CALIFORNIA LIFE SCIENCES

July 19th 2021

The Honorable Anna Eshoo
272 Cannon House Office Building
Washington, DC 20515

Dear Representative Eshoo,

On behalf of the California Life Sciences (CLS), thank you for the opportunity to submit feedback regarding your draft legislation known as the **Diverse and Equitable Participation in Clinical Trials (DEPICT) Act.**

CLS is privileged to be the statewide public policy association representing California's innovative life sciences sector, with a membership spanning biotechnology, pharmaceutical, medical device and diagnostics companies, venture capital firms, research universities and institutes, as well as our sector's nearly 350,000 California employees.

Our state's innovative life sciences companies are vital to the development of groundbreaking therapies, devices, and diagnostics that offer cutting edge tools to diagnose and treat patients in need. We very much appreciate your recognition that California's innovators have been working around the clock to combat the COVID-19 pandemic and played a vital role in our collective fight against this virus through the development of new devices, diagnostics, therapeutics, and vaccines.

We are also very appreciative of your deep commitment to healthcare equity and the need for representative diversity within the patient populations involved in clinical trials. California is currently an active hotbed of clinical research, thanks in no small part to the excellent universities and research hospitals, community health centers, and the private research facilities located there.

Earlier this year, CLS convened a conversation with thought leaders that examined the very issues raised by the draft DEPICT Act, chief amongst them being how we can constantly improve our approach to increasing diversity in clinical trial participation and subsequently how we can measure the effectiveness of the guidance issued by the FDA in November 2020. The panel was made up of experts representing industry, patient, regulatory, and clinical perspectives.

Perhaps not surprisingly, the unified panel consensus was that we can always do better, but that incentives and flexibility provide more positive impact than mandates or quotas. With the evolution of medicine making patient care much more tailored and personalized, the need to allow for individual trial designs that consider as many variables as possible with as many options and strategies as needed to find the right mix of patients with which to conduct the study is imperative.

It also highlighted that the COVID-19 pandemic elevated the issue of inequality in ways that also forced clinical trial sponsors to adapt to pandemic conditions, resulting in more flexible yet innovative approaches to achieving the desired results with the blessing and partnership of regulators. Access, awareness, and trust are key requirements of any such endeavor and require community partnerships and strategic initiatives that leverage the power of trusted voices via key internal and external collaborations.

The pandemic has also certainly accelerated the design of trials that reduce barriers to participation and expand access, which can be as simple as providing transportation services or home visits for those who are housebound. Providing home health services and follow-up visits also helped alleviate time and financial burdens to mitigate certain barriers such as travel, parking, time off work, and child-care. Regrettably, these challenges are certainly not new, but the circumstances required and allowed for different solutions, many of which are now becoming best practices.

Trial sponsors have for some time now prioritized matching talented investigators who work closely with underrepresented communities and are closely wedded and supportive of the communities they treat. By working with doctors and other providers within these communities, it expands access to new therapies and increases awareness for patients who might have previously been unaware of what was available to them, but we must be cognizant that these efforts do take time. Access, awareness, and trust are not hurdles easily or quickly overcome, nor are the solutions easily extrapolated from studies and reports.

The move to blend and tailor trial design has already evolved the historical trend to choose major academic medical centers with a high volume of clinical trial work, where the pool of patients often quickly becomes very homogeneous and primarily white as the available statistics often show. It is critical to bring more trials into the community setting by including new sites that can reach underrepresented groups. CLS members are amongst the leading innovators in this space, and many have been seeking more inclusive data since well before the COVID-19 pandemic.

One important factor to note is that there exists some variance between company sponsored trials and National Cancer Institute (NCI) sponsored trials for example. Drug development for a global market often leads to roughly only one in three patients making up the data packet sent to the FDA being from the United States. With two thirds of patient data coming from other parts of the world, it is not uncommon for certain geographic origins to be over-represented. This is an important distinction when considering the concern that the data being used for U.S drug approvals does not now, and maybe never will, be a true reflection of the U.S population simply because of the global variance in patient demographics.

In the case of oncology, the median size of a trial is 191 patients, meaning that half of cancer trials involve fewer than 200 patients and therefore are limited by a sample size that simply may not allow for statistically significant extrapolation of effectiveness across a proportional representation of the patient pool. As a result, oncology research often requires additional research such as real-world evidence, comparative effectiveness research or the pooling of multiple trials. This scenario is also often the case for disease states with smaller patient populations such as rare and ultra-rare. On the other side of the ledger are more prevalent diseases that affect larger portions of the population where statistical modeling and recruitment are more readily accomplished. All this to say that in the design of clinical trials, one size does

not fit all, and maximum flexibility should be allowed to achieve the desired outcome of increasing participation and inclusion while enhancing patient access to care.

Transforming the face of clinical research will require elimination of barriers at the systemic level, the study sponsor level, and the patient level. Embedding inclusive research principles at the beginning of any trial and a thorough examination of exclusion/inclusion data that currently may be outdated due to the skewed ethnic and gender origin of most of the genomic material available to scientists are imperative. In addition, it would add tremendous value if all clinical trial researchers had access to continuing education about working with diverse populations and increasing minority representation in the clinical trial setting.

Geographical location criteria for site selection should match a representative variety of locations throughout the country and include both rural and urban locations, and site-specific feasibility questionnaires are becoming the norm when determining the suitability of sites with respect to study staff, facilities, and appropriate patient databases for outreach and enrollment. Phase 1 studies, which are conducted at a single site, may pose unique challenges and so again we would caution against overly prescriptive approaches but rather a comprehensive evaluation of the study needs and suitability.

Monitoring diverse enrollment will always require on-going evaluation, as demographic data is collected for patients who are screened for every study, and as we continue to learn from and implement best practices for increased inclusion. Existing databases such as the National Institutes of Health's National Library of Medicine clinicaltrials.gov database might be the ideal repository and could perhaps benefit from grant funding as suggested in your draft. Convening all stakeholders and truly utilizing and sharing data could lead to increased awareness and participation. The digital age has made some outreach more convenient, but it is by no means a standalone solution.

With respect to diversity enrollment targets, the trial sponsor will have the largest impact as discussed above. Company trials designed around a global market will vary. For many domestic trials, the initial target should be representative of the target population within the U.S. and later studies can be done to address the international communities. Many CLS members currently partner with companies in Asia to conduct studies on their population in addition to including Asian Americans in their trials.

Post-marketing commitments should be targeted to addressing additional questions around assets that have not been sufficiently answered in the registration-based clinical development programs. Such questions may include long-term safety data and registries, efficacy in other study populations (pregnancy, pediatrics, etc.), potential effects on key outcome markers (as appropriate). Additionally, phase 4 programs (not necessarily included in post-marketing requirements) are often designed as part of asset lifecycle management strategies and should be part of the on-going discussion with regulatory agencies.

Lastly, from a regulatory perspective, we must commend the FDA for the proactive guidance they have issued to date. CLS and our membership welcomed the initial guidance in the fall of last year and the more recent guidance around decentralized trials designed to address access issues and standardize best practices and other recent learnings. When combined with the Biden Administration's strong commitment to health equity as a priority, and the actions we are likely

to see from HHS, we should celebrate the focused attention and capitalize on the opportunity to bring these champions together and make even greater strides forward. The elevated attention described above allows FDA the opportunity to be the catalyst for change by incentivizing trial sponsors to share, learn, and improve. The very spirit of increasing diversity within clinical trials is based on collaboration, trust, outreach, education, and a unified mission to learn and improve that is perhaps best served without strict mandates. As we prepare for on-going dialogue around a possible 21st Century Cures Act part two and reflect on the resources that have been allocated to specific population research, we have a tremendous opportunity to convene the best minds on these issues and continue this important conversation. If Cures 2.0 seeks to improve how new treatments and therapies are delivered to patients, then it is imperative that the trials that validate this innovation accurately reflect the patient population.

On behalf of the thousands of California life sciences companies that make up our membership, thank you for the opportunity to provide feedback on the DEPICT Act. Please do consider us a resource moving forward, and if we can help provide more detailed expert opinion from within our membership or connect you directly with leading experts in this field, we would welcome the opportunity to do so.

Thank you,

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