

January 9, 2024

Carolyn M. Mazure, PhD
Chair, White House Initiative on Women's Health Research
White House Gender Policy Council
1600 Pennsylvania Ave NW
Washington, D.C. 20500

Dear Dr. Mazure:

The Endocrine Society is excited about the White House Initiative on Women's Health Research, your leadership of the task force, and the opportunity to contribute to this important effort. Founded in 1916, the Endocrine Society is the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology. Our membership of over 18,000 includes leaders in the field of women's health research, such as medical endocrinologists who treat patients with thyroid disease, osteoporosis, diabetes, and other diseases; reproductive endocrinologists who treat conditions like infertility, polycystic ovarian syndrome, and menopause; and basic scientists who study estrogen receptors and central mechanisms that control reproduction. Collectively, we are dedicated to improving women's health through the application of scientific advancements to patient care.

In this letter, we identify several areas of opportunity that we encourage the initiative to consider, but we also want to call general attention to the important role of hormones in women's health research. Hormone signaling is fundamental to human biology and impacts (or is impacted by) disease in myriad ways; for example, as you know, sex steroid hormones influence the incidence and progression of many conditions including cardiovascular disease, fertility disorders, bone disease, hormone-dependent cancers, metabolic disease, mental health, and neurodegenerative diseases, contributing to differences in disease outcomes for men and women¹². Consequently, a better understanding of hormone biology and signaling, and the engagement of endocrine scientists and endocrinologists, is necessary to achieve the goals of the Initiative.

We therefore suggest that the Initiative prioritize:

1. Fostering multidisciplinary research on hormone biology and endocrine science with relevance to women's health.
2. Supporting a better understanding of how the prevalence and progression of some diseases (e.g., cardiovascular disease, cognitive decline, and autoimmune disorders) across the lifespan is different in women.

¹ Vegeto et al., *Endocr Rev.* 2020 Apr; 41(2): 273–319.

² Ryzkowska et al., *Arch Med Sci.* 2023; 19(2): 458–466.



3. Developing capacity, including resources and infrastructure to support a robust pipeline of scientists, clinicians, and allied professionals, to identify and address gaps in our understanding of women's health, including the aforementioned diseases.

We believe that focusing on these areas will help drive high-impact, transformative approaches to women's health. In addition to these overarching priorities, we highlight specific areas of opportunity below:

Building Infrastructure and Capacity at the NIH Office of Research on Women's Health

As the coordinating office at the National Institutes of Health (NIH) for women's health, the Office of Research on Women's Health (ORWH) is responsible for working across NIH and with other federal agencies to advance research that improves the health of women. Such coordination is necessary because the NIH Institutes and Centers (ICs) have unique mission areas, often focused on specific diseases or organ systems, while women's health requires a comprehensive research agenda to identify gap areas that do not fit into the specific missions of each IC. To advance women's health and ensure that all areas of opportunity are addressed, we support a more prominent role of ORWH, including enhancements that will enable its grantmaking authority to "promote the interests of women in research." Grant administration requires facilities and full-time employees, which ORWH lacks in sufficient amounts. To allow for ORWH to build on its success over the past 30 years and directly fund research that advances women's health research we therefore also support additional funding for ORWH, proportional to increases to other ICs, as part of steady, sustainable increases in the overall NIH budget.

Advancing Sex as a Biological Variable (SABV)

We commend NIH and ORWH for introducing the SABV policy, which went into effect in January 2016. This policy set an expectation that SABV will be factored into research designs, analyses, and reporting in basic and clinical research studies funded by NIH. While the policy is an important milestone that has improved researchers' knowledge of sex-specific effects and the importance of investigating sex differences, improved enforcement and accountability across the research enterprise would enable a more complete implementation of the policy as intended. Indeed, researchers report varying levels of adherence to the policy with differences between fields using different animal models and systems³. We encourage NIH to advance SABV across the biomedical research enterprise through comprehensive evaluation and training for researchers and grant reviewers that is recognized and prioritized by leadership at each IC. Further, we urge NIH to consider updating policies to ensure that journal articles and published research results funded by NIH comply with SABV or Sex and Gender Equity in Research (SAGER) guidelines. Through better implementation of the SABV policy, researchers will further advance our understanding of

³ Waltz et al., *J Womens Health (Larchmt)*. 2021 Oct;30(10):1395-1405..



sex differences in the development and progression of disease, and enable more tailored approaches to interventions, including for chronic diseases.

Participation in clinical trials

We recognize that women's representation in clinical trials has increased in recent years; however, analysis of trials within fields shows persistent areas where women are underrepresented, such as in cardiology, oncology, neurology, immunology, and hematology.⁴ This is concerning given that women in general are willing and able to participate in clinical trials at high rates, as evidenced by data collected through the All of Us research study indicating that nearly 60% of participants in the cohort are women⁵. In addition to prioritizing inclusion in clinical trials, there is an opportunity to better understand the fundamental drivers of different outcomes between men and women in clinical research through better assessment of hormonal status (prepubertal, reproductive phase, peri- and postmenopausal, and pregnancy) during trials. Ensuring this data is captured will give everyone more insights into why some interventions are successful or unsuccessful in certain populations and lead to additional public health benefits for women and men.

Workforce

We emphasize the importance of diversity, equity, and inclusion, including representation of women, across the biomedical research enterprise and at leadership levels. We are concerned that, despite accounting for approximately half of healthcare and science-related advanced degree recipients, women remain underrepresented at leadership levels in the biological and biomedical sciences. We encourage the Initiative to consider solutions to address this disparity, including for women from underrepresented groups in biological sciences, and we emphasize the success of cohort programs such as the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) and the Women's Reproductive Health Research (WRHR) program in developing peer and mentor networks to advance the careers of underrepresented groups in research⁶. The Endocrine Society's Future Leaders Advancing Research in Endocrinology (FLARE) is another example of a cohort program that has positioned early career scientists from underrepresented groups to achieve success in their field and career⁷.

Specific Priorities for Consideration

In the field of endocrinology, our members have identified several areas where additional focus and investment could improve women's health. These include:

⁴ Steinberg, et al. JAMA Netw Open. 2021;4(6):e2113749. doi:10.1001/jamanetworkopen.2021.13749

⁵ <https://www.researchallofus.org/data-tools/data-snapshots/> Accessed Jan 4, 2023.

⁶ McCoy et al., Am J Obstet Gynecol. 2023 Oct;229(4):425.e1-425.e16. doi: 10.1016/j.ajog.2023.06.050.

⁷ <https://www.endocrine.org/our-community/career-and-professional-development/future-leaders-in-endocrinology> Accessed Jan 4, 2023



- Understanding the menopausal transition, including its metabolic effects, and developing therapies to address symptoms e.g., hot flashes, cardiovascular risk, and bone density decline.
- Understanding the relationship between reproductive hormones and mental health and cognitive function.
- Research on pubertal development, including why early puberty is more often observed in Black and Hispanic women and what environmental factors e.g., endocrine-disrupting chemicals (EDCs) found in cosmetics are involved.
- Continued study of the long-term effects and benefits of GLP-1 agonists for treating obesity.
- Elucidating risk factors for osteoporosis in women as well as interventions and treatment strategies.
- Research on maternal nutrition and the reproductive health of offspring.
- Research on the overlapping and independent effects of sex chromosomes and sex hormones on the development and progression of disease, including auto-immune diseases.
- Recognizing the menstrual cycle as a sixth vital sign of health and disease.

We note that this list is not exhaustive, and a comprehensive approach to women's health research should not be limited to those diseases and conditions that are exclusive to women.

In conclusion, we are grateful for the Administration's commitment to advancing women's health through research and welcome the opportunity to support you in this important endeavor. We are eager to serve as a partner throughout this process, and we believe our members' unique expertise will help drive high-impact innovations to improve women's health. Thank you for considering our comments. If we can be of further assistance or if you would like to meet with us to discuss specific opportunities in endocrinology, please reach out to Joe Laakso, PhD, Director of Science Policy at jlaakso@endocrine.org.

Sincerely,

Stephen R. Hammes, MD, PhD,
President
Endocrine Society