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May 19, 2020

The Honorable Diana DeGette
2111 Rayburn House Office Building
Washington, DC 20515-0601

The Honorable Fred Upton
2183 Rayburn House Office Building
Washington, DC 20515-2206

Dear Representatives DeGette and Upton:

The Society for Women's Health Research (SWHR) is pleased to provide initial comments in response to your recent concept paper, *21st Century Cures 2.0*. SWHR is a 30-year-old national nonprofit organization dedicated to promoting 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.

Here, we provide comments on the need for language on consideration of SABV in research and inclusion of women in clinical trials. We also provide feedback on the first section of the concept paper, titled "National Testing and Response Strategy for Current and Future Pandemics." We intend to follow up with considerations in other areas in the near future.

Language Focused on Sex Differences and SABV

SWHR applauds efforts to include specific language on sex and gender differences and SABV within upcoming Cures 2.0 legislation. SWHR strongly supports the use of research designs that 1) prioritize the representative inclusion of women and diverse patient populations, and 2) explore SABV in regard to patient outcomes and response to treatment. It is well-known that sex differences exist at all levels: cellular, molecular, and systems. Furthermore, it is understood that these differences affect response to treatment for a variety of drugs and biologics.

SWHR has long supported the idea that studying, analyzing, and reporting on sex differences should be standard practice across all research. Exceptions should only occur in

scientifically justified cases, such as when a study focuses on a sex-specific condition (e.g., pregnancy) or prior evidence suggests no sex differences exist. Improved transparency and consistency in reporting findings on sex differences will help to shed additional light on disparities.

The NIH Revitalization Act of 1993, signed into law on June 10, 1993, directed the NIH to establish guidelines for inclusion of women and minorities in clinical research. Statutory language on this topic can be found within PL 103-43 (Public Health Service Act sec. 492B, 42 U.S.C. sec. 289a-2):¹

Including information on SABV within research has been a focus area within the National Institutes of Health (NIH) since 2016. The NIH guidance document titled, "Consideration of Sex as a Biological Variable in NIH-Funded Research"² includes specific language on SABV:

NIH policy on the consideration of sex as a biological variable. Anticipated changes to FY2016 research grant applications, to be in effect for FY2017 funding, will include accounting for sex as a biological variable in the Research Strategy section. In this section, applicants are asked to "explain how relevant biological variables, such as sex, are factored into research designs and analyses for studies in vertebrate animals and humans." Furthermore, "strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex." Anticipated changes to review criteria will include evaluation of the adequacy of the research plan with regard to consideration of sex as a biological variable.

Your 21st Century Cures Act, PL 114-255, enacted in 2016, required NIH to provide guidance for reporting on sex differences within preclinical research. The statute further required that NIH consider, as appropriate, whether scientists and research institutions have complied with this reporting requirement when awarding any future grants, and that NIH encourage the reporting of the results of valid analysis through any additional means determined appropriate.

To expand and build upon these efforts on SABV, SWHR recommends that a second iteration of the Cures Act:

1. Includes language directing NIH to provide information regarding compliance with the above requirements laid out in the original Cures Act and an update on this process.
2. Uses NIH's definitions of sex and gender — as outlined in the NIH SABV guidance document — to ensure appropriate implementation of the original statutory requirement.
3. Makes the study of SABV a priority in federally funded research by expanding initiatives such as the NIH's Sex & Gender Administrative Supplement Program, which grants supplemental funding as an incentive to add a sex component to an existing research program.

¹ Public Health Service Act sec. 492B, 42 U.S.C. sec. 289a-2. Accessed at: <https://www.govinfo.gov/content/pkg/USCODE-2011-title42/pdf/USCODE-2011-title42-chap6A-subchapIII-partH-sec289a-2.pdf>

² National Institutes of Health (2016). Consideration of sex as a biological variable in NIH-funded research. Accessed at: https://orwh.od.nih.gov/sites/orwh/files/docs/NOT-OD-15-102_Guidance.pdf

The 21st Century Cures Act also emphasized the critical importance of women's participation in clinical trials.³ One way it achieved this was by establishing the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC). To date, insufficient attention has been paid to pregnant and lactating women, and the dearth of research means that these women and their health care providers lack the information needed to make knowledgeable decisions about medication use. PRGLAC's 2018 report to the Secretary of Health and Human Services and Congress⁴ includes specific recommendations related to the inclusion of pregnant and lactating women within clinical trials. The full PRGLAC implementation plan is expected in August 2020.

To continue to prioritize research that includes all women, SWHR recommends that a second iteration of the Cures Act:

1. Ensures the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) has adequate authority and resources to implement PRGLAC's recommendations.
2. Ensures 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).⁵
3. Establishes incentives that encourage financial investment in women's health research across public and private sectors.

National Testing and Response Strategy for Current and Future Pandemics

Your Cures 2.0 concept paper calls specifically for improvement to our nation's surveillance and testing capabilities to support the U.S. response to the current coronavirus pandemic, as well as in considering the possibility of future pandemics.

The current COVID-19 pandemic is providing a stark example of why sex and gender must be critical considerations in pandemic response and preparedness. COVID-19 appears to be infecting similar numbers of women and men, but the majority of people dying from the virus are men. The initial data revealing this disparity analyzed more than 40,000 COVID-19 cases in China and showed that men accounted for nearly two-thirds of deaths.⁶ Available data show that, in most countries, men have been upwards of 50% more likely to die following COVID-19 diagnosis than women.⁷

³ Huneycutt, B. et al. (2019). Exploring the Impact of the 21st Century Cures Act. *Milken Institute & Society for Women's Health Research*. Accessed at: <https://swhr.org/report-cures-act-pushes-womens-health-research-forward/>

⁴ NICHD, Task Force On Research Specific To Pregnant Women And Lactating Women. (2018). Report to Secretary, Health and Human Services and Congress. Accessed at: https://www.nichd.nih.gov/sites/default/files/2018-09/PRGLAC_Report.pdf

⁵ NIH (2019). Advancing science for the health of women: The trans-NIH strategic plan for women's health research. Accessed at: https://orwh.od.nih.gov/sites/orwh/files/docs/ORWH_Strategic_Plan_2019_02_21_19_V2_508C.pdf

⁶ Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (2020). The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) — China, 2020. *China CDC Weekly*. Accessed at: <http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51>

⁷ Global Health 5050 (2020). COVID-19 sex-disaggregated data tracker. Accessed at: <https://globalhealth5050.org/covid19/>

There are a variety of hypotheses as to why we are seeing clear gender disparities, but research is still in the early stages and the answers to these questions are not yet clear.⁸ In order to do this research, we need reliable, consistent data about COVID-19.

Unfortunately, the data currently released by the Centers for Disease Control and Prevention (CDC)⁹ do not break down U.S. COVID-19 infections and deaths by sex, although some individual states and cities are collecting this information. For example, as of May 16, of the 15,888 deaths in New York City, about 61% are men¹⁰. Meanwhile, other COVID-19 hotspots like Louisiana don't appear to be reporting data by sex.¹¹

The lack of a unified standardized process for reporting information on sex and gender differences in COVID-19 puts the United States at a distinct disadvantage in trying to understand the virus and respond adequately.¹² The study of sex and gender differences in COVID-19 must be made a priority. Understanding the sex disparities in this disease will help us develop better vaccines, treatments and public health policies.

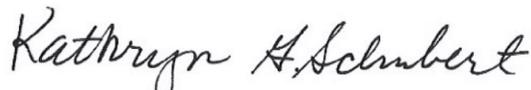
SWHR highly recommends that legislation surrounding pandemic response stipulate a uniform standardized data collection strategy, requiring all states to:

1. Collect comprehensive data from patients testing positive for the disease as well as those who receive tests but test negative for the disease.
2. Track sex differences in deaths, symptoms, risk factors, and virus exposure.
3. Include information about pregnancy status and response to the virus.

Thank you for your leadership in advancing this important legislation. We look forward to continued engagement with your offices on this and other topics.

If you have any questions, please feel free to contact our Director of Science Policy, Melissa Laitner, PhD, MPH, at melissa@swhr.org.

Sincerely,



Kathryn G. Schubert, MPP
President and Chief Executive Officer
Society for Women's Health Research

⁸ Ortman, Emily (2020). Sex and gender: Critical considerations in COVID-19 research and response. Accessed at: <https://swhr.org/sex-and-gender-critical-considerations-in-covid-19-research-and-response/>

⁹ Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19). Accessed at: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html>

¹⁰ New York City Government (2020). Coronavirus disease 2019 (COVID-19) daily data summary. Accessed at: <https://www1.nyc.gov/assets/doh/downloads/pdf/imm/covid-19-daily-data-summary-deaths-04232020-1.pdf>

¹¹ See: <http://ldh.la.gov/Coronavirus/>

¹² Gupta, Alisha Haridansani (2020). Does Covid-19 hit women and men differently? US isn't keeping track. *The New York Times*. Accessed at: <https://www.nytimes.com/2020/04/03/us/coronavirus-male-female-data-bias.html>