FDA Offers Guidance for Boosting Diversity in Clinical Trials

Joan Stephenson, PhD

The US Food and Drug Administration (FDA) has issued final guidance for addressing the diversity of individuals participating in clinical trials of new drugs or biologics. The aim is to increase enrollment for underrepresented groups to ensure a broader understanding of these products' risks and benefits.

Issued earlier this month, this document comes at a time when the coronavirus disease 2019 (COVID-19) pandemic has highlighted differences in how various patient groups—such as older adults, racial and ethnic minorities, pregnant women, and children—are affected by COVID-19. Such differences have led to calls for COVID-19 vaccine trials to step up efforts to recruit racial minorities and others disproportionately affected by the disease.

“This difference in impact illustrates why we must encourage developers of any medical product such as treatments or vaccines for COVID-19—as well as medical products more broadly—to endeavor to include diverse populations to understand their risks or benefits across all groups,” said FDA Commissioner Stephen M. Hahn, MD in a statement.

The 21-page document, “Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry,” notes that in general, despite the FDA’s promotion of enrollment practices that would result in clinical trials better reflecting the population most likely to use the drug under study, certain groups remain underrepresented in many trials.

The FDA advises trial sponsors to enroll individuals “who reflect the characteristics of clinically relevant populations with regard to age, sex, race, and ethnicity,” noting that not doing so can result in insufficient information about the safety and effectiveness of a medical product that should be part of its labeling. To achieve this, the agency said that in addition to enrolling individuals from racial and ethnic minorities, children and adolescents should be included in confirmatory clinical trials involving adults, when appropriate; women also should be represented in adequate numbers to allow for analysis by sex, to permit detection of significant sex-related differences in drug response.

In advising inclusion of racial and ethnic minorities and analysis of clinical trial data by race and ethnicity, the FDA explains that for a variety of reasons, racially and ethnically distinct subgroups of the US population sometimes differ in their responses to medical products (such as how a drug is metabolized, its efficacy, or its safety). “Therefore, FDA recommends that for drugs and biologics, sponsors include a plan for inclusion of clinically relevant populations no later than the end of the Phase 2 meeting,” the guidance says.

The document also encourages study sponsors to design trials that, early in the trial process, account for individuals who may metabolize drugs differently, such as older adults or people with liver or kidney disease. Doing so will help avoid later exclusions and allow dose adjustments “to optimize effectiveness and safety across different populations,” the guidance says.

In addition, the agency suggests use of an adaptive clinical trial design. When an interim analysis of trial data becomes available, adaptive trials allow for making prespecified changes during the study, including altering the makeup of the trial population.

For some individuals, clinical trial participation includes such challenges as the cost of travel or missing work. A requirement to make frequent visits to a specific research site may also be problematic for certain groups, such as older adults, children, disabled or cognitively impaired...
individuals who need transportation or help from a caregiver, or those who live far from the research site.

To help make trial participation "less burdensome," the FDA urges trial designers to consider measures such as making potential participants aware of the availability of reimbursements for travel and lodging expenses related to trial participation; reducing the frequency of study visits; considering whether site visits could be replaced by communication through telephone, secured email, or other means; and using "mobile medical professionals," such as nurses and phlebotomists, to visit and evaluate participants and collect blood samples.

In addition, the FDA provides recommendations for studies of experimental drugs targeting rare diseases, including advice on broadening eligibility criteria, improving enrollment, and retaining participants with rare diseases. Noting the existence of patient advocacy groups that are committed to finding new treatments and supporting clinical trials for rare conditions, the agency says that trial sponsors should consider early engagement with such organizations, experts, and patients for suggestions about designing trials that participants would be willing to enroll in and support.

"FDA encourages sponsors to consider the approaches outlined in this guidance and develop other approaches as appropriate," the guidance notes.