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February 14, 2019

Submitted via email to: NICHDStrategicPlan@nih.gov

Diana W. Bianchi, MD

Director, Eunice Kennedy Shriver National Institute of Child
Health and Human Development (NICHD)

Re: Request for Information (RFI) NOT-HD-18-031: NICHD
Strategic Plan Fiscal Years 2020-2024

Dear Dr. Bianchi:

The Society for Women's Health Research (SWHR) commends the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) for its leadership in research on pregnancy and women's reproductive health and for developing a five-year strategic plan to guide the research. We greatly appreciate the opportunity to provide input on the plan as outlined in the January 2, 2019, Request for Information (RFI) Notice (NOT-HD-18-031).

SWHR is a nearly 30-year-old national nonprofit dedicated to its mission of promoting research on biological sex differences in disease and improving women's health through science, policy, and education.

SWHR supports the objectives outlined in the NICHD strategic plan for fiscal years 2020-2024 and is pleased to provide the following comments on the specific themes.

Research Theme #1: Understanding Early Human Development

SWHR supports NICHD's goal to better understand human development at the cellular level. To achieve this goal, it is critical that this research includes sex as a biological variable (SABV) in the design, analysis, and reporting. Accounting for sex differences, even down to the cellular level, may help discover crucial information about the varied development, function, and biology between women and men, and the role these differences may play in health and disease. As research demonstrates, sex differences exist from "womb to

tomb,”¹ thus it is critical to examine SABV even in early human development.

The NIH Policy on Consideration of Sex as a Biological Variable in NIH-funded Research (NOT-OD-15-102) only requires that investigators *consider* the role of SAVB in research designs, analyses, and reporting — stopping short of requiring it — and there is a lot of variability in the testing and reporting of sex-difference findings in NIH research.

SWHR strongly believes that examining sex differences should be standard practice, except when prior evidence suggests no differences exist, and that there needs to be greater transparency and consistency in reporting of sex differences research. **SWHR recommends that NICHD ensure sex is incorporated as a variable in this scientific research, from the development and design of studies to the analysis and reporting of study results.**

Research Theme #2: Setting the Foundation for a Healthy Pregnancy and Lifelong Wellness

More women die of pregnancy-related complications in the United States than in any other developed country, and the U.S. maternal mortality rate is increasing.^{2,3} In addition, pregnancy-related complications have been associated with increased risk for diseases such as cardiovascular disease, obesity, and diabetes for women and their children later in life.⁴⁻⁶ As such, NICHD's goal to “improve pregnancy outcomes to maximize the *lifelong* health” of women and their children is critical. Increasing our knowledge about pregnancy-related complications could not only help prevent them, but could also assist women and their health care providers in managing downstream health risks related to these complications.

Efforts to better understand the biological and environmental factors that influence pregnancy and contribute to complications must consider the stark differences in pregnancy outcomes in diverse populations. For example, African American women are three to four times more likely to die during or after delivery than white women.⁷ **SWHR recommends NICHD ensure adequate inclusion of diverse populations in this research so that new treatment and prevention strategies are appropriately targeted and tested in those groups affected the most by adverse pregnancy-related events.**

Research Theme #3: Promoting Gynecological, Andrological, and Reproductive Health

An estimated 10% of reproductive-aged women are living with endometriosis, and an astounding 80% of African American women and 70% of white women will develop uterine fibroids at some point in their lifetime.^{8,9} These conditions often cause debilitating pelvic pain, heavy and irregular bleeding, and problems with fertility. Despite the prevalence of these diseases and their potentially severe effects on women, their families, and society, we still lack a clear understanding of the basic biology behind these conditions, resulting in delayed diagnosis and limited treatment options.

For example, women with endometriosis on average experience delays in diagnosis of 7 to 12 years, and three-quarters of women experience a misdiagnosis.^{10,11} Diagnosing gynecologic diseases such as endometriosis, adenomyosis, uterine fibroids, and pelvic inflammatory disease

can be challenging, in part because their symptoms can overlap with each other and with non-gynecologic diseases such as irritable bowel syndrome and fibromyalgia.¹² In addition, the current diagnostic gold standard for endometriosis, laparoscopic surgery, is invasive and costly. Improving understanding of the biological underpinnings of this disease will facilitate the development of new noninvasive or less invasive diagnostic tools (e.g., biomarkers, imaging tests), which are greatly needed.

Our limited understanding of endometriosis also means treatment options are limited. Current medical therapies provide pain relief for many women, but not all, and most medications cannot be used when women are trying to get pregnant. Even surgical approaches like laparoscopy and hysterectomy are not curative, have implications for fertility, and pain can recur.¹³ These surgical therapies mainly focus on eliminating lesions, but the relationship between lesions and symptoms is not well understood.¹⁴ A better understanding of the underlying biology of endometriosis and possible endometriosis subtypes could lead to new therapeutic avenues and more individualized treatment plans.

We commend the NICHD's goal to help women "manage fertility and minimize the impact of gynecological conditions" such as endometriosis and uterine fibroids. **SWHR urges NICHD to take a patient-centered approach to studying these diseases in order to achieve meaningful outcomes that focus on the patient as a whole, rather than just individual disease characteristics or symptoms such as infertility or pelvic pain.**

Research Theme #6: Ensuring Safe and Effective Therapeutics and Devices

About 94% of the 6.5 million pregnant women in the U.S. each year take at least one prescription or over-the-counter (OTC) medication during pregnancy.^{14,15} Yet the exclusion of pregnant and lactating women from research has led to significant, unacceptable gaps in knowledge about the safety and efficacy of therapies for these women, making health care providers uncertain about whether to prescribe needed medications. In many instances, this uncertainty has resulted in ill-informed decisions and suboptimal care for pregnant or breastfeeding patients with an illness.¹⁶⁻¹⁸ Further, without the availability of reliable information, women who are pregnant or nursing may decide to stop taking drugs or stop breastfeeding, even though this may not be the best health option for the woman, fetus, or baby.

SWHR applauds NICHD's goal to "develop, test, and validate safe and effective therapeutics and devices specifically for pregnant and lactating women" and supports NICHD's efforts to address this issue through digital health tools like NICHD's crowdsourcing website [PregSource](#), for which SWHR serves as a partner. Another great example of a digital health tool used to collect information from this special population is the FDA's MyStudies Application, a new open-source computer code technology to foster collection of real-world evidence via patients' mobile devices. In a pilot study conducted by FDA and Kaiser Permanente, 64 pregnant women used the app to report on health outcomes.¹⁹

Only by including pregnant and lactating women in research can we ensure we are providing them with safe, effective treatments. **SWHR encourages NICHD to work toward this goal by implementing the recommendations outlined in the recent report issued by the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC).**²⁰

Thank you for providing this opportunity to comment on the NICHD Strategic Plan Fiscal Years 2020-2024 9 (RFI NOT-HD-18-031). We hope you will take our comments into consideration as you finalize your plan, and we look forward to continuing our partnership with NICHD.

If you have questions, please contact Sarah Wells Kocsis, Vice President of Public Policy, at 202.496.5003 or swellskocsis@swhr.org.

Sincerely,



Amy M. Miller, PhD
President and Chief Executive Officer
Society for Women's Health Research

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