Thought Leaders in Precision Medicine:  
Fulfilling the Potential of the All of Us Research Program for Populations that are Historically Underrepresented in Biomedical Research  

February 7, 2018  
Washington, DC  

BRIEFING DOCUMENT  

The Challenge  

Improving the health status of populations historically underrepresented in biomedical research (HUBR) has long been recognized as both a desirable and a feasible objective. Unfortunately, the indisposition of individual research sponsors to identify study cohorts of sufficient size and diversity to power statistically significant findings has stymied efforts to redress healthcare inequities for these populations. A paradigm shift is imperative: a fundamental redesign of the American health services research, delivery and financing system so that it can assign value to the content and outcomes of healthcare for American children, American families, and American business. The All of Us Research Program can be an invaluable resource in that endeavor.

Annual reports issued by the US Agency for Healthcare Research and Quality have documented the failure of the American health services research, delivery and financing sector to implement effective, sustained change. Reports issued by the NHS R&D Health Technology Assessment (HTA) Programme for the United Kingdom’s National Health Service, and by the Baylor College of Medicine Eliminating Disparities in Clinical Trials (EDICT) Project, have addressed this challenge, as well. The HTA report, *The causes and effects of socio-demographic exclusions from clinical trials* notes: “In general, the exclusion from trials of those who are seen as ‘different’ or would require increased resources to be included…cannot be defended ethically and is against the principle of wide inclusion criteria to maximize generalizability of trial findings.” The HTA report also notes, “Under-representation occurs, but in drug trials at least this may not always affect the external validity of relative effect estimates. However, measures of absolute effect size, absolute harm and cost-effectiveness are associated with underlying risk levels in different socio-demographic groups. Under-representation will therefore bias absolute effect estimates.”

*Major Deficiencies in the Design and Funding of Clinical Trials*, issued by EDICT in April 2008, reports, “When it comes to the makeup of clinical trials, the National Institutes of Health requires that women and members of minority groups be included in all NIH-supported biomedical and behavioral research projects involving human subjects. Despite this requirement, little measurable improvement has been made in increasing clinical trials participation in such populations.” Most importantly, the EDICT report states, “Under-representation of specific populations in clinical trials is also at direct odds with the current state of medical science and
drug discovery. With the successful sequencing of the human genome, scientists are faced with
the new challenge of documenting, describing, and understanding the non-random pattern of
human genetic variation and its link to disease risk in different patient groups. Findings from the
large amount of genetic data generated to date show that more than 90 percent of the observed
genetic variations occur within rather than between groups. This underscores the fact that
ethnicity — which incorporates multiple variables including genetics, economic, social, dietary,
religious, and linguistic background — has biomedical consequences when studying health
outcomes.”

The long-anticipated demographic shift of the US population has reached the tipping point. It has
been predicted for decades that by the first quarter of the 21st century, approximately 40% of the
US population will be composed, collectively, of racial and ethnic population groups that have
been classified as “minorities”; by 2050, these groups will constitute at least 50% of the
population. In some cities and geographic areas, this demographic shift is already the reality.
Given the relatively younger ages of the “minority” population groups, it can be assumed that an
increasing percentage of the American work force and school age children will be members of
population groups that are currently classified as non-Hispanic single race Caucasian.

Persistent health status and health care quality gaps exist between the non-Hispanic White
majority and the other race or ethnic population cohorts in the U.S. These gaps include
substantially higher rates of acute and chronic diseases, premature mortality, and documented
disparities in the quality of care provided. Yet, as a rule, when national health policy has been
deliberated and promulgated, the implications for America’s emerging biodiverse majority have
been largely ignored. The legacy of this inattention is a health services research, delivery and
financing system that is unable to meet the needs of the American healthcare consumers who
invest in the system through taxes, insurance premiums, and out-of-pocket expenditures. The
evidence of this inability is found in scientific research that is skewed toward a diminishing
majority, in quality metrics that ignore patient variability, in health care policies that promote
inequalities, in differences in reimbursement that systemically under-compensate providers who
treat emerging populations, and in poor health outcomes and medical errors for an increasing
number Americans.

The All of Us Research Program offers an innovative and unique pathway to the imperatives of
the 21st century. All of Us has the potential to inform the efforts required to redress the
fundamental misalignment between our past and our future. Realizing that potential, however,
requires structured and continuous input and guidance from the clinical, advocacy and policy
leadership that is committed to maximized, measurable health outcomes among populations that
have historically not been included in biomedical research. We must engage. In the 21st century,
we cannot build effectively if we are hobbled by the incomplete foundation of science and
evidence grandfathered in from the 20th century.
Tapping into the Potential of the *All of Us* Research Program

The *All of Us* Research Program, directed by the National Institutes of Health, is a nationwide, longitudinal research effort that aims to improve the ability of the American health care system to prevent and treat disease based on individual differences. *All of Us* is the cornerstone of the Precision Medicine Initiative, which was authorized by the 21st Century Cures Act and launched in 2015. The primary objective of *All of Us* is to engage at least one million volunteers living in the US to contribute their health data over many years to improve health outcomes, fuel the development of new treatments for disease, and catalyze a new era of evidence-based and more precise preventive care and medical treatment. Participants will share information over many years in a variety of ways, through surveys, electronic health records, physical measurements, blood and urine samples, and wearable technologies. The *All of Us* Research Program will also transform how research is done through the development of authentic partnerships with researchers and participants, who will control how they participate and how the data are used.

The *All of Us* database will be one of the world’s largest and most diverse data sets for precision health research — an unprecedented resource that can be an invaluable resource to inform the development of new evidence and science-based approaches to measure risk for a range of diseases based on environmental exposures, genetic factors, and interactions between the two; identify the causes of individual differences in response to commonly used drugs (commonly referred to as pharmacogenomics); discover biological markers that signal increased or decreased risk of developing common diseases; and develop new disease classifications and relationships.

*All of Us* is currently in the beta-testing phase, with full launch anticipated in Spring 2018. NIH, through the *All of Us* program leadership, is currently seeking input through different channels to explore scientific opportunities, and chart future directions for the *All of Us* Research Program.

**Thought Leaders Meeting Discussion and Recommendations**

The National Minority Quality Forum is partnering with *All of Us* through the Community Influencer Initiative that is coordinated by HCM Strategists. This first Thought Leaders in Precision Medicine Roundtable is a product of that partnership. It will enable the discussants to enhance their understanding of the *All of Us* Research Program, and to develop a set of recommendations that will be communicated to the *All of Us* leadership in a written report. Presenters will address the *All of Us* research design, inadequacies of current approaches to obtaining data and information to support biomedical research, and anticipated barriers to access for biomedical researchers. The facilitated discussion will enable participants to develop specific recommendations to eliminate these barriers that will be included in the formal report that will be sent to the *All of Us* Research Program no later than February 28, 2018.
Suggested Discussion Questions are included here to trigger a robust exchange and a broad range of recommendations:

- What are the desired outcomes for the All of Us Research Program? What three things must All of Us accomplish to enhance health research and the quality of care available for HUBR populations and communities? What opportunities for All of Us are particularly intriguing?

- What steps are being taken to achieve representative diversity? What are the inclusion criteria for participants? Is there a limit on the total number of participants?

- When will the information in the All of Us database be available for use by academic and/or commercial researchers? Will priority be given to certain categories of researcher or All of Us partner (public, private, not-for-profit)? Will access to the All of Us database be available without constraints or costs? Will the research questions or protocols be subject to review or approval before access is granted? If yes, by whom?

- How have the protections outlined in the Common Rule been factored into the All of Us research protocol?

- As researchers, clinicians and advocates, what are our concerns regarding our ability to access or use the All of Us data set? What steps can All of Us take to address those concerns?

- Do our institutions and organizations have the capacity to incorporate into clinical or applied research the type of data that the All of Us Research Program will collect? If not, what additional capacity is needed in our communities, institutions, or organizations?

- Are there particular participant characteristics (e.g., disease classification, phenotype, genotype, state/county/zip code of residence, age, sex, gender) that we believe must be included to support research projects that yield statistically significant results for HUBR populations?

- Is there anything that All of Us can or should do to create incentives for research that will accrue to the benefit of populations that are historically underrepresented in biomedical research? What should All of Us do to facilitate the translation of that research into therapeutic options that are reimbursable by CMS and/or commercial insurers?

If you have any questions or comments regarding this Briefing Document or the Thought Leaders in Precision Medicine Roundtable, please contact Gretchen C. Wartman, Vice President for Policy and Program, National Minority Quality Forum, at gwartman@nmqf.org.