American College of Clinical Pharmacology® Response to FDA Docket No. FDA–2021–D–0789, Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials, Draft Guidance for Industry

The FDA draft guidance entitled "Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials" issued on April 14th is to be commended for its timeliness. With the recent intense development of vaccines to prevent COVID infections as well as other treatments, the public and health care providers are more aware than ever of the importance of enrollment of all members of society into clinical trials. Moving forward with the formalization of a comprehensive process to thoughtfully develop plans to enroll participants in clinical trials will greatly enhance the benefit and utility of clinical trials. The American College of Clinical Pharmacology (ACCP) fully supports this guidance.

The scientific literature provides ample and well-documented evidence for pharmacokinetic, pharmacodynamic, and drug-related outcome differences in patients not only based on race/ethnicity but also sex, age and developmental stage, comorbidities, and socioeconomic status.[1] The lack of enrollment of these groups, especially representatives of different racial and ethnic groups may lead to delayed availability of new medical products to these populations and may result in either suboptimal outcomes or increased rate of adverse events. Determination of differences in pharmacodynamic and pharmacokinetic parameters in diverse populations prior to marketing of new drugs is hence a combination of the ethical, public health and safety issues.

While the draft guidance provides a general approach to inclusion of racial/ethnic minorities, it could be strengthened by indicating the criteria when a drug development program has successfully met inclusion of underrepresented populations. In other words, what should be the target enrollment for underrepresented populations and how should this target be set for a drug development program? Should sponsors use country Census data, real-world evidence and epidemiological data indicating prevalence or incidence of the disease being treated to set target enrollment for underrepresented populations? It is also advisable to set target enrollment at the drug development program level and not at the individual clinical trial level to maintain agility and avoid delaying drug development program progress.

The draft guidance emphasizes the importance of accurate assessment of the pathophysiology of diseases among different populations. Could the FDA share suggested methods for obtaining information given the acknowledged lack of information in underrepresented groups? If there has been a long-standing gap in data collection among under-represented groups, how can sponsors trust published literature? Are there methods for collaboration with other government agencies who have treatment and outcome data among rural populations as well as those being cared for by the US Public Health Service?

One recent example of underrepresentation of racial/ethnic minorities and the elderly was in SARS-CoV-2 trials.[2] These same populations are disproportionately impacted by COVID-19 infections. Hence, inclusion of these populations, is crucial to evaluate safety and efficacy of a vaccine candidate among those who bear the highest burden of the disease. Another example is the development of HIV vaccine and antiretroviral drugs, where, despite the successful increase in clinical trial participation by affected racial/ethnic populations, significant gaps remain.[3] Although data to inform effective approaches to assure increased representation of racial/ethnic minorities are limited, engagement with community

stakeholders from the design to the conduct of clinical trials has been proven to be an effective strategy to implement in future studies.[4]

The draft guidance signals the importance of inclusion of race/ethnicity as an important factor in drug development by the FDA. ACCP as a professional organization further encourages all stakeholders involved in drug development, drug utilization and assessment of safety and patient education to consider inclusion and adequate representation of all races and ethnicities, sex (both cis- and trans-gendered populations), age and developmental stage (children, including neonatal populations, and the elderly, puberty, menopause), and diverse socioeconomic status populations (such as uninsured, underinsured, and Medicare/Medicaid patients) in clinical trials to further strengthen patient outcomes that translate into real world applications.

Not included in the current draft guidance, but important to the continued participation of all members of society, are the availability of communication plans to share data from clinical trials with those who have not previously participated. A sixth element in the Plan is needed to provide direction for expectations of provision of the results of clinical trials with the various stakeholders who contributed. Are the current practices of provision of lay summaries adequate for those who have not previously participated?

Expanding diversity plans to consider contributing factors in medication effectiveness will lead to optimized patient care and can provide a framework for future drug development. While this draft guidance is an important step to diversify clinical trial enrollment reflective of the target population, other determinants of health and treatment outcome need to be considered in the regulatory framework as well.

References

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