PERSONALIZED MEDICINE COALITION

July 16, 2021

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

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

Sent electronically

Re: Cures 2.0 Discussion Draft

Dear Representative DeGette and Representative Upton:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 220 institutions and individuals from across the health care spectrum, thanks you for releasing the *Cures 2.0 Discussion Draft*.[i] The preceding *21st Century Cures Act* made meaningful regulatory changes and provided essential financial support for many of the breakthroughs in personalized medicine that patients are benefitting from today. We appreciate the opportunity to provide feedback on the draft legislation and suggest how it can continue to advance an individualized approach to care.

Personalized medicine is an evolving field in which physicians use diagnostic tests to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health. By combining data from diagnostic tests with an individual's medical history, circumstances and values, health care providers can develop targeted treatment and prevention plans with their patients.

Personalized medicine is helping to shift the patient and provider experience away from trial-and-error treatments of late-stage diseases in favor of more streamlined approaches to disease prevention and treatment, which will lead to improved patient outcomes, a reduction in unnecessary treatment costs, and better patient and provider satisfaction. PMC's members are leading the way in personalized medicine and recommend that patients who may benefit from this approach undergo appropriate testing and tailored treatment as soon as possible during their clinical experiences.

Personalized medicine is delivering better efficacy, improvements in overall survival, and a reduction in adverse events for patients.[ii] However, PMC has observed that the field continues to experience challenges in delivering timely individualized care. Obstacles impeding the integration of personalized medicine are often caused when scientific developments outpace updates to our regulatory, coverage and payment, and health care delivery systems. In the current environment, patients, providers, and other health care stakeholders are not always prepared to make informed decisions about personalized medicine based on an assessment of all available diagnostic and

treatment options. We believe that *Cures 2.0* could alleviate some of these challenges.

Statement of Neutrality

Many of PMC's members will present their own responses to the *Cures 2.0 Discussion Draft*. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance, and are not intended to impact adversely the ability of individual PMC members, alone or in combination, to pursue separate comments with respect to this legislation or related issues.

TITLE I: PUBLIC HEALTH

The COVID-19 pandemic was an unprecedented moment in history for the world and the entire personalized medicine community. Leaders in personalized medicine worked rapidly to scale the United States' diagnostic capacity, develop treatments for patients suffering from COVID-19 infection, and develop vaccines, all while continuing to learn about individual response to the SARS-CoV-2 virus and its variants. As vaccination rates climb and infection rates slow in this country, we appreciate the bipartisanship you continue to demonstrate by ensuring that the *Cures 2.0 Discussion Draft* allows for further understanding the implications of COVID-19 as well as our opportunities to enable a better response to any future pandemics.

Sec. 101 of the *Cures 2.0 Discussion Draft* calls for a series of national meetings to serve as the basis for an ongoing long-COVID learning collaborative with individuals and organizations representing key sectors of the health care community. PMC supports the creation of this collaborative but notes that clinical laboratories are not mentioned among the required stakeholders in Sec. 101. Clinical laboratories were the first to validate and scale novel tests for the SARS-CoV-2 virus and they continue to perform millions of tests for COVID-19. We urge you to include clinical laboratories along with the other important health care leaders listed in the *Cures 2.0 Discussion Draft*.

The COVID-19 pandemic revealed vulnerabilities to our nation's health and security that must be dealt with before the United States faces another devastating emergency. **Sec. 102 of the *Cures 2.0 Discussion Draft* calls for a national testing and response strategy based on lessons learned, and best practices developed, as a result of the COVID-19 pandemic. PMC supports the emphasis in this section on testing, data sharing infrastructure, administration of vaccines and therapeutics, and medical supply readiness to mitigate future pandemics and public health emergencies. However, strategies for testing should be comprehensive, addressing all testing types, and should not focus solely on point-of-care tests and tests at non-medical sites. In addition, we would strongly encourage making resources available to support the execution of the national strategy including the development of additional infrastructure and partnerships between federal agencies and the private sector.**

Sec. 105 of the *Cures 2.0 Discussion Draft* provides incentives and pathways for the development of critically needed innovative antimicrobial drugs. We applaud the inclusion of these provisions in the *Discussion Draft* but urge that the *Discussion Draft* be amended to require, rather than merely

permit, the development of appropriate use plans for such antimicrobial drugs in partnership with the Secretary, infectious disease experts, diagnostics experts or developers, and laboratory experts, to ensure that all appropriate expertise is included in the development of such plans. This is particularly important to the extent that personalized diagnostics may be used to guide drug selection or dosing.

TITLE II: PATIENTS AND CAREGIVERS

The diagnostic tests underpinning personalized medicine can sometimes reveal genetic mutations that make some patients more susceptible to diseases than others. These tests may also uncover molecular characteristics of cells and tumors, or the functional status of specific biochemical pathways, that can be targeted by available therapies. For some patients, targeted therapies are safer and more effective than traditional treatments.

Health systems are still working on developing and adopting the procedures that will be necessary to facilitate the widespread utilization of personalized medicine. For this reason, patients and their caregivers must educate themselves about the field and discuss it with their physicians. To facilitate patient and caregiver education, PMC launched a campaign called *More Than a Number*, which introduces the concept of personalized medicine, includes a list of questions for patients to ask during six key stages of their interactions with the health care system, and describes the ins and outs of insurance coverage in the United States.[iii]

Because we are moving away from a "one-size-fits-all" approach to medicine to one that is based on the individual patient's particular characteristics of disease, it is important that patients collaborate closely with their physicians in developing prevention and treatment plans. **PMC therefore supports the provisions detailed in Sec. 201 and Sec. 202 of the *Cures 2.0 Discussion Draft* that would fund educational programs for caregivers and require the Centers for Medicare & Medicaid Services (CMS) to solicit input on promoting greater health literacy. We urge the agency to incorporate content that helps guide patient interactions with physicians in this era of personalized medicine.**

Personalized medicine also depends on a diverse, equitable, and inclusive biomedical research enterprise to generate reliable evidence to inform health care interventions that affect subsets of heterogeneous patient populations differently. But the health care system too often fails to engage adequately representative cohorts of patients in basic biomedical research and drug development studies. As a result, clinical care is often delivered and therapies prescribed based on assumptions that have gone untested in underrepresented groups of patients, risking disease progression and exacerbating health disparities.

PMC recently convened leaders from across the health care spectrum who are contributing to the development of research programs in the public and private sectors to uncover sociocultural, behavioral, and systemic factors that perpetuate inequities in research participation and outcomes.[iv] Other recent initiatives spearheaded by PMC members have identified ideas that are essential to effective strategies that reduce disparities and accelerate cures for all patients such as working with health systems outside of academic medical centers, developing community networks, leveraging technology, and even going

directly to patients.[v] **By requiring updates from federal health agencies on efforts to improve diversity in clinical trials while identifying barriers to participation, Sec. 203 of the *Cures 2.0 Discussion Draft* would facilitate positive steps toward broadening our collective understanding of strategies that can be adopted to cultivate a more inclusive biomedical research enterprise. This section should be further improved by including contract research organizations among the entities designated to serve on a task force for making ClinicalTrials.Gov more user friendly**. PMC plans to release a report on related topics in the coming months. The report may be useful for Department of Health and Human Services (HHS) leadership if the provisions in the *Cures 2.0 Discussion Draft* are enacted.

PMC generally supports Sec. 204 of the *Cures 2.0 Discussion Draft*, which will continue work on the collection and reporting of patient experience data (PED). Patients are experts in their own experiences of their diseases and conditions. They are also the end consumers of medical products. We believe that considering patient journeys and understanding patient preferences about their care can advance activities to positively impact the design and conduct of premarket clinical studies, benefit-risk assessments, and post-market evaluation. PED collection is largely qualitative and methods are still emerging. PED can also be collected by anyone and submitted to the U.S. Food and Drug Administration (FDA) as part of a clinical trial or outside of a specific trial. **Thus, the call for "standardizing" PED in Sec. 204 will prove challenging. PMC recommends removing this requirement and instead encouraging "models" of PED development and presentation. Models may inform PED generation and its use in various therapeutic contexts.[vi]**

TITLE III: FOOD AND DRUG ADMINISTRATION

FDA serves as an important gateway for many breakthrough personalized medicine products entering the market. Various centers at the FDA have responsibilities for evaluating medical products for their safety and efficacy. As personalized approaches to treatment and prevention have grown, new types of drugs, tools, and technologies using a patient's genetic and other personal health information have challenged existing regulatory frameworks and processes.

Digital health is an approach focused on using such technology to monitor and provide relevant health-related data about individuals. These technologies include a rapidly expanding array of consumer products and wearables, as well as complex clinical care platforms.[vii] The collection of accurate digitized information that can be integrated with other data is essential to personalized medicine, and we are pleased to see it highlighted as a priority in the *Cures 2.0 Discussion Draft*.

In 2020, FDA's Center for Devices and Radiological Health launched the Digital Health Center of Excellence to build partnerships advancing the development and FDA's review of cutting-edge digital health technologies. Over the past year, FDA has also released an action plan for innovation in medical device software using AI and machine learning, held a public meeting to discuss the use of real-world data generated from patients through digital health technologies, and published learnings from its pilot precertification program for medical device software. **We believe the report to Congress from HHS on collaboration and alignment in regulating digital health technologies proposed in Sec. 301 of the *Cures 2.0 Discussion Draft* can assist FDA in building on the foundation it has already**

established and further inform FDA's approach to regulatory oversight of these emerging technologies.

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. The FDA released an RWE (real-world evidence) Framework in 2019 and subsequently acknowledged that pragmatic and hybrid clinical trials, including decentralized trials conducted at the point of care incorporating RWE, can help clinical trials become more agile and efficient and can allow patients to receive treatments from community providers without compromising the quality of the trial or the integrity of the data collected. **The proposed grants for novel trial designs and other innovations in drug development contained in Sec. 302 of the *Cures 2.0 Discussion Draft* could further build the science in these areas, however it is unclear how "novel" would be interpreted. What is novel in some therapeutic areas is not in others. Thus, we urge you to define what constitutes a novel trial design in Sec. 302. Furthermore, PMC believes that, in addition to the grant program, the FDA should accelerate the use of decentralized trials by issuing guidance regarding digital technology issues, including the acceptance of decentralized trials.**

Thanks in part to a responsive regulatory agency, personalized medicine has seen steady progress in recent years. As of 2020, more than 286 personalized treatments are available for patients.[viii] Personalized medicines accounted for 39 percent of the new drugs FDA approved last year, topping one-third of new drug approvals for the third time in the last four years.[ix] Cell and gene therapy is a fast-growing area of personalized medicine development. As of January 2020, FDA had over 900 active Investigational New Drug applications for gene therapies.[x] The scientific review of gene therapies requires the evaluation of highly complex information and, thus, reviewers with highly specific expertise. By 2025, the FDA anticipates it will be approving 10 to 20 cell and gene therapy products per year.[xi] **Sec. 303 of the *Cures 2.0 Discussion Draft* requires a report to Congress on the current state of cell and gene therapy regulation and foreseeable challenges for the FDA in the future. PMC hopes that this report will include recommendations for meeting the FDA's anticipated resource needs to bolster its workforce and keep pace with the growing workload, as well as identification of challenges associated with long term follow-up studies deemed necessary based on risk of delayed adverse events.**

The *21st Century Cures Act* also placed an additional focus on the use of RWE to support regulatory decision-making, including the approval of new indications for approved drugs. Congress defined RWE as data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than traditional clinical trials. FDA expanded on this definition and now defines RWE as clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of data routinely collected from electronic health records (EHRs), claims and billing sources, product and disease registries, patient-generated data, and mobile devices.[xii]

RWE is enabling researchers to go beyond the scope of traditional clinical trials and to gain insights from information collected in routine clinical care. However, using this data to tailor care at an individual patient level is complex because providers do not always have the resources to assess every piece of information that could help a patient achieve their specific health outcomes. Advanced tools

like artificial intelligence, machine learning, and other analytics technologies are playing an increasingly important role in continually assessing records and other data sets to extract pertinent information.

Health care delivery informed by RWE is an important part of personalized medicine's future. PMC appreciates your desire to build on the initial RWE provisions in the *21st Century Cures Act*. **The provisions contained in Sec. 304 of the *Cures 2.0 Discussion Draft* requiring HHS to outline how it will maximize and expand the use of RWE and establishing a task force to develop recommendations on patient engagement in data generation will support ongoing RWE activities at the FDA and across the federal government to foster technologies that will make data-driven health care a reality**. **The recommendations under Sec. 304 should include clear mandates such as key performance indicators demonstrating how FDA is using RWE in review decisions. To provide additional clarity to the personalized medicine community, PMC would encourage further FDA guidance development on RWE that includes an overarching framework for its uses in clinical trials, the discovery of predictive and prognostic biomarkers, and clinical decision support. We also believe Sec. 304 should be amended to include provisions authorizing the use of RWE for pre-market evaluation of drugs, biologics and devices.**

To ensure that patients have access to personalized medicine, PMC advocates for flexible coverage policies and adequate payment rates for personalized medicine treatments and technologies. PMC has been working with CMS and private payers to inform strategies that facilitate timely access to personalized medicine based on the value it provides to patients, the health care system, and society. We have been fortunate to see many transformative treatments and technologies come to market in recent years. Chimeric antigen receptor (CAR) T-cell therapies in oncology, gene therapies for pediatric rare diseases, and next-generation sequencing technologies are just a few of the innovations that are unlocking a new era of personalized care.

Unfortunately, the process for seeking and securing patient access to some technologies and treatments by CMS and private payers has been challenging. In some cases, inconsistencies in coverage and inadequate reimbursement have impacted patient access. **Sec. 305 of the *Cures 2.0 Discussion Draft* requires the establishment of a communication mechanism between FDA and CMS on breakthrough therapy drugs.** Given the complexity of delivering many of these therapies to patients and the barriers created for reimbursement to hospitals and healthcare providers, we encourage the inclusion of representatives from CMS in any conversations to consider not only coverage for the drugs, but also diagnostics used to inform treatment as well as provider reimbursement for the true costs of care associated with the delivery of a breakthrough therapy. **The existing language in Sec. 305 is problematic due to the possibility that the authority for FDA and CMS to share information with each other as may be appropriate to inform and coordinate such decisions could change the clear and distinct remits of each agency making such approval and coverage decisions more difficult. We believe Sec. 305 should be modified. Appropriate communication between agencies should be based on a process that provides a concrete way to facilitate communication without changing authorities and includes additional stakeholders.**

One of the major pillars of personalized medicine is the development of targeted treatments based on increased understanding of the molecular basis of disease. Tremendous progress has been made in

defining the molecular basis and mechanisms of disease through the use of large datasets, advanced genomic technologies, and analytical methods. As a result, personalized medicine drug approvals doubled between 2016 and 2020, jumping from 132 to 286. In order for research advances to be realized

rapidly, the regulatory approval processes in the United States have evolved to facilitate the development of novel, safe, and efficacious interventions in a timely manner. Four expedited pathways were developed for distinct reasons. Priority review aims for FDA review in 6 months (vs. 10 months for standard review). Accelerated approval permits approval based on surrogate endpoints. Fast-track and breakthrough therapy programs both intend to reduce the duration of clinical trials through more intensive FDA guidance including regular meetings and communication throughout the full drug development cycle. Between 2011 and 2017, the majority of newly approved drugs were associated with at least one expedited FDA review pathway.[xiii] With the increasing identification of new molecular drug targets, use of these pathways may also grow. A recent working group determined that enhancements to the Accelerated Approval pathway will help to ensure continued benefit from this program as medicines and drug development evolve.[xiv] **Sec. 307 of the *Cures 2.0 Discussion Draft* remedies some unforeseen impediments to sponsors, which will allow them to gain Accelerated Approval designations for investigational drugs if they meet proper criteria.**

TITLE IV: CENTERS FOR MEDICARE & MEDICAID SERVICES

PMC is interested in additional opportunities to modernize coverage and reimbursement processes at CMS that could ensure patient access to personalized medicine.

In recent years CMS made national coverage determinations for types of technologies versus a product-by-product basis, such as for next-generation sequencing diagnostic tests used in advanced stages of cancer. Given the rapid pace of innovation and the challenges in securing coverage or reimbursement for some technologies, **we believe the GAO report to Congress from the Comptroller General on recommendations to enhance Medicare coverage and reimbursement for innovative health technologies proposed in Sec. 401 of the *Cures 2.0 Discussion Draft* would identify opportunities to improve interagency collaboration and communications under the Medicare program, specifically between CMS and the FDA, as well as other opportunities to streamline the coverage process.**

Sec. 401 could be improved by defining "innovative technologies," which should include cell and gene therapies, individualized therapies, clinical decision support and patient management algorithms and platforms, and new biomarker tests, among others. Since the initial evidence base for novel technologies may be more limited, this report should apply to innovative technologies that "may" increase access to health care, improve health care quality, decrease expenditures or otherwise improve the Medicare program or health care for beneficiaries. Furthermore, similar to our earlier comments on Sec. 305 in the *Cures 2.0 Discussion Draft* that FDA's and CMS' decision-making processes should remain distinct, we encourage Sec. 401 to clarify that improved interagency coordination should not be interpreted to include activities that would lead to coordinating approval and coverage decisions or to changing the agencies' respective remits.

Despite the consensus that personalized medicine approaches have significant value, their implementation – and consequently patient access – across the United States is highly variable.[xv] Telehealth can improve patients' access to personalized medicine by making it easier for a patient to connect with a health care provider, including providers a patient would not normally have access to at their current health care institution, to discuss appropriate treatment and prevention options, which may involve diagnostic testing. For example, genetic tests used to assist in medication selection for patients with depression have demonstrated improved patient outcomes[xvi] and reduced costs.[xvii] Telehealth also has the potential to mitigate barriers that disproportionately impact individuals from minority, low-income, and rural communities, and may be especially helpful for individuals who have to travel long distances to a provider or may face logistical or other challenges to accessing care in-person, such as the stigma often associated with seeking mental and behavioral health care. Finally, Congress' temporary expansion of Medicare beneficiaries' access to telehealth services during the coronavirus public health emergency has played a critical role in ensuring the continuity of care for patients.

PMC therefore supports the inclusion of Sec. 403 in the *Cures 2.0 Discussion Draft* that would allow the Secretary of HHS to permanently expand telehealth flexibilities and remove Medicare's geographic and originating site restrictions, which require a patient to live in a rural area and be physically in a doctor's office or clinic to use telehealth services. PMC also appreciates that this provision includes language requiring the Secretary of HHS to consult with stakeholders on services that are clinically appropriate via telehealth.

However, before modifying coverage policies that may remove or limit patient access to telehealth services currently covered under the public health emergency, such as policies for ordering testing services via telehealth, PMC believes the Secretary should first consult with stakeholders, including through public notice and comment rulemaking. PMC recognizes that in some instances additional oversight may be required to ensure the appropriate use of telehealth and prevent fraud, but no additional requirements should create additional burdens on patients. Instead, oversight requirements should focus on monitoring provider deployment of telehealth services.

PMC also encourages Sec. 403 to include Medicare coverage for audio-only telehealth services and to allow reciprocity between states in telehealth licensure requirements. We believe patients should have full access to telehealth services and the ability to choose the type of visit most appropriate to their circumstances, whether that is by video, audio or in-person. Audio-only telehealth services can benefit beneficiaries facing broadband access or other technological issues that may create challenges for conducting video-based telehealth visits. Expanding coverage for audio-only visits would minimize these barriers and ensure as many Medicare beneficiaries as possible can benefit from access to telehealth services. State reciprocity in licensure requirements would also make it easier for health care providers located near state borders to deliver telehealth services to their nearby patient populations, which may be split across state lines, and easier for patients to access remote second opinions from out-of-state providers or consult with, for example, genetic counselors on their genetic test results.

PMC has strongly supported CMS' recent efforts to establish a Medicare Coverage for Innovative Technologies (MCIT) pathway that would extend coverage for breakthrough devices immediately upon the date of FDA approval for up to four years. For devices addressing areas of unmet medical need,

which may include diagnostic and screening tests underpinning personalized medicine, the newness of the device, and in some cases small patient population sizes, can create challenges to gathering the clinical evidence needed for coverage and reimbursement determinations, subsequently increasing the time between introduction to the market and patient access. **We support the inclusion of Sec. 404 in the *Cures 2.0 Discussion Draft* that would codify a transitional coverage and payment pathway for breakthrough devices under the Medicare program, including for "specified" breakthrough devices that do not fall into a defined Medicare benefit category.** Creating this pathway would mitigate the upfront evidence burden required to meet the current coverage standard and allow for additional evidence collection while addressing patients' unmet medical needs. The transitional pathway proposed in the *Cures 2.0 Discussion Draft* would create an opportunity for timely Medicare coverage of breakthrough devices, including in vitro diagnostic (IVD) test kits as well as laboratory-developed tests (LDTs) in the event a laboratory voluntarily seeks breakthrough designation and clearance or approval from FDA.

However, Section 404 should be amended to clarify that breakthrough devices to be covered include not only devices for "treating indications," but also for "informing treatment of indications," to ensure that personalized diagnostics are included. As Congress finalizes the *Cures 2.0 Discussion Draft,* PMC believes the pathway outlined in Sec. 404 should not be changed to include provisions that can be construed as a requirement for laboratories to seek FDA approval as a necessary precondition for Medicare coverage of all tests either within or outside of the pathway, nor should the pathway be expanded to apply to drugs or biologicals.

Digital health technologies play a key role in advancing personalized medicine by generating data from individuals in a real-world setting. This information can be used with other data sources to generate RWE informing coverage and payment decisions, future medical product development, and treatment decision-making. **We support the inclusion of Sec. 405 of the *Cures 2.0 Discussion Draft* that would require the Secretary of HHS to submit a proposal to Congress on how to provide coverage and payment for digital alternatives to treatment, including wearables and digital applications and platforms.** We believe this provision complements other regulatory proposals in the *Discussion Draft* advancing digital health and would help prepare CMS for the future as patients assume a larger role in managing their own health care and are more informed by their ability to access their personal data, including their genomic information.

Since 2017, PMC has supported legislative efforts to establish a demonstration project identifying ways in which genetic and genomic testing can be better utilized to improve patient outcomes. We appreciate your inclusion of Sec. 407 in the *Cures 2.0 Discussion Draft* to expand access to diagnostic testing for some pediatric patients with rare diseases. Many rare disease patients experience lengthy delays in receiving diagnoses and treatments necessary for their diseases. Federal support for coverage of DNA sequencing clinical services for children on Medicaid who have unresolved diseases with suspected genetic causes will enable patient access to services that would otherwise be financially out of reach. **Sec. 407 should be expanded to include whole genome sequencing, whole exome sequencing, and multigene panel testing as DNA sequencing clinical services eligible for coverage under this section. Furthermore, the services to be evaluated should include not only those that improve the diagnosing of rare diseases, but also those that improve appropriate treatment selection. In**

addition, the National Academy of Medicine study and report should require consultation with the clinical laboratories that will be performing many of the services that are the subject matter of the report.

Cures 2.0 presents an opportunity to expand access to personalized medicine for patients outside of the pediatric rare disease community as well. For example, genetic and genomic testing can improve health outcomes for individuals with cancer by detecting genetic mutations earlier and informing treatment. Consider that a recent study found that of the more than 300,000 patients diagnosed with breast cancer in the United States each year, 10 percent of cases have hereditary causes. Between 50 and 80 percent of those individuals at risk have not received genetic testing, in part because insurance seldom reimburses for their cases. In addition to improving patients' diagnoses, the results of diagnostic testing are increasingly relevant for informing treatment.[xviii] **If feasible, the language in Sec. 407 should address barriers to diagnostic testing and targeted therapy more broadly.**

Certain personalized medicine tests, called pharmacogenomic tests, predict which medications at which doses will be most effective and safest for individuals based on their genetic makeup and known drug-gene interactions.[xix] This information can help guide the safe application of medicines for many health conditions, including drug selection and dosing. For example, one case study in retirees over age 65 found that leveraging pharmacists' expertise to recommend medication changes based on patients' genetic information and known pharmacogenomic implications resulted in a 17 percent reduction in cost-to-plan spending and a 29 percent reduction in hospitalizations.[xx] Another study found that combining information from pharmacogenomic testing with provider access to related clinical decision support tools led to a decrease of about 40 percent in hospitalizations, a reduction of about 70 percent in emergency department visits, and reduced health care costs.[xxi] Given the important role of these and other tests in personalized medicine, **PMC supports the inclusion of Sec. 408 in the *Cures 2.0 Discussion Draft* that would provide Medicare coverage for personalized medicine consultations between a beneficiary's health care provider and qualified clinical 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.

In addition to the current provision, we support adding to Sec. 408 the text of H.R. 2144, the *Access to Genetic Counselor Services Act*, in its entirety. Genetic counselors are specifically educated, trained and qualified to provide consultations about genetic tests and their appropriate uses and applications in personalized medicine. In some cases, genetic counselors may be better positioned than clinical pharmacists to provide the consultations needed. For example, they are trained to help patients understand their genetic information and the implications of their genetic test results on their medical conditions, levels of health risk, and the health of their families. PMC believes it is important to involve both clinical pharmacists and genetic counselors in delivering personalized medicine to patients.

Since drug-gene interactions can have varying levels of evidence supporting their validity and to ensure providers understand which drugs have pharmacogenomic information included in their FDA-approved label, PMC would also support the addition of language in Sec. 408 requiring clinical pharmacists, genetic counselors, and/or other accredited experts to mention in their "genomic precision medicine consultations" with providers which drug-gene interactions are or

are not included in a treatment's FDA-approved label and if not included in a treatment's FDA-approved label, to describe the basis for any consultations on drug-gene interactions, such as guidelines of the Clinical Pharmacogenetics Implementation Consortium (CPIC) that may be based on more current evidence than the FDA-approved label.

To further assist providers in implementing personalized medicine, PMC would also support expanding Sec. 408 to include coverage for the use of clinical decision support tools and consultations with other experts beyond pharmacists and genetic counselors, like pathologists. This provision could be expanded beyond genetic and genomic tests to include consultations on interpreting any kind of diagnostic test result that reveals information about the underlying pathways for a disease and could thereby improve the selection of appropriate treatment or prevention approaches.

TITLE V: RESEARCH

Decades of research on the genetic and biological underpinnings of disease has made it possible to develop new personalized medicine treatments for cancers as well as rare, common, and infectious diseases. Foundational advances in genetic and genomic technologies also paved the way for scientists' rapid response to COVID-19. The progress we have seen, from mRNA vaccine development, diagnostic testing, and variant sequencing, to beginning to understand how human genomic variation influences infectivity, disease severity, vaccine efficacy, and treatment response, relies on years of personalized medicine research.[xxii, xxiii]

PMC believes creating the proposed Advanced Research Projects Agency for Health (ARPA-H) as a distinct division within the National Institutes of Health (NIH) and with a unique culture and organization that embraces the risk of failure and fosters collaborations similar to those we have seen throughout the COVID-19 pandemic and during the Human Genome Project has the potential to significantly benefit patients and the health care system by expediting the development and application of new personalized medicine technologies. **PMC therefore supports the interest from Congress in establishing President Biden's proposed ARPA-H under the placeholder in Sec. 501 of the *Cures 2.0 Discussion Draft* that would help drive transformational innovation in health research and speed the application and implementation of health breakthroughs.**

NIH investigator-led research generates fundamental knowledge about the molecular basis of a disease and points to pathways for developing new treatments and potential cures. Thus, diligently investing in NIH research is key to bringing us closer to a future in which every patient benefits from an individualized approach to health care. **PMC shares some stakeholders' concerns that funding ARPA-H could ultimately reduce appropriations to NIH for traditional basic and translational research. We believe that forming priorities for ARPA-H that are distinct from NIH's existing centers and institutes will help avoid this tradeoff.**

Some have raised specific concerns about ARPA-H's potential overlap with NIH's National Center for Advancing Translational Sciences (NCATS). NCATS develops, demonstrates, and disseminates innovations that reduce, remove or bypass costly and time-consuming bottlenecks in translational

research. This research leads to the more predictable and successful development of new medical interventions, such as drugs, diagnostics, and medical devices, for all human diseases. **To minimize overlap, NACTS should continue to focus on supporting a national network of clinical research centers, and other pivotal projects around platform technologies, gene therapy, and others. In addition, NCATS' broad portfolio is critical to rare diseases, and as the only dedicated place for rare disease research in NIH, the Office of Rare Disease Research should not be compromised moving forward. Meanwhile, ARPA-H could focus on initiatives that require sustained and extensive cross-sector collaborations, novel partnerships, and significant upfront capital. ARPA-H leaders should also coordinate with the directors of the Biden Cancer Moonshot and *All of Us* Research Programs established in the original *21st Century Cures Act* to avoid duplication.**

Despite advances in the science behind personalized medicine and efforts to modernize the United States' regulatory and reimbursement systems to foster this approach to care, including many of the provisions outlined in the *Cures 2.0 Discussion Draft*, challenges to implementing personalized medicine remain across health care delivery settings.[xxiv, xxv] Realizing the full potential of personalized medicine requires a paradigm shift in how our health care system provides care to patients. **We think ARPA-H could help understand and address these clinical integration challenges by prioritizing implementation research as it relates to personalized medicine.**

Transparency, sustained stakeholder engagement, and the incorporation of diverse perspectives, including the perspectives of stakeholders from underserved communities, will be key to building patient trust around any new technologies. PMC therefore appreciates the Administration's suggestion that equity considerations be woven throughout ARPA-H's mission and that APRA-H have a senior leader who can ensure that issues of equity are considered in all aspects of ARPA-H's work.[xxvi] **ARPA-H's design should emphasize transparency and patient engagement throughout the research process to ensure the agency develops technologies that improve patient care in ways that are meaningful to them. Patients and other health care stakeholders, including providers, health care administrators, payers, industry representatives, and representatives of other federal agencies, should be involved in identifying ARPA-H's research priorities. Program managers should also engage patients and other health care stakeholders throughout the research and development process.**

We appreciate Congress' request for information from stakeholders on shaping this provision and encourage Congress to provide additional opportunities to review the legislative text establishing ARPA-H.

Conclusion

Thank you for releasing the discussion draft and for considering our comments. PMC welcomes the opportunity to serve as a resource for you as you continue the *Cures 2.0* effort to ensure it can support the ongoing development and delivery of personalized medicine products and services for all patients. If you have any questions about the content of this letter, please contact me at 202-499-0986 and cbens@personalizedmedicinecoalition.org or David Davenport, PMC's Manager of Public Policy, at 804-291-8572 and ddavenport@personalizedmedicinecoalition.org.

Sincerely yours,

Cynthia A. Bens
Senior Vice President, Public Policy

---

[i] Representative Diana DeGette and Representative Fred Upton. *Discussion Draft: Cures 2.0*. June 21, 2021. https://degette.house.gov/sites/degette.house.gov/files/Cures%202.0_DISCUSSION%20DRAFT.pdf?_cldee=Y2JlbnNAcGVyc29uYWxpemVkbWVkaWNpbmVjb2FsaXRpb24ub3Jn&recipientid=contact-11b930a79e5a48a98a8ee0b217e795da-a7b01da44d8e44a8899fd55531655594&esid=0786fb00-26df-eb11-a2f1-000c2959e3d7.

[ii] Charles River Associates. *The Benefits of Personalized Medicine to Patients, Society and the Healthcare System: Final Report*. Prepared for the European Biopharmaceutical Enterprises and the European Federation of Pharmaceutical Industries and Associations. July 6, 2018. https://www.ebe-biopharma.eu/wp-content/uploads/2018/07/CRA-EBE-EFPIABenefits-of-PM-Final-Report-6-July-2018-STC.pdf.

[iii] Personalized Medicine Coalition. *More Than a Number*. September 20, 2020. https://www.genomecreative.com/mtan/.

[iv] Personalized Medicine Coalition. *Advancing Personalized Medicine Through Inclusive Biomedical Research.* April 22, 2021. https://www.youtube.com/watch?v=SXtPVd9sJ98.

[v] Kathy Giusti and Richard Hamermesh. *You Can't Have Precision Medicine if You Still Have Disparities.* https://www.hbs.edu/kraft-accelerator/assets/pdf/HBSKraft2021Disparitieswhitepaperv6.pdf. Accessed July 13, 2021.

[vi] Eastern Research Group, Inc. *Assessment of the Used of Patient Experience Data in Regulatory Decision-Making*. June 18, 2021. https://www.fda.gov/media/150405/download

[vii] University of California, San Francisco. *The Elements of Personalized Medicine*. https://precisionmedicine.ucsf.edu/digital-health. Accessed December 13, 2019.

[viii] Personalized Medicine Coalition. *Personalized Medicine at FDA: The Scope and Significance of Progress in 2020.* February 11, 2021. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC_The_Personalized_Medicine_Report_Opportunity_Challenges_and_the_Future.pdf.

[ix] Personalized Medicine Coalition. *Personalized Medicine at FDA: The Scope and Significance of Progress in 2020.* February 11, 2021. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_The_Scope_Significance_of_Progress_in_2020.pdf.

[x] U.S. Food and Drug Administration. *FDA Continues Strong Support of Innovation in Development of Gene Therapy Products*. January 28, 2020. https://www.fda.gov/news-events/press-announcements/fda-continues-strong-support-innovation-development-gene-therapy-products.

[xi] U.S. Food and Drug Administration. *FDA Continues Strong Support of Innovation in Development of Gene Therapy Products*. January 28, 2020. https://www.fda.gov/news-events/press-announcements/fda-continues-strong-support-innovation-development-gene-therapy-products.

[xii] U.S. Food and Drug Administration. *Real-World Evidence*. https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence. Accessed December 13, 2019.

[xiii] Ariel Kantor and Susanne Haaga. "The Potential Benefit of Expedited Development and Approval Programs in Precision Medicine." *Journal of Personalized Medicine*. January 11, 2021. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7828670/.

[xiv] Friends of Cancer Research. *Optimizing the Use of Accelerated Approval*. November, 2020. https://friendsofcancerresearch.org/sites/default/files/2020-11/Optimizing_the_Use_of_Accelerated_Approval-2020.pdf.

[xv] Arushi Agarwal et al. "A Quantitative Framework for Measuring Personalized Medicine Integration into US Healthcare Delivery Organizations." *Journal of Personalized Medicine*. Vol. 11(3):196. March 12, 2021. https://doi.org/10.3390/jpm11030196.

[xvi] John F. Greden et al. "Impact of Pharmacogenomics on Clinical Outcomes in Major Depressive Disorder in the GUIDED trial: A Large, Patient- and Rater-Blinded, Randomized, Controlled Study." *Journal of Psychiatric Research*. Vol. 111: 59-67. April, 2019. https://doi.org/10.1016/j.jpsychires.2019.01.003.
[xvii] Joachim Benitez, Christina L. Cool, and Dennis J. Scotti. "Use of Combinatorial Pharmacogenomic Guidance in Treating Psychiatric Disorders." *Personalized Medicine*. Vol. 15(6). November, 2018. https://doi.org/10.2217/pme-2018-0074.
[xviii] Peter D. Beitsch et al. "Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle?" *Journal of Clinical Oncology.* November 2, 2018. https://pubmed.ncbi.nlm.nih.gov/30526229/.
[xix] Personalized Medicine Coalition. *The Personalized Medicine Report: Opportunity, Challenges, and the Future*. 6th edition. November 17, 2020. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC_The_Personalized_Medicine_Report_Opportunity_Challenges_and_the_Future.pdf. Accessed July 9, 2021.
[xx] Coriell Life Sciences. *Case Study: Teachers' Retirement System of Kentucky*. https://www.coriell.com/wp-content/uploads/CLS-Case-Study-TRS-04.pdf. Accessed July 8, 2021.
[xxi] D. Brixner et al. "The Effect of Pharmacogenetic Profiling With a Clinical Decision Support Tool on Healthcare Resource Utilization and Estimated Costs in the Elderly Exposed to Polypharmacy." *Journal of Medical Economics*. Vol. 19(3). November 11, 2015. http://dx.doi.org/10.3111/13696998.2015.1110160.
[xxii] Joshua C. Denny and Francis S. Collins. "Precision Medicine in 2030 — Seven Ways to Transform Healthcare." *Cell*. Vol. 184(6): 1415-1419. March 18, 2021. https://doi.org/10.1016/j.cell.2021.01.015.
[xxiii] Eric D. Green et al. "Strategic Vision for Improving Human Health at the Forefront of Genomics." *Nature*. 586: 683–692. October 28, 2020. https://doi.org/10.1038/s41586-020-2817-4.
[xxiv] Arushi Agarwal et al. "A Quantitative Framework for Measuring Personalized Medicine Integration into US Healthcare Delivery Organizations." *Journal of Personalized Medicine*. Vol. 11(3):196. March 12, 2021. https://doi.org/10.3390/jpm11030196.
[xxv] Personalized Medicine Coalition. *Understanding Genomic Testing Utilization and Coverage in the US.* June, 2020. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC_Understanding_Genomic_Testing_Utilization_and_Coverage_in_the_US2.pdf. Accessed July 13, 2021.
[xxvi] Francis S. Collins et al. "ARPA-H: Accelerating Biomedical Breakthroughs." *Science.* Vol. 373(6551): 165-167. July 9, 2021. https://science.sciencemag.org/content/373/6551/165.