August 2, 2024

The Honorable Representatives Diana DeGette and Larry Bucshon, M.D.
U.S. House Committee on Energy and Commerce

*Submitted electronically to cures.rfi@mail.house.gov*

Dear Representatives Bucshon and DeGette,

Thank you for the opportunity to provide policy considerations as you develop legislation that builds on the 21st Century Cures Act. Arnold Ventures is a philanthropy dedicated to investing in evidence-based policy solutions that maximize opportunity and minimize injustice. Our work in health care is driven by the recognition that the system costs too much and fails to adequately provide access for the people it serves. We aim to strengthen innovation through stronger U.S. Food and Drug Administration (FDA) approval standards, greater clinical trial transparency, and accountability into FDA reviews of clinical data, as well as assuring that insurance coverage reflects available clinical evidence. We advance these strategic priorities through research, policy development, technical assistance, advocacy, and education.

The 21st Century Cures Act was sweeping legislation that touched on a variety of issues related to biomedical research. Arnold Ventures' comments focus on two sets of issues: (1) real-world data (RWD) collection to formulate real-world evidence (RWE), and (2) evidence generation through executive agency coordination.

**Real World Data and the Formulation of Real-World Evidence**

The 21st Century Cures Act accelerated consideration of new uses of RWD to generate RWE. This means that FDA can consider, for example, studies of patient health data from administrative sources such as electronic health records in real-world settings when assessing risks and benefits of medical technologies. However, we do not believe that RWE can replace randomized trials because such studies lack the necessary scientific or statistical analysis required to determine whether a medical product is effective. Researchers have found that there is limited ability to replicate clinical trials using RWE.[i] FDA later studied and confirmed that among 589 drug approvals, 339 had end points that could not be reliably measured in administrative claims data.[ii] These results show that the lack of rigor in RWD collection, which is the basis of RWE, adds uncertainty to understanding which patients will benefit most from a new technology.

There are already documented concerns surrounding the quality and strength of evidence used by FDA at the time of medical product approval.[iii,iv,v] Nearly half of physicians (47%) believe that the FDA threshold for drug approval has fallen in the past 5 years.[vi] We are concerned that if policymakers indicate a willingness to have RWE become one of the main sources used by FDA to determine whether new medical products are effective, then evidence standards would be weakened further. The consequence of weak or unavailable evidence is that it shifts the cost of further research on product safety, effectiveness, and durability onto patients and the health care system.

We do believe that the collection of RWD for studies of RWE can inform and improve clinical trial design, conduct, and analysis when used to:

i. Study the course of disease to inform clinical trial design;

ii. Understand the standard of clinical care to inform diverse clinical trial participant recruitment; and
iii. Compile post-market data on adverse events to inform post-approval safety surveillance.

Without reliable evidence at the time of FDA approval, payers such as the Medicare program which currently covers 67.3 million older people and people with disabilities,[vii] cannot determine whether (1) a product's benefits are outweighed by their harms and (2) results are generalizable to the Medicare population. The next section explores several policy solutions to bolster evidence generation.

**Clinical Evidence Generation**

Congress can build on the 21st Century Cures Act through efforts that enhance coordination throughout the Department of Health and Human Services (HHS), but specifically between regulatory functions at FDA and coverage functions at The Centers for Medicare & Medicaid Services (CMS). FDA and CMS have separate and distinct statutory authorities. FDA approves medical products when they are determined "safe and effective" for their intended use. After FDA approval, CMS determines if Medicare coverage of a new medical product is "reasonable and necessary". Each agency's distinct but complementary authorities can serve as an important system of checks and balances that can lead to more robust data collection on clinical outcomes. This can result in patients and providers having access to better information when determining the right treatment options.

With enhanced authority from Congress, FDA can apply even more scientific and clinical rigor to evaluate and confirm clinical benefits of new medical products, particularly for drugs in the accelerated approval program and devices with breakthrough designation. This includes more consistent use of scientific and clinical expertise from advisory committees to inform the technical aspects of drug development and safety. The advisory committee meetings promote transparent data analysis and could be strengthened to more conclusively demonstrate that benefits to patients outweigh both known and potential risks. Finally, Congress must continue to hold FDA accountable for continuously monitoring research on drug products after approval to assure the durability of assumptions on the safety and effectiveness of a drug in real-world settings of care.

The Medicare population deserves appropriate access to medical products that improve health outcomes. In the post-FDA-approval setting, Medicare would benefit from additional tools to make more reasonable and necessary determinations of drug uses for chronic conditions.[viii] This includes more resources to perform comparative effectiveness studies that will enable regular updates to national coverage decisions, as well as generate more evidence that an FDA-approved product meaningfully improves health outcomes for Medicare beneficiaries. These enhancements can build sustainable processes for both agencies to generate information that fosters better coordination that results in the delivery of better health outcomes.

**Conclusion**

Thank you again for the chance to comment and for your consideration of potential policy levers to address clinical evidence generation. Arnold Ventures welcomes being a resource to you as you work to develop federal policies that address these issues. This letter was prepared by Katherine Szarama Ph.D., Director of Health Care with support from Andrea Noda, MPP, Vice President of Health Care and Mark E. Miller Ph.D. Executive Vice President of Health Care.

Please contact Mark E. Miller at mmiller@arnoldventures.org or Andrea Noda at anoda@arnoldventures.org with any questions.

Sincerely,

Andrea Noda

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[vi] Dhruva, S.S., Kesselheim, A.S., Woloshin, S., et al., Published January 2024 at https://doi.org/10.1377/hlthaff.2023.00466.
[vii] Medicare Monthly Enrollment, Accessed August 2024 at https://data.cms.gov/summary-statistics-on-beneficiary-enrollment/medicare-and-medicaid-reports/medicare-monthly-enrollment.
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