Society for Women's Health Research

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

Re: 21st Century Cures 2.0 Discussion Draft and ARPA-H RFI

Dear Representatives DeGette and Upton:

On behalf of the Society for Women's Health Research (SWHR), I appreciate the opportunity to provide comments on the 21st Century Cures 2.0 discussion draft and request for information (RFI) on the Advanced Research Projects Agency for Health (ARPA-H). For over 30 years, SWHR has promoted research on biological sex differences in disease and improving women's health through science, policy and education. Because of SWHR's advocacy efforts, women are now routinely included in most major medical research studies, and scientists funded by the National Institutes of Health (NIH) are required to consider sex as a biological variable (SABV) in their research. SWHR is committed to ensuring researchers consider the unique needs of women across all areas of health care.

Cures 2.0 presents an opportunity to continue the original legislation's legacy in furthering women's health. We encourage you to consider a national, collaborative and prioritized approach to an investment in women's health. Women often serve as the chief medical decisionmaker in their families, take on the role of primary caregivers in their families, and as we have seen during the global health pandemic, are bearing the burden of family care, school, and are experiencing higher levels of stress than ever before. A comprehensive approach to women's health that explores health across the lifespan would benefit the entire population.

As SWHR previously commented, we ask that Cures 2.0 prioritize research that includes all women. Specifically, we ask that you ensure that the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) has adequate authority and resources to implement PRGLAC's recommendations, that the NIH has adequate resources to implement its the 2019-2023 Trans-NIH Strategic Plan for Women's Health Research, which focuses both on research broadly (see pp. 12-14) and research methodology (pp. 16-18), and that establishes incentives that encourage financial investment in women's health research across public and private sectors.

Further, we echo the Women First Research Coalition's request to engage with the National Academy of Medicine (NAM) to conduct a study on gaps in women's health research, and provide $1.5 million dollars to support this work. The NAM study should look at research of a wide range of conditions affecting women's health across the lifespan, such as maternal mortality, cancer, and chronic conditions, including menopause and cardiovascular disease. This study could be designed to explore the proportion of research on conditions that are more common or unique to women as well as those that differently or disproportionately impact women, establish how these conditions are defined, evaluating sex and gender differences and racial health disparities, and determine the appropriate level of funding that is needed to address gaps in women's health research. Historically, there has been an inadequate representation of minority women as both researchers and research participants. The NAM is well

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suited to ensure standardized data points, definitions and common data points to women's health research, with an eye toward women's health across the lifespan.

We offer the following specific comments to the discussion draft:

Section 101. Further Understanding the Implications of Long COVID. We appreciated the inclusion of better understanding the implications of Long COVID, and urge the recognition of the biological sex differences in Long COVID that are being observed. Research has suggested that anywhere from 10-30% of those who contract COVID-19 will experience prolonged effects, including fatigue, headache, difficulty breathing, and loss of smell. Although men are at greater risk of more severe symptoms and death from COVID-19, studies have suggested that women are more vulnerable to prolonged autoimmune-related symptoms following COVID-19. A hospital in Paris saw about 30 COVID long haulers a week from May to July 2020, with the average age of 40 and a ratio of 4:1 women to men. A study from King's College in London found that women ages 50-60 were at highest risk for sustained COVID symptoms. Another study published in early March also identified women as more likely to become long haulers. A Mayo Clinic physician who leads post-COVID syndrome research recently said about 60% to 80% of COVID-19 long hauler patients there were women. In addition to experiencing long COVID at a higher rate, women may also face a wider range of symptoms, including menstrual health issues.

Section 101(b) of the Cures 2.0 discussion draft directs the Secretary of HHS to convene a series of national meetings to serve as the basis of an ongoing long-COVID learning collaborative with individuals and organizations representing key sectors of the health care community. Due to the known sex differences that have been described above, we ask that you include experts in sex differences research as well as women's health who can contribute to the learning collaborative in a meaningful way.

Section 102. National Testing and Response Strategy for Future Pandemics. SWHR appreciates the inclusion of provisions related to future pandemics. It will be critical that legislation stipulate a uniform standardized data collection strategy that requires the collection of comprehensive data from patients testing positive for the disease as well as those who receive tests but test negative for the disease; that tracks sex differences in deaths, symptoms, risk factors, and virus exposure, and that includes information about pregnancy status and response to the virus.

Section 104. Vaccine and Immunization Programs. Vaccine education and awareness is paramount, and we urge you to ensure that public education and community outreach programs on vaccines and immunizations are culturally appropriate and relevant, and include multiple perspectives, including that of women as the chief medical decisionmaker of the family.

Sec. 201. Educational programs and training for caregivers. SWHR supports the inclusion of programs and training for caregivers, particularly from the perspective of caregivers' growing role in health care.

Section 203. Increasing Diversity in Clinical Trials. SWHR was founded on the idea that women and minorities were not being included in clinical trials. Although much progress has been made in terms of including women in trials, women of color and those from historically excluded populations must be built into the trials process from the beginning. Removing barriers to inclusion in addition to a cultural shift that promotes a willingness to volunteer for biomedical research endeavors will be critical to ensuring cures, innovations in treatment and can only be done if the trial population reflects the

treatment population. Such diversity efforts should include race, ethnicity, geography, life stage/age and socioeconomic status.

During the COVID-19 pandemic, there was a significant delay in getting pregnant and lactating women included in the COVID-19 vaccine trials. This was due in part to poorly justified concerns about the safety of medications and vaccines during pregnancy. For the duration of the COVID-19 pandemic and during any future pandemics, every attempt should be made, based on sound scientific and clinical data, to include pregnant women in clinical trials designed to prevent the disease, and mitigate and gain a better understanding of its severity. When determining study design, pregnant and lactating women must be included at the outset.

Due to the original 21st Century Cures Act, the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) was established to provide a path forward on the inclusion of pregnant and lactating people in research. We urge you to continue this legacy and make sure that the recommendations and implementation plan of the PRGLAC Task Force is included in Cures 2.0.

Additionally, section 203(d) should include language to ensure that the established task force not only look at ways to make clinicaltrials.gov more user- and patient-friendly, but also to enhance participation from diverse populations, including pregnant and lactating women.

Section 204. Patient Experience Data. SWHR is supportive of efforts to include patient experience data as part of clinical trials. We encourage this provision to not only include the patient in the "patient experience," but also the caregiver's perspective as part of this effort. Women comprise more than half of the U.S. population and provide the majority of caregiving- nearly 70% of caregivers are female, and women assume multiple roles while caregiving: hands-on, case manager, companion, decision-maker and advocate. Further, women make more than 80% of health care spending decisions. This perspective should be included as a data point for patient experience.

Section 304. Increasing the Use of Real-World Evidence: SWHR appreciates efforts related to the increased collection of and use of real-world evidence in FDA's work. Specifically, we hope that the task force established under this proposal would include the caregiver perspective. The majority of caregivers are women, and this perspective is not one typically included in clinical trials, as well as pertinent evidence from stakeholders that may not be available in published literature. We look forward to seeing how this task force might incorporate this key perspective. Additionally, real world evidence should incorporate the perspective of women has chief medical decisionmaker within families.

Sec. 402. Strategies to increase Access to Telehealth under Medicaid and Children's Health Insurance Program (CHIP). SWHR supports efforts to incorporate telehealth into Medicaid and CHIP, particularly the provision for a study on telehealth's impact on health care access to include multiple datapoints including race, ethnicity, sex, age disability status and zip code. We hope that this will provide insight into women's health access and the impact of telehealth within the Medicaid program.

Section 403. Extending Medicare Telehealth Flexibilities. SWHR supports efforts to ensure access to telehealth services post-pandemic, and the inclusion fo the Telehealth Modernization Act in this legislation. Removing Medicare's geographic and originating sit restrictions permanently will offer greater access, choice and health services to women throughout the country. Unfortunately in the beginning of the pandemic women were delaying their routine care and other screenings. Telehealth helped ease some of this burden, and further allowed women to continue receiving services with

respect to primary care, gynecologic care, perinatal care, postpartum care, oncology, and others. Telehealth has made it possible for women regardless of their stage of life, location, health status or family/home situation to receive care without leaving their homes.

Section 407. Expanding Access to Genetic Testing. We applaud your work to increase access to genetic diagnostics, and encourage you to consider including access to genetic screenings for women who are considering becoming pregnant, like expanded carrier screening, or for those who are pregnant, like noninvasive prenatal screening. Noninvasive prenatal screening (NIPS) and expanded carrier screening (ECS), both forms of genetic screening, allow families to gain insight into the risk posed by certain heritable conditions.

Section 501. Advanced Research Projects Agency for Health

Advanced Research Projects Agency for Health (ARPA-H) Request for Information (RFI)

We also greatly appreciate the opportunity to respond to the questions in the RFI related to the ARPA-H initiative. the responses to which will help inform an authorization for ARPA-H originally proposed by the Biden-Harris Administration in the fiscal year (FY) 2022 budget request.

Despite the fact NIH has implemented policies related to sex as a biological variable as authorized by the 21st Century Cures Act, as well as stemming from the original 1993 law mandating the inclusion of women in clinical trials, significant gaps remain in our understanding of health conditions both specific to women or that disproportionately or differently affect women. Given the gaps in knowledge and research and rising public health crises where women are the focal point: uterine fibroids, maternal mortality, Alzheimer's Disease, cand cervical cancer, just to name a few, more must be done to prioritize women's health. Women's health is underfunded and there is little incentive for investment in women's health in certain areas. Given this, we offer the following comments on the RFI:

To ensure it has the biggest impact, on what activities or areas should ARPA-H focus? What activities or areas should ARPA-H avoid?
ARPA-H should support high-risk, high-reward projects that address cross-cutting priorities and the development of technologies and platforms which can benefit a wide variety of diseases and organs and should avoid replicating the organ system approach taken by the existing NIH institutes and centers which tends to provide greater benefits for high-visibility diseases and conditions. A. lifespan approach that investigates the whole-woman is essential to ensuring progress. ARPA-H has the potential to benefit areas of health and diseases that have not received robust funding, like many conditions unique to or more common in women. Additionally, it will be critical that ARPA-H adopt and implement the NIH's policies on sex as a biological variable (SABV) to ensure that any resulting discoveries can improve health on a broad scale.

Some assert ARPA-H's ability to operate independently and transparently will be essential to its success. Do you agree? If so, what is the best way to design ARPA-H in order to accomplish this?
ARPA-H represents a new biomedical research paradigm, and ensuring that ARPA-H is complementary and additive to NIH research will be critical. ARPA-H should share its research focuses, funding opportunities, review processes, and outcomes and incorporate opportunities for public input and comment to ensure transparency.

What is the appropriate funding level for ARPA-H? How do we ensure ARPA-H funding does not come at the expense of traditional funding for the National Institutes of Health?
ARPA-H funding should be complementary and separate from the existing NIH budget allocation, and should be proportional in increases to overarching NIH funding. The existing NIH Institutes and Centers play a critical role in improving human health as evidenced by the work done by the agency in the development of effective COVID-19 treatments and vaccines and this work must continue to receive robust, sustained support. The basic science supported by the agency are the foundation for the transformational work envisioned for ARPA-H and must remain along parallel tracks.

Section 502. Research Investment to Spark the Economy. SWHR appreciates the provision of $25 billion to independent research institutions, public laboratories and universities throughout the country. The authorization of $25 billion for pandemic-related research relief for independent research institutions, public laboratories, and universities will be invaluable throughout the country to support research that was interrupted due to the COVID-19 pandemic. We ask that you consider how to ensure that this investment will lead to direct improvements as well as to keep early-stage investigators in the biomedical research workforce.

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Thank you for the opportunity to provide comment on this important legislative proposal. It has great potential to move the needle forward in women's health. Should you have any questions or require additional information, please do not hesitate to contact SWHR's chief advocacy officer, Lindsey Horan, at lindsey@swhr.org.

Sincerely,

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