AMERICAN LUNG ASSOCIATION.

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National President and
CEO

August 5, 2019

Norman E. "Ned" Sharpless, M.D.
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Avenue, Room 2217
Silver Spring, MD 20993

Re: Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs; Draft Guidance for Industry (Docket No. FDA-2019-D-1264)

Dear Dr. Sharpless:

The American Lung Association appreciates the opportunity to comment on the Food and Drug Administration's (FDA) draft guidance for industry, *Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs*.

The American Lung Association is the leading organization working to save lives by improving lung health and preventing lung disease through research, education and advocacy. The Lung Association works on behalf of the 35 million Americans living with lung diseases including asthma, lung cancer and COPD.

Broadening Eligibility Criteria in Clinical Trail Enrollment

The American Lung Association appreciates FDA's previous efforts to promote inclusion in clinical trials and to ensure Caucasian males are no longer considered the norm study population. However, there continues to be populations that are either under-represented or un-represented in the clinical trial process. Clinical trial populations must appropriately represent the patient population that will later use the drug when approved. The absence of certain populations can lead to misrepresentation of the efficacy and safety of a new drug. The Lung Association is encouraged by the FDA's issuance of guidance for the need to enhance representation and diversity in clinical trials.

In the draft guidance, FDA highlights several populations that are frequently excluded from clinical trials without strong justification. These include "the elderly, those at the extremes of the weight range, individuals with organ dysfunction, those with malignancies or certain infections such

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as HIV, and children." The Lung Association encourages these populations' inclusion in clinical trials. In addition to the aforementioned populations, the Lung Association recommends the FDA also include people with physical and mental disabilities in their list of underrepresented populations to include in clinical trials.

In the U.S., approximately 26 percent of adults have some type of disability – either physical and/or mental[1]. People with disabilities experience poorer health, greater incidence of chronic conditions, higher healthcare expenditures and are more likely to smoke compared to people without disabilities[1,2]. People with disabilities are consistently marginalized in the context of clinical trials, despite needing the treatment. Yet, they continue to be excluded from clinical trials without strong justification. The American Lung Association advises that the FDA include people with physical and mental disabilities in their list of excluded populations. The Lung Association also recommends the FDA issue a population-specific guidance to address the need to include people with physical and mental disabilities in clinical trials.

Improving Enrollment and Retention

Clinical trial participants face several barriers including financial costs, mistrust, time spent and more. The Lung Association agrees with the FDA's outline to make trial participation less burdensome for participants. For example, FDA needs to include language around ensuring research sites are accessible for people with physical disabilities. The final guidance must work to include all types of patients, including those with disabilities, from many different angles.

The American Lung Association agrees with the FDA's guidance on working directly with communities to address participant needs. Involving patients, patient advocates and caregivers is extremely important and the insight they can provide would be invaluable. The Lung Association also believes that involving practicing healthcare providers in the community can help improve enrollment of a more diverse population. Healthcare providers need to be comfortable enough to discuss and refer their patient to clinical trials as an opportunity for a care option. The Lung Association urges FDA to include educating healthcare providers about the trials and expand their awareness of clinical trials, to improve the diversity of enrolled participants.

Continued Efforts to Improve Diversity in Clinical Trails

Appendix A and Appendix B in the guidance list current FDA initiatives to broaden eligibility criteria in clinical trials, however there continues to be consistent under-representation of racial and ethnic minorities and women in clinical trials.

Racial and ethnic minorities make up approximately 39 percent of the total U.S. population, however there continues to be stark under-representation of racial and ethnic minorities in clinical trials[3, 4]. Asian participants account for less than two percent of the U.S.-based trials, American Indian participants were not reported in nearly two-thirds of clinical trials. This can have a negative impact on health outcomes because evidence suggests that drugs may have different effects on different populations. For example, albuterol, a common asthma medication, is less effective in African American and Puerto Rican children compared with European American and

Mexican children. In the U.S., Puerto Rican and African American children have the highest prevalence of asthma nationwide, yet over 95 percent of studies on lung disease have been performed on people of European descent[5]. The Lung Association appreciates the FDA's 2016 guidance titled *Collection of Race and Ethnicity Data in Clinical Trials*, but also insists that the FDA remain vigilant in promoting the inclusion of racial and ethnic minorities to ensure the efficacy and safety of drugs on the market for all patients.

Women, regardless of pregnancy status, also continue to be under-represented in clinical trials. There are distinct differences in health outcomes between women and men. In addition to lifestyle, environmental and behavioral differences, there are also biological differences at the molecular and cellular level[6]. These biological differences can lead to differences in clinical outcomes and can have significant health consequences. The Lung Association acknowledges the FDA's issuance of guidance in 1993 discouraging unjustified exclusion based on gender in clinical trials. Yet, thousands of clinical trials are enrolling annually, and women are still less likely to be aware of or to participate in clinical trials[7]. The American Lung Association asks the FDA to continue developing strategies to improve representation of women in clinical trials. This will help safeguard drugs on the market are safe and effective for everyone.

Conclusion

The Lung Association supports the FDA's issuance of this guidance to enhance the diversity of clinical trial populations, however does have several recommendations to improve it:

- Include language around providing healthcare providers with adequate knowledge and awareness of clinical trials as a strategy to improve enrollment and diversity;
- Include people with physical and mental disabilities as a population that has been excluded from clinical trials without any strong justification;
- Issue a population-specific guidance to address the need to include people with physical and mental disabilities in clinical trials; and
- Include language around making research sites accessible for people with physical disabilities.

The American Lung Association recognizes the work FDA has already done to improve enrollment of racial and ethnic minorities and women in clinical trials, however these populations continue to be under-represented. As such, the Lung Association encourages the FDA to continue developing more guidance and strategies to improve their representation. Thank you for the opportunity to provide comments on this draft guidance.

Sincerely,

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Chief Mission Officer

[1] Center for Disease Control and Prevention (2019). *Disability Impacts All of Us. Retrieved from* https://www.cdc.gov/ncbddd/disabilityandhealth/infographic-disability-impacts-all.html
[2] Rios, D., Magasi, S., Novak, C., & Harniss, M. (2016). Conducting Accessible Research: Including People With Disabilities in Public Health, Epidemiological, and Outcomes Studies. *American journal of public health*, *106*(12), 2137–2144
[3] U.S. Census Bureau. *Quick Facts, 2018. Retrieved from* https://www.census.gov/quickfacts/fact/table/US/PST045218
[4] Food and Drug Administration (2018). *Minorities in Clinical Trials. Retrieved from* https://www.fda.gov/consumers/minority-health/minorities-clinical-trials
[5] Mak et al., 2018 "Whole-Genome Sequencing of Pharmacogenetic Drug Response in Racially Diverse Children with Asthma." *American Journal of Respiratory and Critical Care Medicine*, vol. 197, no. 12, 15 June 2018
[6] Wizemann T, Pardue M. Exploring the biological contributions to human health: does sex matter? Washington DC: National Academies Press; 2001
[7] Pal S. Inclusion of Women in Clinical Trials of New Drugs and Devices. US Pharm. 2015;40(10):21

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