. Critics have also expressed concern that this proposal could lead drug companies to increase their efforts to encourage off-label prescribing with the goal of gaining new indications. They believe these practices compromise patient safety and have already resulted in billions of dollars in civil and criminal fines. They also contend drug manufacturers that wish to market their products for other uses should be willing to finance clinical studies of off-label uses. The APA will carefully follow the FDA’s evaluation and guidance, especially to ensure the APA Registry is prepared to help provide rigorous “real-world evidence” to the FDA that can benefit psychiatrists and their patients. *(Section 3022)*

- **Permits the FDA to rely on qualified data summaries to support approval of a supplemental drug application.** Calls for the use of “data summaries” to support the approval of certain drugs for new indications. It allows the FDA to use data previously submitted for a different purpose to expedite the development of certain drugs and establish a streamlined data review program for drug approvals for additional indications.

Critics have expressed concern the FDA could become more dependent on these industry-developed data summaries and less focused on their own independent data analysis resulting in lower standards for new drug indications. *(Section 3031)*

- **Requires manufacturers to publish their guidelines for expanded access (compassionate use) of unapproved drugs.** The content of the policy shall include contact information for the manufacturer to facilitate communication; procedures for making such a request; criteria that will be used to evaluate such a request; and the length of time the manufacturer requires to respond. This section also makes clear that the posting of guidelines shall not serve as a guarantee of access to any investigational drug. *(Section 3032)*
- **Clarifies the scope of permissible manufacturer communications regarding healthcare economic information to certain entities.** Broadens the current definition of healthcare economic information (HCEI) to expand the types of HCEI materials and analyses firms could prepare and use with payors or formulary committees, including allowing HCEI to be comparative to the use of another drug, intervention, or no intervention. Such claims are required to still utilize an appropriate methodology, be truthful, and non-

misleading. Also extends the dissemination of HCEI explicitly to payors and formulary committees. Clarifies that HCEI is required to only “relate” to an FDA-approved indication rather than “directly” related to such approved indication. This clarification allows firms to disseminate HCEI that contain data on both approved and unapproved uses of a product (for example, broader than just on-label patients). Requires that manufacturers affix to HCEI information, where applicable, any material differences between the HCEI and the labeling of an approved drug.

Given these modifications, it will be important to ensure that such information is not misused and remains based on competent and reliable scientific evidence. *(Section 3037)*

- **Establishes breakthrough device pathway, building on existing priority review device pathway at FDA.** Creates an accelerated approval pathway for medical devices similar to the pathway that currently exists for drugs.

Some critics have raised concerns that this would weaken the standards for reviewing new medical devices. It will be important to ensure that the FDA implements the new approval pathway in such a way that the definition of a breakthrough device is appropriately narrow and limited to only those devices that represent a clear and demonstrable improvement over what is already on the market. *(Section 3051)*

- **Requires FDA to clarify when it is appropriate to waive clinical laboratory improvement requirements.** Requires that the FDA update its existing regulatory guidance to clarify the criteria for waiving Clinical Laboratory Improvement Amendment (CLIA) requirements, which aims to expand patient access to point-of-care diagnostics. *(Section 3057)*
- **Implements a “least burdensome” device review process.** Facilitates the dissemination of health care economic information to payers, formulary committees, or other similar entities.

While this provision might provide helpful information to these entities, some have cautioned that it will be important to ensure that such information is not misused, so it will be critical that it is based on competent and reliable scientific evidence. Yet many of the promising new modalities in the development pipeline for mental health and substance use disorders involve devices (e.g., for new diagnostics, neuromodulation, cognitive training, etc.). Both a breakthrough device 3031 pathway as well as least burdensome review process will improve the currently cumbersome regulatory process for devices and benefit both psychiatrists and their patients. *(Section 3058)*

- **Assists doctors and hospitals in improving quality of care for patients through electronic health records.** Directs the Secretary of HHS in consultation with multiple stakeholders to establish a goal for reducing regulatory or administrative burdens related to the use of EHRs. Such a strategy shall include public comment and prioritization of meaningful use of certified EHR technology for medical specialties and sites of service. In addition, authorizes a grant program for the purposes of developing reporting criteria that reflects relevant stakeholder input, including from healthcare providers. The criteria will reflect information gathered on EHR interoperability, usability, and security. The goal is to assist healthcare providers in selecting EHR products.

Psychiatrists are relatively late adopters of EHRs; providing this unbiased information will likely help psychiatrists choose an EHR and promote adoption in the field. *(Sections, 4001, 4002)*

- **Promotes EHR interoperability to improve patient care.** Defines the term interoperability and provides for the support of a trusted, secure interoperable network-to-network exchange of health information. A component of this exchange will be the creation of a digital healthcare provider directory. The HIT Policy and Standards Advisory Committee is reformed to ensure the Committees’ duties are targeted toward achieving a HIT infrastructure nationally and locally; the promotion and protection of privacy and security of health information; and the facilitation of secure access by an individual of a person’s protected health

information. Further, requires EHRs to be capable of transmitting, and where applicable, receiving and accepting data, from registries. This includes clinician-led clinical data registries. Additionally, an HIT developer shall be treated as a provider for the purposes of reporting and conducting patient safety activities concerning improving clinical care. The Secretary of HHS shall also complete a report concerning best practices and current trends voluntarily provided, without identifying individual providers or disclosing PHI, by patient safety organizations to improve integration of HIT into clinical practice.

Creating standards for and promoting EHR interoperability will likely help psychiatrists exchange information, especially with teams in which they are members (e.g., collaborative care teams). Greater EHR interoperability will also help facilitate inclusion of more psychiatrists in the APA Registry. *(Sections 4003, 4005)*

- **Improves patient access to their EHR.** Directs the Secretary of HHS to use existing authorities to encourage partnerships between health information exchange organizations, networks, and health providers for the purposes of offering patients access to their electronic health information in a single format that is easy to understand, secure, and automatically updated. Encourages the Secretary, in coordination with OCR, to educate healthcare providers on ways to leverage capabilities of health information exchanges to provide patients with access to their electronic health information and clarify misunderstandings by healthcare providers about the use of health information exchanges. Directs HHS, through ONC, to educate providers and individuals in understanding a patient's rights to access and protect personal health information under HIPAA, including providing best practices for requesting such information.

These provisions emphasize the importance of developing patient dashboards (in addition to physician dashboards) in the APA Registry so patients can view their results. *(Section 4006)*

- **Includes cost offsets, determined after months of negotiations.** The offsets include: a drawdown of the strategic petroleum reserve; reductions in funding available from the Affordable Care Act, including the Prevention and Public Health Fund and funding available to territories; limitations of federal Medicaid reimbursement to states for durable medical equipment, prosthetics, orthotics and supplies to Medicare reimbursement rates; elimination of federal Medicaid matching funds for prescription drugs used for cosmetic purposes or hair growth, unless medically necessary; increased oversight of termination of Medicaid providers; and measures to reduce Medicare spending, including provisions focusing on payments for infusion drugs and home infusion drug services, and contracting and fraud penalties. *(Sections 5001-5012)*