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The Honorable Diana DeGette
United States House of Representatives
2111 Rayburn House Office Building
Washington, DC 20515

The Honorable Fred Upton
United States House of Representatives
2183 Rayburn House Office Building
Washington, DC 2051

RE: 21st Century Cures 2.0 Discussion Draft

Dear Representatives DeGette and Upton,

On behalf of the Alliance for Aging Research (the "Alliance"), we applaud your commitment to improving medical research and healthcare delivery in the United States. The Alliance was honored to provide input on, and support passage of, the 21st Century Cures Act. Our organization advocated for the $10 billion increase in NIH funding, the NIH provisions for young and emerging scientists to encourage careers in medical research and adjust loan repayments, and creation of the Inclusion Across the Lifespan effort. To advance clinical development at the FDA, we've advocated for funding to support the qualification and use of drug development tools, the provision to modernize trial design and real-world evidence development, the section to develop a new FDA pathway for antibiotic drug development, the establishment of priority review for medical devices, and the FDA workforce provisions to enhance hiring and retention at the agency.

We appreciate your continued passion for clinical and regulatory science, and your dedication to ensuring it is as well-funded, efficient, and meaningful as possible for the patients and families it is supposed to help. We enthusiastically support the 21st Century Cures 2.0 (Cures 2.0) effort and appreciate the opportunity to provide comments on several provisions in the discussion draft and how they could best serve the needs of older adults.

Sec. 104 Vaccine and Immunization Programs

The Alliance is supportive of the bill's efforts to fund educational activities on 1) the importance of vaccinations and 2) data collection on immunization activities. In addition to these activities, we recommend that your offices explore extending the Pharmacy Partnership for Long-Term Care (LTC) Program, a Centers for Disease Control and Prevention (CDC) initiative that offers on-site vaccination of residents and staff at LTC facilities. The COVID-19 pandemic has delayed routine healthcare for many Americans due to a combination of an overwhelmed healthcare system and patient fears of contracting COVID-19. A June 2021 analysis from Avalere found that adults in the markets studied (commercial healthcare, managed Medicaid, Medicare Advantage, and Medicare FFS) missed an estimated 17.2 million doses of recommended vaccines from January to November 2020 compared to

vaccination levels over the same period in 2019. **The Alliance suggests that the CDC explore expanding and utilizing the Pharmacy Partnership program for all long-term care communities and for older adults and people with disabilities living at home and in community-based settings.**

The Alliance also supports the investment that Cures 2.0 would make in infrastructure to support ongoing immunization efforts and combat future pandemics. The ability to exchange immunization information across multiple jurisdictions through the Immunization Information Systems (IIS) will improve immunization rates by informing healthcare providers of appropriate CDC-recommended vaccines for a patient given their previous vaccination history.

Sec. 105 PASTEUR Act

The Alliance has publicly supported the Pioneering Antimicrobial Subscriptions to End Up surging Resistance (PASTEUR) Act, which establishes a subscription model to pay for novel antimicrobial products while providing funding for hospitals to develop stewardship programs. Unfortunately, most large pharmaceutical companies have suspended novel antibiotic research and development, while at the same time, existing antibiotics are losing their efficacy due to inappropriate and overprescribing. This legislation decouples sales from a company's ability to recover investment in the product, providing a pathway to correct a market failure that disincentives companies from investing in antibiotic research and development.

Sec. 203 Increasing Diversity in Clinical Trials

The Alliance supports legislative efforts to increase diversity and the representation of older adults in clinical trials. We are encouraged by the provisions within Cures 2.0, including funding for a study on barriers to clinical trial participation, funding a public awareness campaign, and establishing a long-overdue redesign of clinicaltrials.gov to make the website more patient and user friendly. However, we encourage consideration of additional efforts to better address the needs of older adults in the development and evaluation of medicines. Our biology changes as we age as metabolism and immune system responses wane. The rate of decline, the onset of comorbidities, and the use of medications vary from person to person and functional status widely differs through the biological aging process. Accordingly, it is important to ensure medications used by older adults are studied appropriately on older adults throughout the medical product lifecycle.

The first 21st Century Cures Act directed the National Institutes of Health (NIH) to collect data on the inclusion of participants in clinical research studies by age and convene a workshop focused on the inclusion of pediatric and older adult populations in clinical research. The Inclusion Across the Lifespan policy applies to all NIH grant applications on or after January 2019. The policy requires NIH-sponsored trials to develop a plan for including individuals across the lifespan and justify any exclusions based on age. The NIH's Scientific Review Groups assess applications for whether they meet this requirement, and NIH may seek additional information and determine if the plans need revision. Funding awards will not be granted until concerns are resolved. **The Alliance would like Cures 2.0 to include a requirement for the U.S. Health and Human Services (HHS) Secretary and the FDA Office of the Commissioner to convene a similar workshop to develop an Inclusion Across the Lifespan policy for industry-sponsored trials.**

Sec. 304: Increasing Use of Real-World Evidence

The enhancement of real-world evidence in regulatory decision-making is a key priority for the Alliance. Older adults are too often excluded from clinical trial due to arbitrary age restrictions and exclusion criteria that often prohibits participation by individuals with one or more co-morbid conditions. Yet, according to the CDC, about 85 percent of older adults have one chronic disease and 60 percent of older adults have two or more chronic conditions. Therefore, real-world evidence is a crucial source of data for understanding a medical product's safety and efficacy profile on older adults.

The Alliance is supportive of requiring the HHS Secretary to issue guidance on how to evaluate the safety and effectiveness of drugs that received breakthrough therapy, fast track, or accelerated approval designations, as well as the creation of an inter-agency Task Force to provide periodic recommendations on how to engage patients in real-world evidence generation.

Furthermore, the Alliance strongly recommends that Cures 2.0 include language to increase transparency and access to patient registries. Patient registries have the potential to help inform—and play an essential role in—decision-making in science, development, and testing of new therapies and devices, and subsequent payment policy for innovations in treatment and care.

Currently, the Centers for Medicare & Medicaid Services (CMS) often includes participation in a patient registry as a condition of coverage for hospitals performing a service—in essence, an additional "condition of participation" specific to receiving reimbursement for a particular service. Specialty societies apply to develop and run these registries and usually charge participating providers annual fees. Input on the health outcomes information collected in the registries is determined by an advisory board appointed by the specialty society. The specialty societies also own the registry data, with control over who can access and what types of analyses may be conducted using the data, for which societies may impose an additional charge. Industry must also pay for use of the registry data, even though their FDA-approved medical product is the reason why the registry exists.

CMS uses the information contained in these registries to determine coverage and payment policy. Yet, CMS has no direct access to the data and no enforcement over whether their registry-related evidence questions are answered at all, let alone within a set period. The specialty societies also determine whether and when annual analyses of the data collected are published. As a result, such Coverage with Evidence Development (CED) national coverage decisions (NCD) may drag out for a decade or more with no definitive end. It is financially profitable for the specialty societies to continue the registries, but prolonged reliance on private data registries with little ability to ensure registries report data necessary to finalize a NCD without CED is not in beneficiaries' interest. These registries are being used specifically to inform Medicare coverage decisions yet exist outside public access. Transparency and accessibility are essential for the public, policymakers, and patients to have confidence in the data and the process.

The Alliance believes that Cures 2.0 should empower CMS with open CED registry data access, the ability to limit charge amounts by specialty societies for provider registry participation, the enforcement authority to sanction registry managers if evidence questions are not answered in a reasonable timeframe, and decision-making authority over the types of analyses the specialty societies and outside researchers may conduct using the data.

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

The Alliance endorses the inclusion of Section 306 in the discussion draft of Cures 2.0, which would create two new inter-center institutes within the Food and Drug Administration (FDA). We believe that these can be modeled after the successful Oncology Center of Excellence, which has helped accelerate the development and review of oncology products while keeping patients at the center of regulatory decision-making.

The Alliance convenes the Accelerate Cures/Treatments for All Dementias (ACT-AD) coalition, which was founded in 2005 with the mission of being a focal point of advocacy for organizations to weigh in with the FDA on issues impacting the research and development of Alzheimer's disease and other forms of dementia. Our organization is well-versed in the difficulties of bringing new safe, and effective therapies to treat neurological disorders, such as Alzheimer's disease and other dementias. These conditions have an enormous burden both financially and emotionally on families throughout our country. There is a disquieting absence of disease-modifying therapies within this disease space. Additionally, the cost of conducting clinical trials for neurological disorders and the high failure rate of therapeutics in the space further adds to the burden of bringing new treatments to patients.

Accordingly, the Alliance believes one of the Intercenter institutes that would be established by Section 306 should be designated as a Neuroscience Center of Excellence within the FDA. Such a Center would consolidate FDA expertise across the review divisions and enable a more efficient process in reviewing new neuroscience products and guidance creation.

Sec. 403 Extending Medicare Telehealth Flexibilities

CMS waivers for geographic and originating site restrictions to telehealth services during the COVID-19 public health emergency have been vital to supporting continuity of care. In many cases, these waivers have removed barriers to telehealth that unnecessarily impeded care access, including the limitation of eligibility for telehealth only to beneficiaries in rural areas. For many beneficiaries, telehealth can address challenges for beneficiaries that have limited mobility, emergent behavioral health needs, or access to specialists for ongoing care needs. The Alliance supports the continuation of waivers of geographic restrictions.

However, for some conditions, diagnostics and an initial in-person consultation are necessary to ensure accurate diagnosis and care plan development. In these cases, telehealth could be offered for maintenance visits after an initial in-person visit. **We support the Secretary consulting with both beneficiaries and clinicians to determine conditions for which telehealth is most likely to provide benefit, as well as when during the course of care telehealth is most clinically appropriate.**

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

The FDA's breakthrough status allows expedited review for devices that provide "more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions."[1] These devices often provide a

[1] U.S. Food and Drug Administration. Breakthrough Devices Program. 16 May 2019. https://www.fda.gov/medical-devices/how-study-and-market-your-device/breakthrough-devices-program#s1

treatment option when no clear alternatives exist or that have significant advantages over existing treatments. In many circumstances, a breakthrough device may deliver a therapeutic pathway for a patient when pre-existing technologies for an indication are not clinically appropriate.

For patients that have a life-threatening or irreversibly debilitating condition, time is of the essence. However, the current national coverage decision (NCD) and local coverage decision (LCD) pathways typically are completed nine to twelve months after an FDA market authorization.[2] For Medicare patients that would benefit from an FDA-approved breakthrough device, this interim period can have real-world impacts on rates of long-term complications and mortality.

The Alliance supports CMS's proposal to begin Medicare coverage upon FDA approval for breakthrough devices and provide a coverage period of up to four years**.** Further, **we support the provision in Cures 2.0 requiring HHS to identify additional data and evidence necessary to establish a national coverage policy within one year and a pathway to permanent coverage approval within two years for FDA-approved breakthrough devices.**

Sec. 501. Advanced Research Projects Agency for Health

The Alliance is generally supportive of the Cures 2.0 provision that would create an Advanced Research Project Agency for Health (ARPA-H). ARPA-H, if appropriately funded and managed, could bolster existing federal biomedical research and development. However, the creation of such an agency should augment the investigator-led work at the NIH and other public health agencies rather than supplanting ongoing efforts. There is concern among the research advocacy community about the potential for ARPA-H to divert funding from the traditional biomedical research model in the United States. Therefore, creating an ARPA-H necessitates parallel increases for basic research elsewhere in the federal biomedical research system. **We recommend that appropriators consider measures to ensure ARPA-H funding and NIH funding remain balanced.**

We agree with NIH Director Francis Collins that the mission of ARPA-H should be to "make pivotal investments in breakthrough technologies and broadly applicable platforms, capabilities, resources, and solutions that have the potential to transform important areas of medicine and health for the benefit of all patients and that cannot readily be accomplished through traditional research or commercial activity." When considering the type of projects that ARPA-H should fund, the focus of the new agency should be on funding potentially transformational research that, for one reason or another, does not fit within the traditional model. For example, ARPA-H could fund breakthrough projects that may be too costly or have a longer duration than supported under the conventional model. It should also support research in which complex coordination between federal agencies is required.

Additional Consideration: CMS Coverage with Evidence Development Reform

We urge your offices to include a section in Cures 2.0 that would create unique statutory authority requirements for CMS' Coverage with Evidence Development (CED) process. Because CED falls under the NCD statutory authority, there is no specific enforcement mechanism to ensure timely research reporting compliance, which results in an ad hoc process that leaves Medicare beneficiaries in a state of uncertainty regarding their treatment.

[2] Centers for Medicare and Medicaid Services. CMS-3372-P: Medicare Program: Medicare Coverage of Innovative Technology and Definition of Reasonable and Necessary. Federal Register. Vol. 85, No. 170. 1 September 2020. https://www.govinfo.gov/content/pkg/FR-2020-09-01/pdf/2020-19289.pdf

In an August 2011 article, "Improving the Quality and Efficiency of the Medicare Program Through Coverage Policy," the authors state, "The current authority is sufficiently ambiguous to prevent CMS from fully developing and implementing coverage with evidence development consistently and systematically."[3]

CMS should be required to clarify what specific evidence is needed to close a CED and provide a timeline for collection of evidence. In its 2014 guidance on CED, within the section "Ending CED," CMS states that the purpose of the studies is to "produce evidence that will lead to revisions in Medicare coverage policies," and cites two examples of completed CED processes—NCDs for oncologic uses of fluorodeoxyglucose positron emission tomography and ventricular assist devices. The implication here is that there would be a clear beginning and end to the CED process.

The "Ending CED" section further states that "a CED cycle is considered completed when CMS completes a reconsideration of the CED coverage decision and removes the requirement for study participation as a condition of coverage." However, CED requirements for study participation have often been continued well beyond the time evidence questions are answered. **Cures 2.0 should require that CMS establish milestones and a targeted end date for CED when utilized in coverage determinations.**

Conclusion

Thank you for considering our views and for the extensive effort you have devoted to developing this discussion draft of Cures 2.0. These provisions would constitute clear advances for patient care and innovation. If you have additional questions on our recommendations, please do not hesitate to contact the Alliance's Vice President of Public Policy, Michael Ward, at mward@agingresearch.org.

Sincerely,

Michael Ward, MS
Vice President of Public Policy

Ryne Carney
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[3] https://www.urban.org/sites/default/files/publication/27516/412392-Improving-the-Quality-and-Efficiency-of-the-Medicare-Program-Through-Coverage-Policy.PDF.