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Achieving Diversity in Pharmaceutical Clinical Trials

Regulating agencies set policies for inclusion of women, minorities

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Research has shown that differences in biology and genetics may influence the efficacy of pharmaceutical treatments. If a potential compound's performance is evaluated in a homogenous trial population, such results may not apply to a heterogeneous patient population. For example, only after it had been on the market for a number of years did the U.S. Food and Drug Administration approve a label change for the active ingredient in Ambien upon determining that women metabolize the drug more slowly than men. Despite this understanding, clinical trials today skew largely white, male and young and often fail to reflect the demographics and genetics of the ultimate recipients of the treatment.

Each of the major federal voices in regulating biomedical research has contributed to the discussion regarding the inclusion of women and minorities in clinical trials. The following briefly summarizes the existing regulatory landscape.

Instutional Review Boards: The Institutional Review Board (IRB) guidebook speaks directly to the importance of including minorities in clinical trials: "The study design should provide for the adequate representation of women and minorities ... so that the findings will be meaningful for those groups and they can, therefore, share in the benefits of the research." By regulation, IRB approval requires "equitable" selection of subject and advises that the IRB should be mindful of research involving vulnerable populations. It does not, however, contain any mandatory rules of inclusion.

The FDA: In 1998, the FDA promulgated regulations to require all new-drug applications to document

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effectiveness and safety data for demographic subgroups including gender, age and racial subgroups, within the selected participants. However, there is no mandate to include such subgroups in the study. In 2011, the FDA issued guidance outlining strategies for enrolling women in medical device trials. Finally, in 2012, the FDA Safety and Innovation Act required a report to Congress on diversity in clinical trials. The resulting report was published in August 2013 and included recommendations for the FDA to increase its focus on understanding how biological and genetic factors influence how individuals react to a drug or device, and to work to ensure clinical trials adequately account for those factors.

National Institutes of Health: The NIH was ahead of the FDA and issued guidelines urging inclusion of women and minorities in clinical research in 1987. These guidelines were strengthened by the NIH Revitalization Act of 1993 that directed the NIH to establish guidelines for inclusion of women and minorities in clinical research. The resulting regulations require a "clear and compelling rationale and justification" for excluding women or minorities from any NIH-supported biomedical research. In addition, the regulations require that if Phase I or Phase II trials indicate significant differences between subgroups, Phase III trial design must include at least two inquiries—in order to investigate the differences identified.

Additional agencies and groups. Other government agencies and groups work to increase diversity in clinical trials, for example, the FDA Office of Minority Health, which was established by the Affordable Care Act and has a mission of reducing ethnic and racial health disparities. In addition, the Office of Women's Health issued a 2011 report on strategies to engage women and minorities in clinical trials, and there has been some industry movement to increase the number of minority physicians conducting clinical trials in hopes of improving outreach and participation.

It has been more than 20 years since the first government regulations and recommendations sought to increase the diversity of participation in clinical trials and to ensure that the proportion of racial minorities and women in clinical trials reflects the composition of the U.S. population at large. Despite these efforts, the continuing lack of racial and sexual diversity is a persistent problem.

Below are some of the continuing challenges faced in attempting to improve diversity in clinical trials along with some strategies to address those challenges.

- **Increasing physician awareness.** Patient recruitment into a clinical trial is often the result of physician referral. Physicians should be educated about the importance of clinical trials to the health care system, the current lack of diversity in clinical trials, and the potential harms to patients resulting from this lack of diversity. Advocacy organizations, medical schools and/or teaching hospitals with large research programs may be well-positioned to provide such education.

- **Communication.** Transparent communication and education regarding the risks and benefits of participation, the importance of clinical trials for medical advancement and the vital role patients perform in moving drugs and devices to market should be part of any recruitment strategy. Different tools and messages may be appropriate for outreach to different groups or subgroups.

- **Health care access**. Another set of challenges arises from disparities in access to the health care system. A patient needs to interact with the health care system in order to be recruited to enroll in a clinical trial, and often must have insurance coverage sufficient to pay for any costs related to such participation (as insurance may cover the non-experimental portions of the trial).

- **Access to clinical trial sites.** Transportation and proximity to trial sites may also be a barrier. The FDA's Office of Women's Health notes that according to the ZIP Code Analysis Project (conducted by the National Association for Elimination of Health Disparities), 80 percent of racial minorities reside in 20 percent of U.S. ZIP codes. This means that, depending upon the trial site, potential minority participants may need to travel farther than others to participate. Child-care needs or an inability to take time from work may also impede access. Thus, recruitment strategies should address not only how minorities and women are recruited but also what support and resources are necessary and offered to facilitate their productive participation.

An increasingly diverse population requires medical products that are safe and effective across distinct population subgroups. Looking ahead, we anticipate continued public and private sector efforts to educate physicians and patients, regulatory efforts to encourage (or require) consistent representation of diverse populations in clinical trials and the consideration of effectiveness across population subgroups during the medical product approval process. As science advances and medicine moves toward more genetic and personalized interventions, equal access to clinical trials will only become a more pressing imperative, and the call for legal intervention to compel inclusive treatment development will only intensify. ■