July 16, 2021

The Honorable Diana DeGette
U.S. House of Representatives
2111 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Fred Upton
U.S. House of Representatives
2183 Rayburn House Office Building
Washington, D.C. 20515

Re: Biocom California's Comments in Response to the Cures 2.0 Discussion Draft

Dear Congresswoman DeGette and Congressman Upton:

Biocom California commends you on releasing the Cures 2.0 discussion draft and appreciates the opportunity to offer comments. We applaud your leadership and continued efforts to improve our nation's innovation ecosystem over the years, especially your landmark, bipartisan legislation, the 21st Century Cures Act. Biocom California had been very supportive of the bill in 2016, which has significantly modernized our regulatory environment and improved the discovery, development, and delivery of care.

We are eager to work with you again to make further improvements to our innovation ecosystem, including emerging infectious disease preparedness, regulation of new products and technologies, and delivery of care. Please find below our feedback on specific provisions of high interest to our industry. We thank you for the opportunity to provide comments and look forward to continuing working with you as the proposal moves through the legislative process.

Biocom California is the largest, most experienced leader and advocate for California's life science sector, which includes biotechnology, pharmaceutical, medical device, genomics and diagnostics companies of all sizes, as well as research universities and institutes, clinical research organizations, investors and service providers. With more than 1,400 members dedicated to improving health and quality of life, Biocom California drives public policy initiatives to positively influence the state's life science community in the research, development, and delivery of innovative products. California's life sciences industry generates $372 billion in annual economic output, boosts the state's total gross product by $212 billion, supports over 1.4 million jobs, and increases labor income by more than $115 billion per year[1].

[1] *Biocom California 2020 Economic Impact Report Databook.* https://www.biocom.org/eir/.

Title I – Public Health

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

Having a strong supply chain is paramount to combating future pandemics. The shortage of products, particularly personal protective equipment (PPE), during the covid-19 pandemic showed a need for a resilient supply chain for medical products in the United States. We appreciate that both Congress and the Administration are looking at proposals to strengthen the supply chain to avoid shortages of drugs, testing supplies and PPE in the future. We also applaud the FDA for quickly approving Emergency Use Authorizations (EUAs) for vaccines, therapeutics, and medical technologies.

Biocom California supports the development of a national strategy that focuses on strengthening testing capacities and medical supply readiness, improving access to testing services, incentivizing research, developing manufacturing capacities, coordinating the delivery and administration of vaccines and therapeutics, and building partnerships between federal agencies and the private sector.

Additionally, we warn against proposals to drastically overhaul the drug supply chain, such as requiring American drug manufacturers to source all their ingredients for medicines from the U.S., repatriating manufacturing operations to manufacture exclusively in the U.S., or mandating that government agencies only purchase American-made medicines. Such policies risk having the opposite desired effect by delaying the development of vaccines, therapeutics and diagnostics, raising prices, and exacerbating shortages of critically-needed medicines.

Sec. 104. Vaccine and Immunization Programs

Covid-19 vaccines have been essential to addressing the pandemic. The FDA approved the first vaccine developed by Pfizer and BioNTech in December 2020, later approving vaccines by Moderna and Johnson & Johnson. The biotech industry developed these vaccines in record time, in part due to the ongoing research on mRNA vaccines, which has made vaccine development faster than traditional vaccines and ensured access to vaccines a year into the pandemic. The industry also worked to ramp up production, including sharing manufacturing space and resources to produce vaccines faster. As it stands in mid-July 2021, approximately 55.6 percent of the population in the United States and 60.6 percent of California have been vaccinated[2]. By day 92 of the Biden Administration, over 200 million vaccines were administered, far surpassing the goal of 100 million in the first 100 days.

Biocom California supports provisions under this section to authorize new funding for education campaigns on vaccination and immunization information systems. We also believe that increased education with respect to the development and regulation of vaccines is essential to combating vaccine resistance and ensuring that more populations receive vaccines faster and reach herd immunity. We also support capacity building for the Centers for Disease Control and Prevention (CDC)'s

[2] *Covid Data Tracker*. CDC. https://covid.cdc.gov/covid-data-tracker/#datatracker-home.

Immunization Information Systems and hope it will ensure the safety of U.S. citizens as they return to public works.

Sec. 105. Developing Antimicrobial Innovations

Anti-microbial resistance (AMR) has become a major threat to global public health and is one of the greatest challenges for the biotechnology industry in the twenty-first century. Within three decades, an estimated 10 million deaths worldwide (from 700,000 today) could be caused by anti-microbial resistant infections[3], potentially surpassing deaths due to cancer. New antibiotics are needed to address growing AMR, yet, only about 1 percent of medicines in development are antibiotics and the pipeline has steadily declined. More biotech companies, which are developing the overwhelming majority of novel antibiotics, are exiting the space as they continue to face difficulties finding financing and large pharmaceutical partners to help carry out research and development (R&D) and ramp-up commercialization.

Indeed, antibiotic R&D faces severe scientific, regulatory, and economic hurdles. Current clinical guidelines and policies with respect to how antibiotics are used have actively discouraged the development of new antibiotics for almost twenty years, undervaluing the benefits of novel antibiotics to society. In addition, current reimbursement systems tend to discourage appropriate use of novel antibiotics, leading to overuse of older antibiotics, which are often less effective and can exacerbate AMR.

Therefore, Biocom California is supportive of the proposed concept for a subscription model to pay for critically-needed novel antimicrobial drugs. Biocom California also suggests reimbursing drug costs separately from bundled hospital payments to better reflect the societal value of novel antibiotics, and addressing other structural impediments to the development of life-saving antibiotics, including reducing the cost of R&D and ensuring a predictable return on investment, such as through market entry rewards and transferrable exclusivity extensions.

Title II - Patients and Caregivers
Sec. 203. Increasing Diversity in Clinical Trials

A diverse test population is vital to having the most comprehensive clinical trials and generating reliable evidence to inform care for different populations. Biological differences between populations can cause diseases to present differently and treatments to vary in effectiveness. Unfortunately, our health care system too often fails to engage diverse groups of patients in clinical trials because of sociocultural, behavioral, and systemic factors that perpetuate inequities in research participation. As a result, clinical care is sometimes delivered based on evidence that did not account for underrepresented groups of patients, risking disease progression and exacerbating health disparities.

[3] *AMR is a public health crisis.* Working to fight AMR. https://workingtofightamr.org/

Biocom California supports enhancing clinical trial diversity and the Cures 2.0 proposal to require updates from federal health agencies on efforts to improve diversity in clinical trials and identify barriers to participation, which have made it difficult for clinical trial sponsors to recruit diverse pools of participants.

In addition, we believe that the proposed "Task Force for Making ClinicalTrials.Gov More User Friendly" should include representation of additional key stakeholders, including clinical trial sponsors (who are key users of and contributors to clinicaltrials.gov), Contract Research Organizations (CROs can carry out clinical trials on behalf of clinical trial sponsors), and academic medical centers and community clinics (who often are the clinical sites enrolling trial subjects and working closely with CROs and clinical trial sponsors)."

Title III - FDA

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

Health care is at the cusp of a sector-wide transformation due in large part to the development of digital health technologies, from genomic testing to mobile applications to remote patient monitoring. Digital health technologies often reduce the need to physically visit a doctor's office or hospital in certain circumstances, allowing patients to communicate with their physicians and receive and transmit health care information instantly in a home setting; thus, containing costs, preventing the deterioration of conditions, reducing the frequency of visits to medical institutions, and ensuring the continuity of care. Digital health also empowers patients to be active participants in their health care decision-making process. Digital health technologies are a complement, but not a substitute, for face-to-face visits, which remain an essential part of health care.

The covid-19 pandemic has highlighted the vital role digital health technologies serve connecting patients to health care services and providing data to physicians that they could monitor remotely. The global digital health market is expected to grow at a compound annual growth rate of 15.1% from 2021 to 2028.[4] North America also accounted for the largest market share of 38.77% in 2020. With this exponential growth, we recommend continued investment in digital health technology evaluation and regulatory alignment.

We commend FDA's existing efforts in the space, including creating the Digital Health Center of Excellence within the Center for Devices and Radiologic Health (CDRH) in 2020 to advance the development and regulation of digital health products and finalizing the discussion paper on Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) in 2021.

[4] *Digital Health Market Size, Share & Trends Analysis Report By Technology (Healthcare Analytics, mHealth), By Component (Software, Services), By Region, And Segment Forecasts, 2021 – 2028.* Grand View Research. https://www.grandviewresearch.com/industry-analysis/digital-health-market#:~:text=The%20global%20digital%20health%20market%20is%20expected%20to%20grow%20at,share%20of%2056.7%25%20in%202019.

Biocom California supports the proposed report to Congress on the Department of Health and Human Services' (HHS) efforts to ensure collaboration and alignment across FDA's centers and offices with respect to the regulation of digital heath technologies, particularly as their prevalence and capabilities grow. We also support ongoing funding for the FDA's Digital Health Center of Excellence to support their staff and growing responsibilities.

Sec. 302. Grants for Novel Trial Designs and Other Innovations in Drug Development

Industry and regulators have both acknowledged the complexities of traditional clinical trials. The 21st Century Cures Act recognized the cost, time, and complexity associated with the research and development of new medicines, calling for the incorporation of novel clinical trial designs.

In 2019, the FDA released a final guidance entitled Adaptive Designs for Clinical Trials of Drugs and Biologics, which outlined how industry should communicate and structure clinical trials whose design is deemed 'adaptive.' This design allows for modifications to ongoing clinical trials without undermining their validity and integrity or introducing bias. The FDA also released a guidance document in 2020 on Interacting with the FDA on Complex Innovative Trial Designs for Drugs and Biological Products. The document clarifies the use of novel trial designs in the development and regulatory review of drugs and biological products, how sponsors may obtain feedback on technical issues related to modeling and simulation, and the types of quantitative and qualitative information that should be submitted for review.

Biocom California supports providing grants to incorporate adaptive and other novel trial designs into clinical protocols and applications for drugs, which would further the development and use of these designs.

Sec. 303. FDA Cell and Gene Therapy

Cell and gene therapies have long been an area of research and promise for modern medicine. In 2017, the first CAR-T cell therapy, Kymriah, was approved in the United States and marked an increase in research and development in the space. The Alliance for Regenerative Medicine estimates an increase of about 10 percent in cell and gene therapy developers just from 2019 to 2020.

The 21st Century Cures recognized the novelty and growth of the field and created the regenerative medicine advanced therapy (RMAT) expediated approval pathway to incentivize and support the development of regenerative products, including cell therapies, therapeutic tissue engineering products, and human cell and tissue products. FDA also recognizes human gene therapies and xenogeneic cell products to meet the definition of a regenerative medicine therapy.

In 2019, FDA finalized its Guidance for Industry, Expedited Programs for Regenerative Medicine Therapies for Serious Conditions to administer the RMAT designation program. Biocom submitted comments in 2018 in support of the guidance. We also applaud FDA's

Oncology Center of Excellence's (OCE) Oncology Cell and Gene Therapy program, which works to streamline the evaluation process of safe and effective products for patients, cognizant of the unique opportunities and challenges of the space.

Biocom California supports the Cures 2.0 proposal to submit a report to Congress on the current state of cell and gene therapy regulation, foreseeable regulatory challenges, how the agency plans to address those challenges, and the resources and authority the FDA needs from Congress. Biocom California has identified through our Cell & Gene Therapy Working Group regulatory areas in the cell and gene therapy space that need attention.

Industrialization and scaling up manufacturing of these products is a major challenge, as cell and gene therapies are very costly and need to be developed specifically for individual patients. Another focus area is the shift from autologous to allogeneic treatments, which would allow for greater patient access to these treatments, as well as larger scale production. We would also like to see more clarity around the reimbursement of these therapies by CMS and how industry can develop greater standardization in Chemistry, Manufacturing and Controls (CMC) regulatory compliance. Lastly, we believe it is very important to educate the public and patients on the realistic benefits and risks of cell and gene therapy and what to expect from clinical trials, as it is a new technology that is often not fully understood by patients.

Sec. 304. Increasing Use of Real-World Evidence

Under the 21st Century Cures Act, FDA created the real-world evidence (RWE) program to evaluate the potential use of real-world data (RWD). The program evaluates RWD's ability to generate RWE on product effectiveness and help support approval of new indications for drugs and medical products. Real world data include a range of information on a patient's health status and/or the delivery of health care, including, but not limited to, electronic health records (EHRs), claims and billing activities, and product and disease registries. EHRs are particularly useful for the generation of RWE, and in 2016 FDA released a guidance for industry on the Use of Electronic Health Record Data in Clinical Investigations. In 2017, CDRH released a final guidance on Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices.

Biocom California supports the Cures 2.0 proposal to require HHS to outline approaches to maximize and expand the use of RWE and establish a task force to develop recommendations to encourage patients to engage in real-world data generation. The inclusion of multiple agencies, CMS, FDA, NIH, and industry would allow for an encompassing perspective on the use and benefits of this data. We strongly support education and outreach to patients on the importance of this data to ensure accuracy and continuous feedback. Lastly, we'd like to suggest you urge FDA to develop a guidance to share considerations on the use of real-world evidence for regulatory decision-making in drugs and biologics, based on FDA's experience thus far.

Sec. 305. Improving FDA-CMS Communication Regarding Transformative New Therapies

Biocom California supports enhanced communication between the agencies regarding transformative new therapies. While the FDA has, for the most part, kept pace with new advances, such as cell and gene therapies and next-generation sequencing technologies, securing coverage for these treatments has been challenging and the barriers created by reimbursement to hospitals and healthcare providers have made it difficult for patients to access these treatments. In addition, CMS' evidentiary standards are different from FDA's, which makes evidence development burdensome and uncertain for manufacturers of new technologies.

Earlier communication could allow CMS the opportunity to work with manufacturers of transformative therapies on evidence development to inform coverage and reimbursement decisions, upon FDA approval. These conversations could result in timelier and more predictable coverage and reimbursement decisions for transformative therapies – and potentially speedier access for Medicare beneficiaries.

We want to highlight that successful implementation of this provision will be contingent on adequate staffing and additional funding at both agencies. We also want to make clear that while our comments focus on the importance of enhanced communication between FDA and CMS in order to improve coverage decisions, FDA is only responsible for reviewing the safety and efficacy of drugs, devices, biologics, and related products, and CMS is charged with coverage decisions. FDA should not be granted authority to impact Medicare coverage decisions and the role of each agency should remain clear and separate.

Sec. 306. Establishment of Additional Intercenter Institutes at the Food and Drug Administration

Biocom California has been very supportive of the creation of FDA's Oncology Center of Excellence and Digital Health Center of Excellence, to join efforts and resources to advance the development and regulation of oncology and digital health products, respectively. However, the creation of an "intercenter" requires the allocation of significant funding and new staff, which is not addressed in this proposal.

While there are many other diseases and conditions that could benefit from additional investment and exploration at FDA, including dedicated Agency staff and resources, many unanswered questions remain. Thus, we welcome learning more about the intent, disease area, and funding considerations for this initiative.

Title IV – Medicare & Medicaid Services
Sec. 403. Extending Medicare Telehealth Flexibilities

Last year, Congress made important strides toward ensuring that all Medicare patients can access Medicare-covered services during the covid-19 pandemic via telehealth technology by enabling HHS to temporarily waive outdated "originating site" and geographic restrictions in Section 1834(m) of the Social Security Act on Medicare coverage of telehealth services for the duration of the public health emergency (PHE). Prior to the PHE, Section 1834(m) limited telehealth services to rural areas only and prohibited coverage of services provided to patients in their homes, forcing beneficiaries to travel to eligible health care sites.

The changes have helped countless Medicare beneficiaries, a population that is particularly vulnerable to covid-19, access care without having to leave their home and risking exposure to the virus. As a result, telehealth usage has increased dramatically, and the broadened availability of such technologies has proven to be a key in limiting the spread of the virus by keeping people at home. Yet, absent Congressional action, geographic restrictions and sites of care will be reinstated at the end of the PHE, resulting in a sudden unavailability of virtual health options for Medicare patients during times that will remain uncertain and challenging. **Therefore, not only does Biocom California support the Cures 2.0 proposal to extend these telehealth flexibilities within Medicare but also urges Congress to make these changes permanent.**

In addition, the covid-19 pandemic has brought to light issues related to licensure across state lines, which has made it more difficult for many providers to offer telehealth services outside of their licensed state. Biocom California urges Congress to consider making changes to current healthcare licensing restrictions to reflect the current state of telehealth practice. We also believe that a pre-existing provider-patient relationship should not be required to qualify for telehealth services, which is important to improve health inequities, and that genetic counselors should be available to patients through telehealth, which would require CMS to designate them as health care providers.

Please note that our support for continued access to telehealth should not be construed as an endorsement of telehealth services in lieu of in-person visits. Face-to-face visits remain an essential part of health care and cannot be replaced by telehealth care for many patients and many conditions where physical assessment is critical for accurate screening, diagnosis, and treatment.

For example, the Substance Abuse and Mental Health Services Administration (SAMHSA) released guidelines last month recognizing the limitations of telehealth for evaluating certain disorders. It is essential to ensure that patients and providers maintain the ability to access medically necessary care as clinically appropriate for each patient and condition, whether it is via telehealth, in person, or, in narrow circumstances, audio-only services.

Sec. 404. Coverage and Payment for Breakthrough Devices Under the Medicare Program

We are very supportive of the Cures 2.0 provision to provide four years of automatic coverage for devices designated as breakthrough by the FDA. We thank you for your efforts to identify more appropriate ways to reimburse transformative technologies, keep pace with emerging technologies, and remove barriers that prevent Medicare beneficiaries from accessing these critical, life-saving products. These medical technologies are revolutionizing health care by enhancing delivery options and improving outcomes.

The 21st Century Cures Act led to the creation of the Breakthrough Devices Program to expedite the review and approval process for innovative devices and diagnostics. However, it did not provide a pathway for the coverage, coding, and payment of these technologies, which is effectively delaying patients' access to these advancements. This automatic coverage would provide Medicare patients access to the most cutting-edge and transformative technologies as soon as they are deemed safe and effective.

Note that Biocom California submitted comments to CMS in 2020 and 2021 in response to its proposed Medicare Coverage of Innovative Technology (MCIT) pathway. Our comments expressed strong support for the pathway, along with recommendations related to inclusion of diagnostic technologies, benefit categories, coverage duration, coverage post MCIT, evidence generation, and payment and coding. You can view our comments here and here.

Sec. 405. Secretary of Health and Human Services Report on Coverage for Innovative Technologies

As noted in Sec. 301, digital health technologies are a rapidly growing area of the healthcare industry. As they become more prevalent, an effective and streamlined process for coverage and payment of these products is vital. Unfortunately, the lack of reimbursement opportunities is indisputably one of the major barriers to the development of digital health technologies. Coverage and coding limitations, outdated Medicare regulations, restrictive formularies, and increased cost-sharing such as specialty tiers, among others, continue to inhibit the development of digital health technologies.

Biocom California supports reimbursement policies that provide appropriate and inclusive coverage, coding, and payment for new digital health technologies and the Cures 2.0 proposal to require HHS and CMS to submit to Congress a proposal that establishes a process for coverage and payment.

Sec. 407. Expanding Access to Genetic Testing

Today, there are 7,000 known rare genetic diseases affecting 350 million people worldwide and only 5 percent have a treatment. Approximately half of the rare disease population is children and it takes on average 5 to 7 years to reach a diagnostic – years during which conditions can worsen and become more difficult to manage. DNA testing is revolutionizing the practice of medicine by facilitating better and faster diagnoses and leading to potential treatments that are tailored to a patient's genetic material. However, limited insurance coverage of these remarkable technologies continues to impede the use of DNA testing in clinical settings and the diagnoses of many children.

Biocom California supports the Cures 2.0 proposal to create a three-year pilot program to incentivize states to provide DNA sequencing to Medicaid-eligible children who are suspected of having a pediatric-onset genetic disease. The proposal also directs the National Academy of Medicine to provide a report to Congress on how genetic and genomic medicine can contribute to improvements in health care and how the federal government can reduce barriers to the utilization of these technologies.

Biocom California strongly urges you to maintain this bracketed provision in the final legislation. We have been working with the bill's sponsors, Reps. Scott Peters and Eric Swalwell, for many years, as well as other stakeholders within the precision medicine community to reach language that is inclusive and reasonable. We urge you to include whole genome sequencing, whole exome sequencing and multigene panel testing as DNA sequencing clinical services eligible for coverage. This provision will help children suspected of having rare or undiagnosed genetic diseases get a more rapid and accurate diagnosis and holds the potential to drive the use of DNA sequencing in larger clinical settings.

Sec. 408. Medicare Coverage for Precision Medicine Consultations

Pharmacogenomic tests help providers prescribe safe and effective medications and dosage based on individuals' genetic material and known drug-gene interactions. Better drug selection and dosing have not only showed to improve patients' conditions but also reduce hospitalizations and cost.[5]

Biocom California supports the inclusion of Sec. 408 in the Cures 2.0 proposal that would provide Medicare coverage for personalized medicine consultations between a beneficiary's health care provider and qualified pharmacists about their genetic or genomic information and the efficacy of particular drugs, biologicals or other treatments. We believe adding this Medicare benefit will improve patient care and reduce health care costs. We also recommend including genetic counselors.

[5] Case Study: Teachers' Retirement System of Kentucky. Coriell Life Sciences. https://www.coriell.com/wp-content/uploads/CLS-Case-Study-TRS-04.pdf.

Title V- Research

Sec. 501. Advanced Research Projects Agency for Health

Biocom California is encouraged by your interest in establishing President Biden's proposed Advanced Research Projects Agency for Health (ARPA-H) to help drive transformational innovation in health research and speed the application and implementation of health breakthroughs by funding high-risk, high-reward projects. **Biocom California generally supports additional funding for research projects, especially for small and emerging biotech companies, but is currently unable to endorse this placeholder provision until legislation is drafted and responsibilities and funding are determined.**

As this provision is drafted, Biocom California urges you to consider two important concerns within the community: overlap of resources and funding. Biocom believes that ARPA-H should be its own division within NIH, with a unique set of responsibilities that are distinct from existing centers, institutes, and initiatives, such as the Cancer Moonshot and *All of Us* Research Programs established by the 21st Century Cures Act to avoid duplication. In particular, ARPA-H's priorities should be different from NIH's National Center for Advancing Translational Sciences (NCATS), which is tasked with developing and disseminating innovations that reduce or remove costly and time-consuming bottlenecks in translational research. **We urge you to include a diverse pool of stakeholders, including industry, academia, and patients to identify ARPA-H's research priorities.**

We are also concerned that funding for ARPA-H could ultimately reduce appropriations for the National Institutes of Health and some of its programs. Funding for ARPA-H should not come at the expense of NIH's base annual budget and other NIH priorities. Currently the external community is requesting a $3.2 billion increase for NIH, which includes a 5 percent increase over last year to provide meaningful growth and about 2 percent for biomedical inflation.

Sec. 502. Research Investment to Spark the Economy

Since the start of the pandemic, many research projects at research institutions and non-covid-19 laboratories had to be paused or shut down, resulting in many years of research lost and post-doctoral researchers missing the required experience for their careers. In late 2020, NIH Director Francis Collins testified in the Senate that the covid-19 pandemic caused over $10 billion in lost research. Congress passed several supplemental measures, but none included funding to restart the research lost over the shutdowns.

Biocom California supports the Cures 2.0 proposal to include $10 billion for HHS to provide supplemental funding to research institutions, research laboratories, or individuals to extend the duration of awards disrupted because of the covid-19 pandemic. We also recommend making this funding mandatory.

Note Regarding Funding

Biocom California commends you on releasing such a comprehensive set of proposals to improve our innovation ecosystem - many of which we strongly support, as expressed throughout our comments. However, it is unclear how some of the programs and initiatives will be funded. Biocom California is concerned that tasking federal agencies to carry out these new programs with flat funding levels will impose serious constraints on the agencies and the existing programs they administer.

Biocom California does not support pulling funding from existing programs within federal agencies and strongly supports authorizing additional funding for the provisions described in the discussion draft.

We appreciate the opportunity to provide feedback on behalf of our members and thank you for your time and diligence in examining our comments. Please contact Biocom's Director of Federal Policy and Government Affairs, Laure Fabrega, at lfabrega@biocom.org for additional information or questions. We look forward to continuing working with you on this very important matter.

Sincerely,

Joe Panetta
President and CEO
Biocom California