WHITMAN-WALKER HEALTH

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June 30, 2017

SUBMITTED ELECTRONICALLY

Lisa Kaeser
Eunice Kennedy Shriver National Institute
of Child Health and Human Development
National Institutes of Health

Re: Request for Information (RFI): Invitation to Comment on Inclusion in Clinical Research Across the Lifespan, Notice No. NOT-OD-17-059

Dear Ms. Kaeser:

Whitman-Walker Health (WWH) is pleased to submit these comments in response to the NIH's "Invitation to Comment on Inclusion in Clinical Research Across the Lifespan," on the inclusion of pediatric and older populations in research studies involving human subjects.

I. Introduction

Whitman-Walker Health is an FQHC providing primary care and behavioral health care and a range of health-enabling services (such as legal assistance and treatment adherence), and community health services, to individuals and families throughout the greater Washington, DC metropolitan area, with an emphasis on specialty HIV and HCV care and the health and wellness needs of the lesbian, gay, bisexual, transgender and questioning (LGBTQ) communities.

WWH has been conducting clinical research since 1987, when the first HIV treatments were being tested. To date, we have conducted more than 150 studies, including a current cohort study comprising more than 2400 participants. Our studies investigate new ways to prevent or treat diseases in our community, particularly HIV and HCV. WWH's research studies include clinical trials that test how well new medications work and how safe the medications are for patients; as well as behavioral studies that look at such topics as disease prevention and medical adherence. We are a clinical site for SHARE (Study to Help the AIDS Research Effort), which is part of the Multicenter AIDS Cohort Study that began in 1984 and continues to make significant contributions to scientists' understanding of HIV. We also participate in a citywide cohort longitudinal study of HIV infection. Today Whitman-Walker is enrolling a wide age range of participants for studies including new HCV treatments; improved methods to screen for anal cancer; HIV and heart health; Pre-Exposure Prophylaxis (PrEP) for HIV prevention; and HIV and cognitive impairment. Our research priorities also include new treatments for opioid

addiction, the health and wellness priorities of LGBTQ youth, and improving HIV prevention and treatment for sex workers.

WWH applauds NIH's progress in including women and minorities as subjects in clinical research, and your commitment to expand that inclusion to pediatric and older populations. Overly strict inclusion/exclusion criteria and artificial age restrictions result in the underrepresentation of some populations in clinical research of diseases and disorders that could benefit them. NIH's commitment is especially meaningful in light of findings that LGBTQ youth and older adults, especially those identifying as transgender, face significant health disparities. The disproportionate burden of health challenges this community encounters is linked to stigma, discrimination, and denial of civil and human rights.[1,2] These barriers, along with the lack of LGBTQ cultural competency among researchers and providers, result in LGBTQ people delaying or deferring needed medical care out of fear of how they would be treated, and a mistrust of the medical and research community.[3] Young and older LGBTQ people are especially vulnerable as they navigate their sexual and gender minority status while highly dependent on others (parents or other caregivers).[4,5,6]

II. Improving LGBT Youth and Elders Representation in Clinical Trials by Emphasizing LGBT Cultural Competency in Institutional Review Board Reviews

Critical to the inclusion in clinical studies of pediatric and older populations that are representative of the real-world population is the need to adopt more LGBT-sensitive strategies during recruitment and throughout all phases of the study. Concerns about social discomfort or self-consciousness rank high in reasons individuals do not join or complete clinical trials.[7]

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[1] HHS Office of Disease Prevention and Health Promotion (2017). Healthy People 2020: Lesbian, Gay, Bisexual, and Transgender Health. https://www.healthypeople.gov/2020/topics-objectives/topic/lesbian-gay-bisexual-and-transgender-health.

[2] Kates, J., Ranji, U., Beamesderfer, A., Salganicoff, A., & Dawson, L. (2016). Health and Access to Care and Coverage for Lesbian, Gay, Bisexual, and Transgender Individuals in the U.S. The Henry J. Kaiser Family Foundation. http://files.kff.org/attachment/Issue-Brief-Health-and-Access-to-Care-and-Coverage-for-LGBT-Individuals-in-the-US.

[3] Lambda Legal (2010). When Health Care Isn't Caring: Lambda Legal's Survey of Discrimination Against LGBT People and People with HIV. https://www.lambdalegal.org/publications/when-health-care-isnt-caring.

[4] Dickey, L.M. (2017). Toward Developing Clinical Competence: Improving Health Care of Gender Diverse People. *American Journal of Public Health*, 107(2), 222-23. http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2016.303581.

[5] Centers for Disease Control and Prevention (2017). Lesbian, Gay, Bisexual, and Transgender Health: LGBT Youth. https://www.cdc.gov/lgbthealth/youth.htm..

[6] Foglia, M. B., & Fredriksen-Goldsen, K. I. (2014). Health Disparities among LGBT Older Adults and the Role of Nonconscious Bias. *The Hastings Center Report*, *44*(0 4), S40–S44. http://doi.org/10.1002/hast.369

[7] Kelly, S., Martin, S., Kuhn, I., Cowan, A., Brayne, C., & Lafortune, L. (2016). Barriers and Facilitators to the Uptake and Maintenance of Healthy Behaviours by People at Mid-Life: A Rapid Systematic Review. Wang Y, ed. *PLoS ONE*. 11(1):e0145074. http://doi.org/10.1371/journal.pone.0145074.

Those concerns are especially important for LGBT youth and elders because of a lack of LGBT cultural competency among many providers and researchers.

Institutional Review Boards should incorporate and continuously update training modules on LGBT cultural competency, and institutions should require researchers working with human subjects to complete those modules. A recommendation from someone they trust is a primary reason people participate in clinical trials.[8] Improved LGBT cultural competency in research will lead to more LGBT people joining and completing clinical studies.

III. Increasing Flexibility in Clinical Trial Designs, along with Greater Transparency and Availability of Relevant Demographic Subgroup Data

Strategies that are successful in ensuring the inclusion of all appropriate ages employ flexible approaches to engage participants, and rely on transparent demographic subgroup data. Researchers can address these issues by adopting innovative approaches to clinical trial design and methodology to increase the enrollment of pediatric and older populations in clinical trials, without compromising study integrity.

Whitman-Walker successfully uses different strategies to engage individuals in research studies (and care) – including telephone calls, text messages, email, post mail, paper and electronic flyers, and suggestions by our health or legal providers made to individual patients/clients during medical or legal appointments. Text messaging is increasingly useful when engaging youth in studies.[9] Text messaging is most effective through a two-way chat, and examples of messages includes words of appreciation after committing to be in the study, receiving care and attention from the study staff, and appointment reminders of their next visit. While multiple ways of contacting participants can increase trial's enrollment and retention, communications in all platforms must be done with LGBT and gender-expansive cultural competence. When reaching out to potential and current study participants, it is important to avoid making unverified assumptions about an individual's gender or chosen name. Mis-gendering a transgender or gender-expansive person, or calling them by the wrong name, can be traumatic for them, and can undermine the trust necessary to enroll that individual and keep them enrolled.

Recognizing the importance of testing drugs on the right patient populations, the FDA's Center for Drug Evaluation and Research (CDER) piloted the Drug Trials *Snapshots* program in 2015 to facilitate access to information about patient representation in clinical studies. CDER

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[8] Kristina, L. (2014). Why Do Some Patients Enroll in Clinical Trials and Others Don't? Forte Research Systems. https://forteresearch.com/news/patients-enroll-clinical-trials-others-dont.

[9] Markowitz, J.T., Cousineau, T., Franko, D.L., et al. (2014) Text Messaging Intervention for Teens and Young Adults With Diabetes. *Journal of Diabetes Science and Technology*. 8(5):1029-1034. https://doi.org/10.1177/1932296814540130.

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developed snapshots that describe participants in each clinical trial, and organize information from the trials by sex, race, and age subgroups. Furthermore, the snapshots provide a brief narrative by subgroup on whether there were any reported differences in the effectiveness of the drug, and differences in side effects among the different groups.[10] The age demographic subgroup was limited to "Age 65 and older" in snapshots reported in 2016, but included two additional age categories in 2015: "Age 75 and older" and "Age 80 and older".

We recommend that similar snapshots reports be developed and employed in all clinical research involving human subjects. Also, to ensure that LGBT individuals of all appropriate ages are adequately represented in studies, the snapshot reports should be improved as follows:

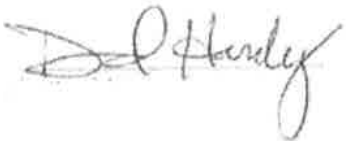
- The category "Age 65 and older" should be broken down into smaller age increments – e.g., "Age 65 to 74" and "Age 75 and older." In addition, "Age 18 and younger" should be employed.
- The snapshots report should include a mean age of study participants, as well as the ages of the oldest and youngest participants.
- While NIH grantees are currently not required to report on specific ages included in research, we believe this requirement would offer greater transparency. A link to this data should be provided with the snapshots report.
- Snapshots reports should include information on sexual orientation and gender identity. Gender identity is particularly important: persons identifying as transgender or gender-expansive face unique health challenges. More research is needed to understand long-term effects of hormone treatments, and potential drug-drug interactions.
- Age restrictions in exclusion criteria should be accompanied by justifications.

[10] U.S. Food and Drug Administration. John, J.W. (2017). FDA Drug Trials Snapshots and Diversity When Testing New Drugs. FDA Voice. https://blogs.fda.gov/fdavoice/index.php/2017/02/fda-drug-trials-snapshots-and-diversity-when-testing-new-drugs.

IV. Conclusion

Whitman-Walker Health appreciates NIH's commitment to encourage the inclusion of pediatric and older population in clinical research. This effort should take into account the alarming health disparities LGBTQ individuals in these populations face, including their high risk of early onset diseases. Given our 30-year history of conducting clinical studies, we wish to continue to serve as a constructive partner to achieve a more complete representation of the real-world population in clinical research, and would be happy to meet with the Agency to further discuss our recommendations. Please do not hesitate to contact us if you have any questions.

Sincerely,



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