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The 21st Century Cures Act: Legislative Update

By David Vulcano

On July 10, the U.S. House of Representatives passed the 21st Century Cures Act with a strong 344-77 bipartisan vote. The Act will now be considered by the Senate Committee on Health, Education, Labor and Pensions (HELP). Making the huge assumption that the Act will not be derailed by Washington politics, the Senate is likely to pass its own version, which would then be reconciled with the House version before being signed into law by the President. In other words, while the details are likely to change, there is an excellent chance the Act will become law.

The Act is intended to decrease the time and cost associated with the discovery, development and delivery of new drugs, devices, biologics and other medical technologies. While the Act focuses on the FDA, it also affects OHRP, CMS, OCR (the office responsible for HIPAA), CDC and other government, academic and industry functions. This article will discuss how the Act, as currently written (https://www.congress.gov/bill/114th-congress/house-bill/6/text), will affect clinical research, without going into over 55,000 words of details that might very well change.

National Institutes of Health

NIH, already the largest funder of medical research on the planet, will get larger still, but with new strings attached. Subtitle I.A-D increases NIH funding, as well as increasing the share of funding that goes to extramural research. To address the aging investigator demographic, the Act calls for NIH to develop a plan to attract, develop and support emerging scientists, included enhanced loan programs. In addition, it expands the "Capstone Grant Program" for senior scientists, provided they waive their eligibility for Principal Investigator status in future NIH grants.

Transparency, Standardization and Interoperability

The Act revises regulations and otherwise supports data sharing.

Subtitle 1.F calls for standardizing information in the clinicaltrials.gov registry to improve consistency and enable more apples-to-apples use of the data.

Section 1.G gives "Institutes of Higher Learning" and other 501(c)(3) organizations access de-identified clinical trial data submitted to the FDA for products no longer in Phase 1-3, i.e., those that have been approved, cleared or withdrawn. This controversial provision will increase *post hoc* analyses of clinical study data, with a variety of consequences.

Section II.F gives companies the ability to share economic information with payors (as they already can do with providers and formulary committees) for off-label conditions, without being challenged for off-label promotion. This section further requires the FDA to issue draft guidance on the responsible dissemination of "truthful and non-misleading scientific and medical information not included in the approved labeling of drugs and devices."

Section II.M requires the FDA to formally recognize interoperability standards from nationally and internationally recognized standards organizations and to train their staff on those standards. The Act revises physician payment transparency requirements (what CMS calls "Open Payments" but is often referred to by its legacy name of "Physician Payment Sunshine Act") by eliminating the reporting requirements for items solely meant to educate

physicians, such as peer-reviewed journal reprints, medical conference reports, and medical textbooks, as well as reporting compensation for preparing and speaking at events that do not commercially promote a product.

Section III.G requires HHS to create a searchable website of provider prices for Medicare recipients (i.e., charges to CMS along with estimated copayments). This website will complement CMS's "Physician Compare" website, which publishes its physician report cards. These websites will provide information that is relevant to investigator selection and clinical trial budgets.

Pediatric, Underrepresented, Rare and Serious Diseases

For those most medically vulnerable, the Act includes numerous provisions to enhance development and access.

Section 1.E calls on NIH to lead in establishing a global pediatric research network with the European Union and the rest of the world. It also demands that NIH create a working group to better define appropriate age groupings in pediatric and geriatric populations for clinical study eligibility.

For serious diseases for which products may be available under FDA's Expanded Access program, Section II.E requires manufacturers to post information about their Expanded Access programs publicly — including contact information and procedures for making requests, criteria for approval, and expected turnaround time — for products in Phase 2 or 3. To alleviate industry concerns that FDA will use any adverse events against them, for example, when reviewing marketing applications, the Act requires HHS to publish final guidance on how adverse event data under Expanded Access will be used.

For those researching antibiotics and vaccines, Sections II.G and H, respectively, provide a pathway for faster FDA reviews of these products, with study designs that require less clinical trial data.

Section II.I rewards manufacturers for conducting clinical trials on rare diseases by granting a six-month extension of marketing exclusivity — on all indications — for adding a rare disease indication. Market forces will determine if and when Sponsors take advantage of these opportunities, as they have for pediatric extensions.

Section III.M expands the rare disease exemption for Humanitarian Use Device classification from <4000 cases per year to <8000 cases per year. Qualifying devices are eligible for HDE approval without the efficacy clinical trials required for IDEs.

Finally, minutes before the vote on the floor of the House of Representatives, the following sentence was added facilitate minority participation: "The Secretary of HHS shall conduct outreach to historically Black colleges and universities, Hispanic-serving institutions, Native American colleges, and rural colleges to ensure their health professionals from underrepresented populations are aware of research opportunities under this Act."

Privacy and Protected Health Information

The Act removes barriers to sharing private health information (PHI), at the cost of limiting protections for individual privacy.

Section I.G states that the exchange of health data for research purposes would now be governed as healthcare operations, meaning that covered entities can exchange data for research purposes as freely as they do for non-research purposes. The Act thus eliminates the extra barriers specific to research, e.g., individual authorization and IRB oversight of protections under a waiver of authorization.

In addition, this section excludes remote data access from the definition of data "removal," thereby permitting remote access under provisions like "preparatory to research" without fear of access being construed as a "removal." This section also further codifies the requirements for a "blanket authorization" for use of data for future unspecified research.

To further persuade covered entities that still resist sharing patient data, Section III.A states that, effective in 2018, except for legitimate exceptions approved by DHHS, providers will lose their EHR "Meaningful Use" certification (with reductions in their government payments) unless they (a) attest that are not restricting the exchange of their data and (b) publish their application programming interface for searching and indexing. By 2018, the Office of the National Coordinator for Health Information Technology Health IT Certification Program (ONCHIT) must create a process for handling public complaints against EHR systems that are not interoperable, as well as against providers for participating in "information blocking," either of which would result in unspecified civil monetary penalties against the EHR vendors and/or providers.

Use of Alternate Data/Inputs

Much of the Act promotes the use of clinical datasets, e.g., EHR data and pharmacy records, to decrease the need for expensive clinical trials. A related objective is to encourage the shift towards patient-centric development, e.g., patients participating in study design and reporting their own health data with smartphone apps and wearable devices in large observational studies.

Section II.A requires the FDA to use and support the development of quality of life "patient experience" data from both patients and caregivers.

Section II.B allocates $10 million/year for 2016-2020 to fund development of biomarkers and other surrogate endpoints and clinical outcome assessments.

Section III.C requires the FDA to issue guidance on how it will use precision medicine in its reviews and how these reviews can be expedited, e.g., by using one sponsor's biomarker data (with permission) for approval of another sponsor's product.

Section III.D calls for the use of clinical experience data for drug approvals, meaning the use of sources other than randomized clinical trials, such as observational studies, registries and electronic health records.

Section II.D also defines a pathway for the FDA to use its Sentinel System to identify potential postmarketing issues and then inform a manufacturer that it intends to initiate an evaluation of a product using clinical experience data, and give the manufacturer the opportunity to comment.

Human Subjects Protections

Provisions motivated by human subjects protection provide interesting regulatory history. In fact, two controversial provisions in earlier versions of the Act have been removed.

First, multicenter studies governed under FDA will not be required to use only a single central IRB. This proposal was seriously considered in committee, but the requirement to use only a single IRB did not make it into the first draft. However, the Act does require the NIH to finalize its draft policy requiring a single IRB for the multicenter studies it funds.

Second, sites performing FDA-governed studies that "checked the box" on their FWA to voluntarily comply with the Common Rule (45 CFR 46) on all studies, regardless of funding, will still be subject to OHRP oversight. The first draft of the Act stated that they would only

have to follow FDA if a study was governed by both FDA and OHRP, but this did not make it to the final.

Other

There's a lot more in the 300+ pages of the Act, including the following:

- To allow more competitive pay for government scientists, Section II.P removes the maximum of 500 individuals that can be eligible for the Silvio O. Conte Senior Biomedical Research Service, with its higher pay rates. This section also raises the salary cap for these employees, as well as FDA scientists and other professionals, to the salary (but not perks) of the President of the United States.
- Section 2161 includes grants to improve pharmaceutical manufacturing processes.
- Section 2241 exempts certain "Health Software" (e.g., smartphone apps) from FDA regulations pertaining to medical devices.
- Much of the act codifies what the FDA already has been doing under its own authority (e.g., expedited review of products designated as "breakthrough therapies"), giving the FDA more confidence that its actions are within the powers granted by Congress.
- Section 4041 orders the Secretary of Energy to sell 80 million barrels of crude oil from the Strategic Petroleum Reserve over the next 10 years to help fund the Act's programs.

Conclusion

The Act will have broad ramifications for clinical research, healthcare and the general public. Given its strong bipartisan support, the Act will probably pass, although most likely with further revisions. If you feel strongly about any of the above provisions, tell your Senator, but do so quickly, while the bill is still in the HELP committee.

Author

David Vulcano is an Assistant Vice President and the Responsible Executive for Clinical Research at HCA, Inc. Contact him at 1.615.344.5260 or David.Vulcano@HCAhealthcare.com.