ENDOCRINE SOCIETY
Hormone Science to Health

Samir Sauma, Ph.D.
Director
Office of Planning, Analysis, and Evaluation
National Institute on Aging

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Dear Dr. Sauma,

The Endocrine Society appreciates the opportunity to respond to the Request for Information (RFI) on the Inclusion Across the Lifespan II Workshop. 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 includes researchers studying how the aging process affects endocrine systems and influences the development of endocrine disease, as well as clinicians who treat patients with these same diseases from infancy through adulthood. We welcomed the announcement of the NIH inclusion policy and support the requirement to report the age of study participants. In our comments, we identify barriers that our members face when seeking to engage broad study populations in research, and we propose some opportunities for NIH to consider as you develop the agenda for the Inclusion Across the Lifespan II Workshop.

Endocrine diseases are widespread and encompass all populations that would benefit from policies to increase inclusion in clinical research. Furthermore, an individual's hormonal profile changes throughout the aging process and during major transitions such as puberty and menopause, necessitating a whole life course approach to the study of endocrine physiology. While many endocrine diseases and conditions may manifest at any point during a person's life, some have origins early in life and are influenced by development. While we are encouraged that many patients with specific diagnoses are highly motivated to participate in clinical research, it remains challenging to recruit healthy volunteers at all ages to participate in clinical research that may inform developmental disease trajectories and potential prevention strategies. This leads to further difficulties in achieving appropriately powered studies that include multiple age categories. Participants at the workshop should discuss how NIH and other stakeholders can facilitate the recruitment of healthy individuals at all ages, including families with healthy children and older adults**.** This can also include discussions related to the preservation of biospecimens for use in the context of longitudinal studies on aging and other secondary studies, and consenting processes that will accommodate the efficient use of biospecimens for such studies.

As NIH expands the concept of inclusion in clinical research, it will be important to consider how the policy might be applied to different types of studies. For instance, discovery-oriented research involving fundamental aspects of human physiology may require a different approach than clinical trials involving drugs or other interventions. Drug trials would clearly benefit from including study populations that are as broad and inclusive as the population that uses the drug or intervention, and

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we share the concern that drugs may be developed and approved through narrowly tailored clinical trials that do not reflect the demographics of the population, often older adults, that are most likely to use the drug. However, for discovery-focused fundamental research, it may be more appropriate to conduct initial studies within a defined age range and then expand the scope of research to include more heterogeneous populations. The biomedical research community would therefore benefit from the development of guidance or suggestions on approaches that are specific for different types of investigations involving human participants.

We applaud recent policy changes and developments intended to include pediatric populations in research, but there remain significant challenges to the recruitment of children for clinical studies. In some cases, studies involving all ages face institutional barriers, e.g., if a hospital that treats children does not want to be liable for studies involving adults. Even where reciprocity agreements exist that allow for more effective partnering between institutions to allow for all-age studies, other logistical barriers exist such as different EHRs for adults and children, or the inability to recruit at certain sites if staff are not trained to work with heterogenous populations. It will be important for NIH to consider ways to reduce liability concerns and other logistical barriers to inclusion and enable institutions to more seamlessly partner on studies involving multiple age groups and populations.

In addition to addressing these and other challenges, we hope that the workshop on inclusion across the lifespan will include a discussion of new opportunities for research that can be accomplished through a more inclusive research enterprise. We note that there is great potential for new drugs that could treat aging in general, and not in the context of a specific disease. For example, some current clinical trials are exploring the effects of metformin on the hallmarks of aging. NIH needs to be thoughtful and open to funding these and other studies that can examine the effects of aging across different populations and with different comorbidities. We also urge NIH to consider opportunities to study how aging populations respond differently to the effects of toxicants such as endocrine-disrupting chemicals (EDCs) and how toxicant exposures can themselves influence the aging process.

We sincerely welcome the expansion of the topics under discussion at the workshop to include underrepresented populations in clinical research, including sexual and gender minority (SGM) populations. One practical barrier that our members report is at the level of determining sex/gender for data collection purposes. Clear, standardized language is needed to facilitate reporting of sex and gender identity. This may require a two-step approach that identifies the sex recorded on the original birth certificate, including no-answer and “X”; and a second question involving gender identity, including non-binary. Other options may also be appropriate, e.g. transgender male/male/masculine spectrum for male.

In conclusion, as you develop the goals and agenda for the upcoming Inclusion Across the Lifespan II Workshop, we urge NIH to:

- Consider ways to facilitate the recruitment of healthy individuals at all stages, including families with healthy children and older adults;
- Investigate how different types of research studies may benefit from development of guidance or suggestions on approaches that are specific for different types of clinical investigations;
- Study ways to reduce liability concerns and other logistical barriers to inclusion and enable institutions to more seamlessly partner on studies involving multiple age groups and populations;
- Consider how sex and gender identity can be clearly reported in a way that includes SGM populations; and
- Explore new approaches to research on aging in general.

Thank you for considering our comments; we look forward to the outcomes of the Inclusion Across the Lifespan II Workshop. If we can be of any further assistance in your efforts, please contact Joe Laakso, PhD, Director of Science Policy at jlaakso@endocrine.org.

Sincerely,

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President, Endocrine Society