

Congress of the United States
Washington, DC 20515

April 30, 2014

The Honorable Gene Dodaro
Comptroller General of the United States
Government Accountability Office
441 G Street, NW
Washington, DC 20548

Dear Mr. Dodaro:

Congress has long had an interest in the inclusion of women in clinical research. Prior Government Accountability Office (GAO) work informed the National Institutes of Health Revitalization Act of 1993, which called for the National Institutes of Health (NIH) to fund research on diseases and conditions that primarily affect women; required that an appropriate number of women be included in all NIH-sponsored clinical research trials; and directed NIH-funded studies to analyze data by sex.¹ The legislation similarly emphasized participation of minorities in clinical research. Later GAO reports evaluated progress made since passage of the NIH Revitalization Act, but GAO has not examined this important issue for more than a decade.

In 2000, GAO reported that NIH has made progress in some areas aimed at increasing the participation of women in research.² For example, GAO reported that NIH considers the inclusion of women and minorities in extramural clinical research as a matter of scientific merit, which affects a proposal's eligibility for funding. NIH reported that in fiscal year 2012, women constituted 57% of enrollees in clinical trials.³ However, the overall inclusion of women does not guarantee that valid analysis by sex can be carried out, nor does it guarantee that women are being represented in proportion to their disease prevalence in the population. GAO reported that NIH still has progress to make implementing the requirement that certain clinical trials be designed and carried out to permit valid analysis by sex, which could reveal whether interventions affect women and men differently. A more recent report from the Institute of Medicine also found the design, analysis, and reporting of clinical research limits researchers'

¹ Pub. L. No. 103-43.

² General Accounting Office, *Women's Health: NIH Has Increased Its Efforts to Include Women in Research* (May 2, 2000) (GAO/HEHS-00-96).

³ Participation is 50.2% if male- and female-only studies are excluded. In domestic intramural clinical research, participation is only 36.5% if male- and female-only studies are excluded. See Department of Health and Human Services, National Institutes of Health, *Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research, Comprehensive Report: Tracking of Clinical Research as Reported in Fiscal Year 2011 and Fiscal Year 2012* (online at <http://orwh.od.nih.gov/research/inclusion/pdf/Inclusion-ComprehensiveReport-FY-2011-2012.pdf>).

ability to perform statistically significant subgroup analysis to determine whether outcomes vary between men and women.⁴

Participation of women in clinical trials is vital to improving our understanding of how women are affected by diseases and conditions that impact their health and lifespan, whether the illnesses are predominately experienced by women, such as breast cancer or osteoporosis, or affect the overall population, such as heart disease or stroke. The onset and progression of some diseases may affect women differently than men, and there are even sex differences in the way that drugs are absorbed, distributed, and metabolized – in part due to differences in body size, hormones, and gene expression. Due to these differences, not all treatments or drugs are equally effective in both sexes, and GAO previously reported that women are more susceptible to adverse drug events.

Ambien dosing highlights the difference between male and female responses to medication. Last year, this prescription drug used to treat insomnia became the first and only prescription drug on the market with different recommended doses for men and women. As early as 1992, a GAO report noted that the Food and Drug Administration (FDA) was not adequately ensuring the representation of women or the analysis of sex differences in clinical drug trials conducted by the pharmaceutical industry.⁵ A 2001 GAO report on FDA noted that although women made up 52% of the study participants overall for new drug applications, women constituted only 22% of the participants in early stage (phase I) clinical trials performed to assess safety and set initial dosing levels.⁶ A more recent review of the clinical trials done to support new drugs approved in 2006 and 2007 revealed that women were still under-represented in phase I trials, comprising only about one-third of participants. A 2013 report required by the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA)⁷ assessed the inclusion and analysis of demographic subgroups in clinical trials supporting new drug and device applications. Overall, this report revealed that while clinical trials are including women and minorities, shortfalls remain in meaningful subgroup analysis and reporting of data to patients and providers. The FDA is currently assembling an Action Plan that will provide recommendations on how to improve women and minority representation, subgroup analysis, and the availability of accurate information to doctors and consumers.

While the FDA is engaged in both data collection and policy development as required by FDASIA, it is critically important that we understand more about the meaningful inclusion of women in NIH-sponsored trials. These trials help to shape our understanding of diseases,

⁴ Institute of Medicine, *Women's Health Research: Progress, Pitfalls, and Promise*. Washington, DC: The National Academies Press (2010).

⁵ General Accounting Office, *Women's Health: FDA Needs to Ensure More Study of Gender Differences in Prescription Drug Testing* (Oct. 29, 1992) (GAO/HRD-93-17).

⁶ General Accounting Office, *Women's Health: Women Sufficiently Represented in New Drug Testing, but FDA Oversight Needs Improvement* (July 6, 2001) (GAO-01-754).

⁷ Pub. L. No. 112-144.

treatment regimens, and care delivery. We are missing an important opportunity to improve women's health if we fail to include women in all stages of clinical trials, analyze sex-specific data, and report the results. At this important 20-year milestone since the passage of the NIH Revitalization Act, we respectfully ask GAO to provide information on the following questions about NIH-supported clinical trials:

Participation rates: What is known about the level of participation of women in clinical trials? Specifically, what is known about the level of participation of women in clinical trials focused on specific diseases or conditions (i.e., heart disease and stroke) and across each phase of clinical trials? Does the proportion of women participating in trials reflect the prevalence of the disease under investigation in women?

Funding: What is known about the distribution of funding for women's health research, including information on investments focused on specific diseases or conditions that predominately affect women (i.e. osteoporosis and breast cancer) as well as the inclusion of women in studies for diseases or conditions that affect both women and men (i.e. heart disease and stroke)?

Statistical power: To what extent is the level of participation of women in clinical trials sufficient for researchers to produce disaggregated analysis and statistically powerful results for the individual sexes? To what extent are sex-stratified data and analyses reported in the literature?

Enrollment: What factors are reported to affect women's enrollment and participation in clinical trials? What, if any, biases in trial design and participant recruitment impact the involvement of women participants in clinical trials? To what, if any, extent do these factors and any identified biases vary by phase of clinical trial? How can the identified challenges, if any, be overcome?

NIH policies: What are the policies and guidance regarding the participation, analysis, and reporting of sex differences in clinical trials? How are these policies overseen?

Thank you for your consideration of this request. Your staff may contact Anne Reid (Waxman), Andi Fristedt (Harkin), Tiffany Guarascio (Pallone), Christine Evans (Mikulski), Chris Bigelow (Lowey), Remy Brim (Warren), Eric Anthony (DeLauro), Lauren Au (Gillibrand), Adriane Casalotti (Capps), and Kim Corbin (Stabenow) for ongoing coordination of this work.

Sincerely,



Henry A. Waxman
Member of Congress



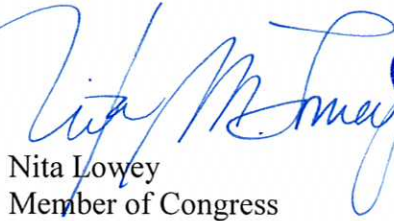
Tom Harkin
Member of Congress



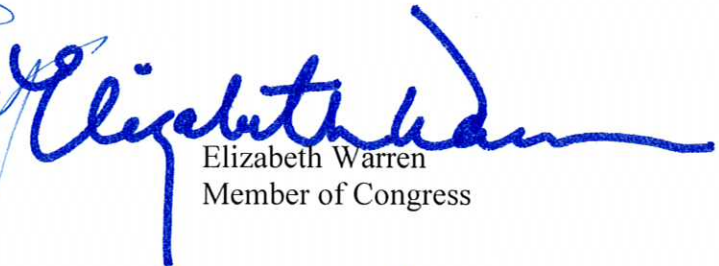
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