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The Honorable Anna Eshoo
Chairwoman
Committee on Energy and Commerce, Subcommittee on Health
United States House of Representatives
272 Cannon House Office Building
Washington, DC 20515

Dear Chairwoman Eshoo:

The Biotechnology Innovation Organization (BIO) is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. Our mission is to advance biotechnology innovation by promoting sound public policy and fostering collaboration, both locally and globally. Our members range from entrepreneurial companies developing a first product to Fortune 500 multinationals. BIO and our members appreciate the opportunity to provide comments to the Diverse and Equitable Participation in Clinical Trials (DEPICT) Act.

BIO is committed to enhancing clinical trial diversity as part of our BIOEquality Agenda published in the fall of 2020. During the pandem we witnessed biopharmaceutical companies achieve increased clinical trial diversity through commitment and regulatory acceptance of certain clinical development tools and approaches. We appreciate the opportunity to provide feedback on the draft legislation.

SEC. 2. Premarket Reporting of Diversity Plan for Clinical Trials and Studies

The DEPICT Act introduces a series of new requirements of clinical trial sponsors and FDA with the intent to promote diversity and representativeness of clinical trial populations. However, many of these new requirements rely on foundational data or knowledge that is inadequate or insufficient. Specifically:

- The draft legislation assumes the availability, and agreement on, source(s) for high quality epidemiology data across disease areas. Unfortunately, U.S. demographic data is incomplete or lacking for many disease areas. This could lead to poorly or inaccurately informed enrollment targets and action plans.
- The draft legislation does not address underlying equity issues that contribute to inequities in clinical trial eligibility. For example, advanced therapies in development for Type 1 Diabetes, due to the risk profile, may require that eligible patients be

aggressively managed with best available therapy prior (e.g., continuous glucose monitor plus a period of stable access to and proper use of insulin) to being eligible for an advanced therapy trial. Due to broader equity issues in the U.S., the overall Type 1 Diabetes population will not be the same as a population of people with Type 1 Diabetes who have had stable access to best available care.

BIO recommends that the legislation provide funding and direction to a federal agency to compile national level reference disease prevalence data or demographic data for various diseases as appropriate. This should be considered a so-called "Gold Standard" reference set that would help to reduce sponsor-by-sponsor variability in demographic target setting due to differences in source data. These data should be publicly available and accepted by FDA for use in drug development. We recommend a public process for nomination of disease areas for which a central repository of regulatory-grade demographic data is most urgently needed.

Targets for the U.S. should be informed by the prevalence of the disease/condition in the target indicated patient population, based on the epidemiology of the disease in the US and important differences associated with various subgroups which would include race and/or ethnic groups in the US. This does not mean that targets should be established that always correspond identically with the prevalence of the disease/condition by each racial and/or ethnic subgroup. Rather, prevalence is important dynamic information that, along with relevant logistical factors, should guide the establishment of appropriate diversity enrollment targets for a particular study. Additionally, where evidence suggests that disease pathophysiology, natural history, and severity differ by demographic subgroup, enrollment targets should most closely match disease prevalence across subgroups. But where disease characteristics do not differ between demographic subgroups, more latitude could be permitted in terms of how closely enrollment targets and disease prevalence match.

Analysis of U.S.-specific demographic enrollment data should be performed to understand the US population's contribution to overall enrollment. However, we note that development programs are often conducted globally, and if a large portion of the clinical program occurs ex-U.S., it may be more difficult to achieve enrollment targets that are based on the US patient population. For this reason, additional flexibility in meeting enrollment targets should be considered. Under circumstances where there are inadequate US data available, there should be flexibility to leverage select international data that may have some generalizability to the US population to help achieve enrollment targets.

The draft legislation should be revised to acknowledge the complexities and nuanced considerations of clinical trial conduct. Particularly for advanced therapies, targeted therapies, therapies for rare disease where clinical trials involve small numbers of patients, the risk-benefit assessment for entering a trial is very individualized, and compliance with trial protocols is essential for patient safety and required long-term follow-up, the inclusion of a patient for demographic reasons should never outweigh inclusion of a patient based on a clinical assessment of suitability for the trial. To ensure safety of participants and the interpretability of data from the trial, clinical trials participants need to be screened and assessed very carefully before enrolling in any clinical trial, but particularly those trials of complex therapies with small patient numbers. We recommend further training of FDA review staff on how FDA's policy on Diversity in Clinical Trials should be implemented across review divisions to ensure consistency and understanding of applying inclusion/exclusion criteria to promote and advance diversity in clinical trials. Additionally, we recommend that the DEPICT Act compels FDA to develop

guidance on the key elements that should be included in a diversity plan for pivotal trials. If a diversity plan were to be mandated by Congress, BIO suggests that FDA integrate this as an expectation at an appropriate point during the drug development process, such as submission of the diversity plan for the pivotal/registrational studies by the end of phase 2 (EOP2). This should be part of the existing FDA submission process, rather than a separate standalone deliverable (e.g., submitted as an appendix to EOP2 briefing document).

The draft legislation seems to apply one approach to all types of patient populations and drug development programs, including targeted therapies. Targeted therapies, specifically those developed for people with a specific genotype, need to be developed with genotype being the primary factor in patient selection and enrollment in a clinical trial. We recommend that the legislation focus first on highly prevalent diseases and exclude/waive rare diseases and targeted therapies from new requirements.

We are developing additional proposals to advance shared understandings between the FDA and sponsors of drug and biologic applications about how to set and evaluate diversity and prevalence targets; approaches to inclusion and exclusion criteria; analysis of subpopulations; and other topics that would enable improved clinical trial diversity and representation.

SEC. 3. FDA Authority to mandate post approval studies due to insufficient demographic subgroup data

The draft bill as written appears to be predicated on the need for efficacy and safety data on each demographic group. It is very important to note that demographic target recruitment data will not necessarily provide sufficient data on diverse subgroups to be able to conduct statistical analysis of the safety and/or efficacy data for each subgroup. To power all studies to enable statistical analysis of trial endpoints across all possible subgroups would require unfeasibly large studies. We do not believe this is the intent of the bill.

We believe the conduct and execution of diversity plans by sponsors in the post-approval setting may in many cases be the most effective and timely way to gather safety and effectiveness information for demographic subgroups in the diseased population. In instances where a drug is intended to treat a serious disease with significant unmet need, the pace of drug development may preclude a sponsor from fully executing its diversity plan(s) pre-approval. In such cases, obtaining safety and effectiveness information in demographic subgroups can be accomplished in the post-market setting. For example, FDA and sponsors should first engage in negotiations on a post-marketing commitment (PMC) to obtain demographic subgroup information. Post-marketing commitments should be tailored in scope to meet the specific informational need, facilitate reasonable study designs that can feasibly achieve enrollment and data objectives, and therefore, are likely to result in trial completion and yield useful results.

BIO welcomes the possibility of utilizing Real World Evidence to satisfy post approval study commitment, and it is likely that Real World Evidence will be the most effective source of data to address these types of post approval study commitments.

SEC. 4. Annual Report on Progress to increase diversity in clinical trials and studies

BIO recommends aggregated reports on progress on increasing diversity in clinical trials and study enrollment that reflects the overall efforts of all sponsors collectively. We encourage the

authors of the legislation to consider the potential negative consequences of the publication of such a report identifying individual sponsors if not aggregated. We understand the intent of the report as the issue is of utmost importance to BIO and our member companies; however, in these times of vaccine and medical products hesitancy and mistrust, a report that identifies that a sponsor was unable to meet their diversity target might lead to a significant subpopulation of patients deciding against a treatment which was, in fact, both safe and efficacious, even if post-approval studies were later conducted in order to build upon understandings of sub-population health outcomes.

SEC. 6. Community engagement and outreach to increase inclusion of underrepresented minorities in clinical trials and research

BIO is supportive and welcomes the effort to increase inclusion of underrepresented groups in clinical trials and research. We are supportive of NIH developing best practices for community engagement and outreach, providing tools and educational resources as well as engaging community stakeholders in underrepresented communities. BIO encourages HHS/NIH to make efforts (*e.g.* public service campaign) to educate healthcare providers and patients about the benefits of participation in clinical trials. Further, academia should be encouraged to develop curricula for healthcare professionals on how to participate in clinical trials as an investigator and how they can enroll patients in trials. Enrollment into a clinical trial should be a routine part of healthcare delivery, and lack of education related to clinical trials is hindering the ability to improve health equity. Additionally, the DEPICT ACT "*Provides funding to NIH for community engagement and outreach efforts to increase inclusion of underrepresented minorities in clinical trials and research"*, the funding could be used to undertake a public service campaign to educate healthcare providers and patients as well as to make clinicaltrials.gov (or a new tool) more patient- and provider-friendly so that those who seek clinical trials can find them easily.

SEC. 7. Grants to increase the capacity of community health centers to participate in clinical trials and research

BIO welcomes effort to increase the capacity of community health centers to participate in clinical trials and research. We understand that current physician reimbursement systems may disincentivize the physicians from enrolling patients to trials. In particular, we would like to see measures implemented that reimbursed primary care and specialist physicians for recommending clinical trials to a patient in a trial, when appropriate. To increase the capacity of Community Health Centers to participate in clinical trials and research, grants awarded should prioritize programs that will create sustainable infrastructure in 3 areas:

1. Clinical Trial Operations and Logistics (*e.g.,* equipment, technology, including EHR/EMR systems)
2. Human Resources (*e.g.,* investigators, study coordinators, data entry staff, patient navigators/supporters)
3. Mentorship/training programs for potential investigators from Community Health Centers in partnership with larger medical centers, particularly those with experience in i) clinical trial operations and ii) implementing benchmarks for ongoing site monitoring that will promote success of participating practices and community health centers.

As mentioned above, BIO is committed to enhancing clinical trial diversity as part of our BIOEquality Agenda. We welcome the opportunity to share and discuss alternative legislative language to advance and improve clinical trial diversity.