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DECEMBER 16, 2019

VIA E-MAIL – cures2@mail.house.gov

The Honorable Diana DeGette
U.S. House of Representatives
2368 Rayburn House Office Building
Washington, DC 20515

The Honorable Fred Upton
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

Re: Cures 2.0 Call to Action

Dear Representative DeGette and Representative Upton:

The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciates the opportunity to provide comments in response to your request for proposals for consideration as part of Cures 2.0. PhRMA is a voluntary nonprofit organization representing the country's leading research-based biopharmaceutical companies, which invest more than $90 billion a year in the research and development of new treatments and potential cures for patients. PhRMA members are dedicated to developing medicines that allow patients to live longer, healthier, and more productive lives.

PhRMA appreciates the opportunity to offer recommendations to achieve our shared goal of modernizing coverage and payment policies to support patient access to new medical advances. Our comments address opportunities to advance the use of digital health tools and real-world evidence (RWE) as well as to promote interoperability and evolve coverage and payment policies for breakthrough therapies, including potentially curative therapies.

Potential public policies in each of these areas are discussed in more detail below.

Advancing the Adoption of Digital Health Tools

Digital technologies are creating new opportunities to modernize health care and empower patients to make more informed decisions about their health. In fact, digital tools have already begun to transform the biopharmaceutical research and development (R&D) process and health care delivery system in myriad ways—including by increasing access to clinical trials, enabling efficient information exchange, accelerating biopharmaceutical R&D and delivery of new treatments, enhancing clinical decision making, and furthering patient engagement. Below we discuss proposals related to the use of digital health tools to improve adherence and patient outcomes and several proposals to accelerate adoption and use of digital tools in the R&D process.

Enhancing the use of digital health technologies to improve adherence and patient outcomes

While progress has been made in adopting digital health technologies, more can be done to harness the full power of these platforms. Digital health tools have the potential to improve clinical outcomes for patients by reducing barriers to adherence, facilitating better use of diagnostics, and improving the post-marketing monitoring of the safety of our medicines. Medicines can lead to life-changing health outcomes for patients but only with appropriate and timely diagnosis and prescribing, prompt initiation of therapy, patient adherence to the treatment regimen, and periodic review of the medication regimen.

As we look to the future of digital health, it will be important to ensure that public policies facilitate its use in the most meaningful and impactful ways. For example, while medicines can lead to life changing health outcomes for patients, the full benefits can only be achieved through optimal treatment adherence. Medication non-adherence costs the health care system hundreds of billions of dollars each year and makes up 7 to 13 percent of all health spending in the U.S.[1] One study found that 45 percent of Medicare beneficiaries with diabetes fail to fill new prescriptions, while 60 percent of beneficiaries with chronic obstructive pulmonary disease (COPD) are non-adherent.[2] Better adherence to treatment regimens can lead to improved patient outcomes, including reductions in hospitalization and physician visits, while providing better health outcomes and improved quality of life for patients. For example, one study found that improved adherence to diabetes medications was associated with 13 percent lower odds of subsequent hospitalizations or emergency department visits. Based on these findings, researchers project that improved adherence to diabetes medication could avert 699,000 emergency department visits and 341,000 hospitalizations annually, for savings of $4.7 billion.[3] Another study of 55,000 COPD patients showed that a 5 percent increase in adherence would lead to a 2.6 percent reduction in hospital visits and a 1.8 percent reduction in emergency department visits.[4]

Digital tools can improve adherence by decreasing patient burden by making it easier for patients to track their dosing schedules, remember when to take their medication, and allow them to easily share relevant medical information with their health care provider(s). Through an interoperable health care system, these data also can be transmitted among a patient's health care team care for review to assess whether any adjustments in the patient's treatment plan are warranted. Once received, patients and their care teams can utilize shared decision making to make decisions about the most appropriate diagnostics, treatment regimens, and monitoring to support improved care. This type of shared decision making can be achieved more quickly and easily with the use of digital technologies. We encourage Congress to direct the Government Accountability Office or the Department of Health and Human Services (HHS) to assess and provide recommendations on the potential of digital health tools to improve adherence and lead to better health outcomes for patients. Congress also should encourage HHS to engage with stakeholders across the health care system to ensure we are harnessing the full

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[1] Prescriptions for a Healthy America. A Treatable Problem: Addressing Medication Nonadherence by Reforming Government Barriers To Care Coordination." October 2017. https://static1.squarespace.com/static/589912df1b10e39bd04eb3ab/t/59f0e439edaed84e6822d9bd/1508959306380/P4HA+WhitePaper+E-DigitalFinal+1017.pdf

[2] Ibid.

[3] Jha, A. et al. "Greater Adherence to Diabetes Drugs is Linked to Less Hospital Use and Could Save Nearly $5 Billion Annually." Health Affairs. https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2011.1198

[4] Van Bove, JFM, et al. "Clinical and economic impact of non-adherence in COPD: A systematic review." *Respiratory Medicine*, https://www.sciencedirect.com/science/article/pii/S0954611113003648

potential of digital health tools. We encourage Congress to direct HHS to engage with stakeholders to identify potential coverage and access barriers related to the adoption and use of digital health tools, particularly given their potential to improve patient outcomes, and to identify potential changes in coverage and payment policies to facilitate use of the full range of digital tools.

Improving interoperability

Biopharmaceutical manufacturers are committed to contributing to the meaningful advancement of health care data flow. PhRMA is therefore a strong supporter of the advancement of clinical and claims interoperability. However, the co-existence of different systems with varying quality standards, formats, and minimum data sets creates challenges to achieving interoperability. As mentioned above, improved interoperability can play a key role in fostering coordination of care and improving patient adherence to treatment regimens. A more interoperable system could result in increased efficiencies and advance patient engagement. Congress should encourage HHS to work with the biopharmaceutical industry, academia, and other relevant stakeholders to support interoperability to facilitate the sharing of information that can lead to improved patient outcomes.

PhRMA also supports policies to increase patient access to accurate and easily understood data that are relevant to their health care needs and which helps them make better-informed decisions about their care. Therefore, we urge Congress to direct HHS to prioritize policies that will advance technologies that provide consumers with meaningful information that facilitates their participation in their care (e.g., information on cost sharing and benefit structure). Congress should encourage HHS to prioritize the development and implementation of patient-centric tools to facilitate patient engagement in health care decision-making, including prioritization of the development of real-time benefits tools (RTBTs). RTBTs could facilitate more meaningful conversations and shared clinical decision making between patients and their providers to improve patient outcomes, reduce health care provider burden, and ultimately generate savings across the health care system. Standardization efforts are necessary to move the nation's health care system forward in a new, highly digitized era. For information to be shared more efficiently, health information systems and technologies must share common processes and frameworks. Therefore, as part of its efforts to advance clinical and claims interoperability, Congress should direct the Center for Medicare and Medicaid Services (CMS) to identify and address key barriers to implementation of RTBTs.

Increasing the application of digital technologies to expedite drug development and enhance regulatory decision making

Applying digital health to biopharmaceutical R&D (referred to as digital R&D) and the FDA-regulated lifecycle of a product is beginning to positively impact biopharmaceutical development. Thanks to advancements in science and technology, the biopharmaceutical industry is leveraging the potential of digital R&D to improve drug development and speed access to those products. Digital R&D is rapidly evolving with the potential to reduce barriers to innovation for novel medical products and therapeutics. Artificial intelligence/machine learning (AI/ML) and connected devices and sensors represent the most commonly leveraged technologies for digital R&D.

From a regulatory perspective, the current framework for medical products presents many challenges to innovation in the digital health space. For example, unlike many other medical products, digital health technologies may constantly update and iterate, “learning” from prior experience. How these continual updates, improvements, and iterations fit within the current regulatory framework is currently unclear

in many respects. Moreover, digital health technologies incorporating AI/ML may present questions as to the appropriate validation to support use. For example, AI/ML tools afford sponsors the ability to analyze large data sets, including safety-related adverse event information, to identify safety signals and better protect the public health. However, there is uncertainty as to how the use of tools may factor into regulatory decision making.

Digital R&D tools hold great promise in the area of clinical trials—spanning the full spectrum of trial design, trial operation and data collection—but those technologies are also being used in areas such as the discovery R&D processes, in manufacturing, and post-approval (for example, in the pharmacovigilance space). As understanding of science and digital technology advances, the regulatory uncertainty and need for a modern flexible regulatory approach is increasing. While rapid integration of digital technologies is occurring, there is an opportunity to expedite and increase use of digital technology throughout the medical product lifecycle by addressing regulatory uncertainty (e.g., addressing validation of technologies and the acceptance by regulators of digitally derived data).

Congress should urge the FDA to prioritize evolving the regulatory framework to allow biopharmaceutical companies to harness the full potential of digital R&D approaches. Specifically, Congress should encourage FDA to accelerate:

- Establishment of a flexible and scalable global framework for digital technology development, validation and usage in the R&D process, with appropriate collaboration and engagement with other regulators to help encourage global harmonization.
- Development of a consistent regulatory approach to digital R&D across all the FDA centers.

Modernizing the FDA's data/information technology (IT) infrastructure

Large-scale benefits from digital technologies will only be accomplished in tandem with a regulatory, policy, and IT landscape that keeps pace with the rapidly evolving, scientific and technological aspects of digital R&D. A modern vision and regulatory and strategic technology framework are needed for a compatible and interoperable, modern data/IT infrastructure, supported by better tools for assessing how digital technologies can be best used in R&D to unlock the full potential of digital R&D for the benefit of patients.

Modernizing and enhancing the FDA's on-going technological advances will be needed to help FDA scale its data/IT infrastructure. The size of datasets used for regulatory decision making is growing exponentially through digital health technology tools, RWE, and patient registries. However, current FDA processes are not suited to transfer this amount of data efficiently. Data and IT modernization is necessary to support initiatives such as dynamic/cloud-based submissions and review. Congress should encourage FDA to work with the biopharmaceutical industry and other stakeholders to develop and finalize a formal and holistic modernization framework that includes provisions on how data requirements will be deployed and managed throughout the regulatory lifecycle. Such work could build upon FDA's recently introduced Technology Modernization Action Plan.

Advancing the use of RWE to support regulatory decisions

In the 21st Century Cures Act, Congress included important provisions to encourage and facilitate the use of RWE in regulatory decision-making. The statute required FDA to establish a program to evaluate the potential use of RWE to help support the approval of a new indication for an approved medicine and to

help support or satisfy post-approval study requirements. In accordance with this requirement, FDA was required to conduct a pilot program and issue guidance to help inform industry and provide regulatory clarity and predictability. FDA issued the required RWE framework in December 2018, outlining a multifaceted approach, which will include "demonstration projects, stakeholder engagement, internal processes to bring senior leadership input into the evaluation of RWE and promote shared learning and consistency in applying the framework, and guidance documents to assist developers interested in using real-world data (RWD) to develop RWE to support Agency regulatory decisions."[5]

Congress intended for FDA to consider RWE's potential to help satisfy or meet the "substantial evidence" requirement. Substantial evidence is defined in statute as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect" specified in the labeling.[6] To fulfill the promise of the 21st Century Cures Act, Congress should encourage FDA to provide additional guidance on how studies using RWE—in the appropriate regulatory context-of-use—can be "adequate and well-controlled" and be sufficient to meet the existing "substantial evidence" standard, including addressing the need to consider RWE in the context of the totality of evidence.

Advancing coverage and payment policy reforms to support emerging technologies

PhRMA appreciates that the initial vision for Cures 2.0 aims to recognize not just the incredible promise of emerging biopharmaceutical advances to save and improve the lives of patients, but the importance of payment policy reforms to unleash this innovation and ensure that new therapies benefit patients as quickly as possible. Because cell and gene and other breakthrough therapies hold great potential to transform care, payment policies should reflect the potential added value of these therapies to the health care system and to patients. Below we provide some detailed policy recommendations that we believe would improve the current new technology add-on payment with a focus on creating a methodology and system that supports patient access to new and innovative therapies.

Evolving Medicare's payment system to support patient access to breakthrough therapies

Ensuring adequate payment for emerging therapies will provide a foundation for the continued advancement toward the availability of expanded treatment options to address unmet medical needs for patients diagnosed with serious, life-threatening diseases. New payment models and mechanisms should be explored to create a level playing field among institutions and to support patient access to new therapies. Adequate reimbursement for emerging therapies is particularly crucial for patients in rural areas, or patients who might not be able to travel long distances because of their condition. Emerging science is proving challenging for existing payment models, and reimbursement for CAR T-cell therapies is a leading example of how current bundles may be inhibiting patient access.

PhRMA appreciates the steps CMS has taken to date to recognize the value of these therapies by including approval of New Technology Add-on Payments (NTAP) for existing CAR T-cell products and increasing the percentage associated with NTAP payments for all therapies so that hospitals

[5] Food & Drug Administration. Framework for FDA's Real-World Evidence Program. December 2018. https://www.fda.gov/media/120060/download.

[6] 21 U.S.C. 355(d).

are not "underwater" when administering breakthrough treatments. However, even with this adjustment, to receive the full payment amount from CMS for current and future therapies, hospitals will still have to increase charges to ensure that the percentage payment they receive covers the acquisition cost of the therapy.[7] We believe that the need to substantially mark up the charges associated with administering therapies or risk financial losses may deter hospitals from providing these services to Medicare patients, and is a likely explanation for the relatively small share of qualified delivery sites that are currently using CAR T to treat Medicare patients outside of clinical trials. Congress should encourage the agency to build on these steps through further payment reform, particularly for treatments that are only available in the inpatient setting, in the following ways:

- In the 2020 Inpatient Prospective Payment System (IPPS), final rule, CMS created a new NTAP pathway for transformative medical devices, stating that if a medical device is approved or cleared with FDA Breakthrough Device designation, the product would be considered new and not substantially similar to existing technology, and therefore eligible for a NTAP. PhRMA recommends that Congress direct CMS to make the same pathway available for medicines that have been approved through FDA's Breakthrough Therapy process, given the high bar that treatments must also meet to obtain a Breakthrough Drug designation. This will help ensure patients are not subject to needless delays to treatments that FDA has deemed of major clinical importance.

- Under IPPS, Medicare pays for a patient's inpatient hospital stay under one bundled payment, which covers all costs for acute care services performed. Although drugs, devices, and supplies typically fall under this bundled payment, there is an exception to this rule, known as new technology add-on payments (NTAPs). When certain criteria are met, CMS may provide additional payment for new, high-cost technologies in the inpatient setting. The NTAP provides additional payment to hospitals above the standard Medicare Severity Diagnosis-Related Group (MS-DRG) payment amount. NTAP payments are the lesser of 65 percent of the amount by which the total covered costs exceed the MS-DRG payment, or 65 percent of the costs of the new technology. PhRMA appreciates CMS recently raising this percentage from 50 in the 2020 IPPS payment rule, however, Congress should urge CMS to consider an additional increase which would ensure that hospitals are able to continue to provide life-saving treatments to Medicare beneficiaries.

- To foster continued biomedical breakthroughs, PhRMA also urges Congress to direct CMS to remove the cost-to-charge ratio (CCR) from the NTAP calculation to provide for a uniform maximum NTAP for all future medicines that receive NTAP status. The application of hospital-specific operating CCRs to estimate costs and calculate NTAPs under the "lesser of" criterion usually results in CMS underestimating the costs incurred by providers in a course of treatment, which leads to hospitals being underpaid for providing certain treatments—which can have particularly negative consequences for adoption of and access to transformative advancements.

Medicare patient access to all cell and gene therapies is at risk if hospitals and health care providers are not adequately reimbursed. While the recommendations above will help provide continued access for treatments administered in the inpatient setting, Congress should encourage CMS to examine innovative ways to ensure Medicare beneficiaries receive the life-saving benefits of future advances.

[7] MedPAC. March 2016 Report to Congress. Medicare Payment Policy. www.medpac.gov/docs/default-source/reports/chapter-3-online-only-appendixes-hospital-inpatient-and-outpatient-services-march-2016-report-.pdf

Future therapies may be administered in the hospital outpatient or physician office settings, similar to physician-administered medicines covered by Medicare Part B, and additional reforms may be necessary to ensure access.

Removing barriers to value-based contracting arrangements

PhRMA strongly supports efforts to remove regulatory barriers to expanding value-based arrangements.[8] By aligning payments for medicines more directly with their value in improving meaningful health outcomes and/or reducing the need for other health care services (such as hospitalizations), value-based arrangements make biopharmaceutical manufacturers accountable for the results their medicines achieve in a more concrete way and can help improve patients' health and maximize the benefits of health care spending.[9] Value-based arrangements have demonstrated these benefits across a wide range of conditions, including spinal muscular atrophy, asthma, COPD, and cardiovascular disease.[10] PhRMA recommends that Congress direct CMS and the HHS Office of Inspector General (OIG) to continue to revisit outdated regulations and guidance developed for a fee-for-service world. In particular, the federal Anti-Kickback Statute and government price reporting rules should be examined to determine how they are limiting the number, scale and types of these arrangements, specifically as related to value-based contracts for medicines.[11]

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PhRMA appreciates the opportunity to share our ideas to improve care delivery and modernize coverage and access to life-saving cures. Please feel free to contact us if we can provide additional information or if you have any questions about the topics discussed in our comments.

Sincerely,

Stephen J. Ubl
President & CEO

[8] PhRMA. Long-awaited FDA guidance addresses one key obstacle to value-based contracting. June 2018. https://catalyst.phrma.org/long-awaited-fda-guidance-addresses-one-key-barrier-to-value-based-contracting.

[9] PhRMA. Delivering Results for Patients: The Value of Value-Based Contracts. February 2018. https://www.phrma.org/en/Report/Delivering-Results-for-Patients-The-Value-of-Value-Based-Contracts

[10] See for example, FiercePharma. Novartis, Spark gene therapies win a boost with soup-to-nuts Cigna coverage. September 2019. https://www.fiercepharma.com/pharma/cigna-gives-gene-therapies-novartis-and-spark-a-boost-comprehensive-payment-plan; Gavidia, M. Outcomes-Based Contract Between Highmark, AstraZeneca Reveals Positive Results for Patients With Asthma and COPD. AJMC Managed Markets Network. https://www.ajmc.com/newsroom/outcomesbased-contract-between-highmark-astrazeneca-reveals-positive-results-for-patients-with-asthma-and-copd.

[11] Goodman, C., et al. Regulatory, Policy, and Operational Considerations for Outcomes-Based Risk-Sharing Agreements in the U.S. Market: Opportunities for Reform. Journal of Managed Care & Specialty Pharmacy. November 2019. https://www.jmcp.org/doi/10.18553/jmcp.2019.19167