ACRO
ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

July 16, 2021

The Honorable Diana DeGette
2111 Rayburn House Office Building
Washington, DC 20515

The Honorable Fred Upton
2183 Rayburn House Office Building
Washington, DC 20515

Dear Representatives DeGette and Upton,

Thank you for the opportunity to provide feedback to the Cures 2.0 discussion draft.

The Association of Clinical Research Organizations (ACRO) is made up of the world's leading clinical research and technology organizations. Our member companies conduct or support the conduct of a majority of clinical trials in the United States and around the world. ACRO members provide an array of specialized services across the entire spectrum of drug, biologic, and medical device development—from discovery, pre-clinical, proof of concept, and first-in-man studies, through post-approval and pharmacovigilance research.

ACRO was pleased to be involved in the drafting of the 21st Century Cures Act, to which we provided input and expertise on issues including the sharing of clinical research data in federally-funded studies, patient protections and IRB operations, the use of real-world evidence in drug development, and some of the barriers to research uses of health data encountered under HIPAA.

Since the 21st Century Cures Act was signed into law in 2016, ACRO members have been at the forefront of innovation in the drug development space. From developing novel trial designs, to streamlining clinical research monitoring practices, and exploring new ways to truly put patients at the center of the clinical research process, ACRO members are delivering on the promise of 21st Century Cures.

Below you will find our feedback on the Cures 2.0 draft legislation released on June 22nd.

Sec. 102. National Testing and Response Strategy for Future Pandemics

This section tasks the Secretary of Health and Human Services with developing and implementing a national strategy to prevent and respond to future pandemics.

Relevant to lessons learned from the COVID-19 pandemic, during a discussion with the ACRO Board of Directors on June 3, 2021, NIH Director Dr. Francis Collins and Acting FDA Commissioner Dr. Janet Woodcock provided an overview of the clinical trials that tested COVID vaccines and therapeutics.

It is fair to say that the vaccines trials, designed and funded by biopharmaceutical companies, (in some cases with assistance from Operation Warp Speed,) and executed in partnership with clinical research organizations (CROs) and technology companies, were,

on the whole, highly successful, recruiting reasonably diverse populations and producing meaningful data in record time, without sacrificing safety or efficacy standards. As one example, in the Moderna vaccine trials, of which ACRO members were a part, 37% of the trial participants were from communities of color.

Meanwhile, the clinical trials aimed at developing COVID treatments, a percentage of which were federally-funded, were largely investigator-initiated—and an overwhelming majority of them (as much as 95 percent) were designed and executed in such a way that not enough patients were enrolled and thus were not statistically powerful enough to produce meaningful results. Even the ACTIV trials, which were overseen by the Foundation for the National Institutes of Health (FNIH), struggled to develop community-based clinical trial networks and to enroll sufficiently diverse patient participants in a timely fashion.

We have learned many lessons as a result of the COVID-19 pandemic. Included is the fact that we shouldn't be asking investigators, academic medical centers, or NIH to set up new community-based clinical trial networks in the midst of a pandemic; rather, they should partner with CROs that have already done this work to better identify communities in which to place trials. Any national strategy to address future pandemics should take these lessons into account.

Based on the lessons learned from the COVID vaccines and therapeutics trials, ACRO suggests inclusion of the following language in the Cures 2.0 draft:

"Within 6 months of enactment, the Secretary of HHS shall provide a report to the House Energy and Commerce Committee and Senate HELP Committee on the COVID-19 therapeutic clinical trials funded by the federal government, including the National Institutes of Health. This report shall include the following:

(1) number of trials funded;
(2) types of trials funded;
(3) number of trials that were designed to be exploratory, or hypothesis-generating;
(4) number of trials yielding statistically valid data adequate for regulatory decision-making;
(5) information on inclusion of populations historically underserved by medical research (e.g., on the basis of race, ethnicity, gender);
(6) number of trials placed at sites located at community hospitals, freestanding research centers, and small medical practices within the community; and
(7) recommendations for addressing issues identified in (4), (5), and (6)."

While the strategy outlined in Sec. 102 includes many important factors like testing and data sharing, it should also include mention of ensuring clinical research (including clinical trials relating to combatting said pandemic) remain up and running. During COVID-19 we made great strides in harnessing new technologies and other strategies—such as the use of telemedicine and remote sensors to allow continuation of the clinical care and evaluation that are part of a clinical trial—to continue, and we should enshrine those learnings going forward. Regarding this section's mention of testing (page 4, lines 24-25), strategies for tests

should be comprehensive to address all testing types and should not focus solely on point of care tests and tests at non-medical sites. It would also be wise to add to Sec. 102(b) a sixth item to address: evaluating COVID-19 regulatory flexibilities that can be leveraged in future pandemics.

Sec. 203. Increasing Diversity in Clinical Trials

ACRO is pleased to see diversity and inclusion be an important piece of the Cures 2.0 package. ACRO and its members have made addressing and improving diversity and inclusion in clinical research an operational priority. Our member companies work with trial sponsors and sites to develop strategies to improve the recruitment of underserved communities in clinical trials. For meaningful improvements to be made, contract research organizations and technology companies should be included in groups tasked with addressing current barriers to participation of diverse populations.

Regarding Sec. 203(a)(1), ACRO recommends including a review of the format and utility of FDA Drug Trials Snapshots as both a consumer tool and a benchmark of progress for the industry. The website has been valuable as a mechanism for increasing industry attention on diversity, however more clarity and context is needed for consumers and other stakeholders to understand:

1. when and if a trial population is in fact representative, and
2. if the full body of research has uncovered differences in treatment effect or safety

To support such context and industry progress on this issue, Congress should also consider actions that would support the publishing of suspected disease-state population epidemiology data on a more extensive range of indications.

We believe that conducting a GAO report on barriers to participation can be useful, but Sec. 203(b) should clarify whether this GAO report is meant to focus on government-funded trials only or if it is meant to be inclusive of all trials intended for filing with FDA. We would recommend that this study includes industry-funded/FDA regulated trials.

We would add to Sec. 203(b)(1): “(C) Assess in particular the effect of digitization and incorporation of remote technologies into clinical trial design on the representation of participant populations in clinical trials to evaluate a potential mode of decreasing underrepresentation through breaking geographical access barriers and other barriers identified in the report.”

We are very supportive of a public awareness campaign to increase awareness, understanding and trust among minority communities and would add to Sec. 203(c)(1): “(D) emphasizing the availability of clinical trials utilizing decentralized elements, where participants are able to be involved regardless of geographical location and to ease patient burden for inclusion of more diverse participants.” We would suggest that the planning and execution involve not only FDA/NIH, academia, and patient organizations but also life science/biopharmaceutical industry experts and key community organizations. We also

suggest the campaign include predetermined metrics and analyses, and that those data be used to refine and redeploy efforts in an ongoing, durable effort.

With regard to improving the user experience of ClinicalTrials.gov, Sec. 203(d)(2) should be amended to say: "(C) academic researchers *and contract research organizations;* and," and a fifth designation should be added to say: "(E) experts who have expertise in deploying technologies to improve diversity metrics."

Clinical research organizations and technology companies have already invested significant resources to make ClinicalTrials.gov more user- and patient-friendly via web crawlers and patient-friendly user interfaces. Inclusion of these companies on the Task Force, particularly representatives from these companies who specialize in patient engagement, would be extremely beneficial to the success of this effort.

Sec. 204. Patient Experience Data

ACRO agrees that patient centricity is essential in clinical research. We would make one addition to Sec. 204(b)(1)(B)(i): "in particular, collecting data on patient experience with regards to the use of various technologies and decentralized trial elements, as well as engaging the patient early on in trial planning and design to build the patient's voice into the trial from inception, with the aim of incorporating patient centricity by design in the future." In a patient centricity by design approach, the patient plays a critical role in the development and planning of the trial, allowing for a truly patient-centric trial design. Within the above analysis, any barriers to technology provision—such as education, access to broadband, etc.—should also be considered.

Sec. 301. Report on Collaboration and Alignment in Regulating Digital Health Technologies

As has been mentioned above, COVID-19 showed us the utility of harnessing various digital health technologies through decentralized clinical trials (DCTs) to ensure trials remain up and running during a pandemic, but also to reach more patients than traditional trials.

Decentralized clinical trials deliver upon three key components of the vision of Cures—(1) patient centricity, (2) modernization, and (3) digital health.

While a myriad of issues should be considered when we begin to think about decentralized clinical trials, from telemedicine to state licensures, beginning with robust direction from the FDA on getting more decentralized trials off the ground would be beneficial to drug development at this stage.

ACRO suggests that in order to provide support and clarity for greater adoption of DCTs, the FDA should:

- Convene a multi-stakeholder meeting, to include representatives from the sponsor community, the CRO community, the technology community, and the patient community, no later than the end of 2022 to explore ways to foster DCT adoption.
- Explore the possibility of appropriate incentives to support DCTs, perhaps using the "Breakthrough Therapies" designation model of dedicated services and recurring, enhanced Sponsor-Agency communication

Sec. 304. Increasing Use of Real-World Evidence

Since the 21st Century Cures Act has become law, FDA has made strides regarding real-world data and evidence (RWD/RWE) in the post-market, pharmacovigilance space but remains stagnant when it comes to the use of real-world evidence in pre-market studies. Sec. 304 of the Cures 2.0 discussion draft similarly lacks attention to the use of RWE for pre-market evaluation of drugs, biologics, and devices, and should be amended to include such provisions. The use of RWE may enhance efficiencies of research and development and accelerate the timelines of clinical trials without compromising the quality of evidence development, and instead greatly enhance trial feasibility, implementation, and data analysis. These gained efficiencies will ultimately lead to improved patient health outcomes.

Conclusion

Thank you again for the opportunity to comment on the Cures 2.0 discussion draft. As we learn from the COVID-19 pandemic and look to the future of drug development ACRO members are thinking boldly about what can be accomplished and how we can improve the clinical research process for patients throughout the country whether on site or virtually. We are excited by this opportunity to contribute to the Cures 2.0 process and look forward to supporting your offices as the legislation is formally introduced.

If you would like to discuss any of these issues further, please do not hesitate to get in touch.

Sincerely,

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