ENDOCRINE SOCIETY
Hormone Science to Health

May 06, 2015

Office of the Director, National Institutes of Health
Shannon Building (Building 1), Room B1-56
1 Center Drive, MSC 0122
Bethesda, Maryland 20892-0122

Dear Dr. Collins,

The Endocrine Society appreciates the opportunity to provide comments on the Precision Medicine Initiative (PMI). We expect that a large-scale study of human biology through the extensive characterization of biologic specimens and associated behavioral and environmental data could become a tremendous resource for biomedical researchers in all fields. The Society also acknowledges that many diseases, including rare endocrine diseases, lack effective therapeutic options and strategies for prevention. We hope that the PMI will address these gaps in care and provide opportunities for biomedical researchers in the United States and worldwide.

We specifically recommend that the PMI collect and link the following data on the cohort to EHRs:

- Information on the hormonal status of the cohort
- A careful assessment of women at various reproductive stages and during pregnancy
- Fertility history of men and women, including pubertal onset and pregnancies
- Exposure to endocrine disrupting chemicals

In doing so, the PMI will be able to accomplish the following:

- Improve our understanding of how hormones may contribute to disease susceptibility and therapeutic responses
- Empower researchers to more effectively and efficiently develop therapies for rare diseases

Founded in 1916, the Endocrine Society is the world's oldest, largest, and most active organization dedicated to research on hormones and the clinical practice of endocrinology. The Society's membership of over 18,000 includes basic researchers, clinical researchers, and clinicians in practice. We anticipate that the PMI will provide numerous downstream benefits to our members and the patients they serve. While the organizational requirements and capabilities of the administering entity are of great importance, we focus our comments on the specific data needs of our members and pressing research questions that could appropriately be addressed by this initiative.

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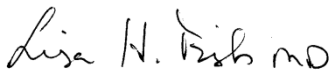
Thank you for considering the Endocrine Society's comments. If we can be of any assistance in your efforts, please do not hesitate to contact Dr. Joseph Laakso, Associate Director of Science Policy at jlaakso@endocrine.org.

Sincerely,



Lisa Fish, MD
President,
Endocrine Society

**Data to be collected at baseline and follow-up, including mode of collection and frequency and length of follow-up.**

Hormones have wide-ranging effects and drive important and long-lasting changes throughout the lifespan. While hormonal status clearly is linked to age-related conditions such as osteoporosis and cardiovascular disease, the complicated influence of hormones on disease progression in many cases remains extremely challenging to study. The PMI presents an important opportunity to combine information on the hormonal status of the cohort with DNA samples for potential genotype and phenotype studies, and link this data to EHRs at various life stages, including a careful assessment of women at various reproductive stages and during pregnancy.

We recommend the PMI elicit fertility history in men and women. Fertility status is a critical indication of overall health. Disturbances in a woman's menstrual cycle are a sensitive signal of general health and it will be important to get a precise, longitudinal menstrual cycle history and timing of menopause. For both sexes, data regarding pubertal onset and pregnancies will be important.

We also note that the discontinued National Children's Study would have included projects to assess how exposures to toxic chemicals influence development and health throughout life. Several institutes anticipate supporting smaller projects that will address this subject; however we hope that the PMI will also assess exposures to endocrine disrupting chemicals and explore methods to connect data on toxic exposures to EHRs.

Finally, the value of the cohort will depend strongly on the length of follow-up. For this investment to be successful, it is imperative that follow-up be planned for at least 20 years, if not indefinitely.

**Potential research questions that could be uniquely or more efficiently and effectively pursued in a large U.S. precision medicine cohort.**

Hormonal status, such as androgen and estrogen status, can promote the progression of diseases or provide protection from disease. Additionally, the relative levels of androgen or estrogen for instance may impact therapeutic response. A large precision medicine cohort will provide opportunities to achieve a much more detailed comparison of hormonal status among different populations, at different developmental points, and with different prevalence of disease. Through a precise assessment of the differences in hormonal status among members of the cohort, the PMI could help researchers more efficiently and effectively elucidate how hormones may contribute to disease susceptibility and therapeutic responses.

Furthermore, developing therapies for rare diseases is challenged by the need to recruit large numbers of patients for clinical research studies. For example, clinical researchers studying disorders of sex development lack sample sizes necessary to address many critical research questions that could impact patient care. The generation of a large cohort may help researchers by facilitating the development of networks for identifying potential participants for clinical studies and allowing geographically disparate researchers to share data in a coordinated way.

In summary, we hope that by systematically collecting data on hormonal status of participants, the PMI will allow researcher to more efficiently and effectively answer questions related to the influence of hormonal status on overall health, and enable researchers to develop therapies for rare diseases.