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Considerations for Patient Advocacy and Engagement in Connection with FDA's Draft Guidance on Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials

On April 13, 2022, the FDA released Draft Guidance entitled *Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials,* The Draft Guidance provides recommendations to industry on how to collect and present race and ethnicity data in submissions to the FDA. Significantly, it recommends developing and submitting a Race and Ethnicity Diversity Plan to increase participation in clinical trials by populations currently underrepresented in such studies**.** This builds on previous guidance regarding the collection of such data from October 2016 and on non-binding recommendations from the 2020 *Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs; Guidance for Industry*.

While the healthcare sector certainly supports increased diversity as an important and long overdue step, we believe the Draft Guidance as issued may have unintended deleterious impacts on the very communities it seeks to help and that Patient Engagement functions can play a significant role in ensuring the Draft Guidance is considered and approached as motivating, meaningful, and lasting change.

In this document, we outline our concerns for how this Draft Guidance on racial and ethnic diversity in clinical trials might create distress and confusion within patient communities, and our recommendations on how the implementation of the Draft Guidance could more likely ensure success in drug development.

What is missing from the Draft Guidance?

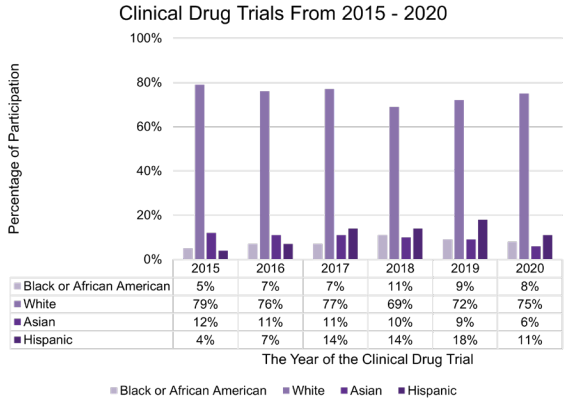
The Draft Guidance offers a clear, elegant rationale for the importance of diversity and inclusion in clinical trials. It notes that:

> *Adequate representation of these populations in clinical trials and studies supporting regulatory submissions helps ensure that the data generated in the development program reflects the racial and ethnic diversity of the population expected to use the medical product if approved and may potentially identify effects on safety or efficacy outcomes that may be associated with, or occur more frequently within, these populations*.

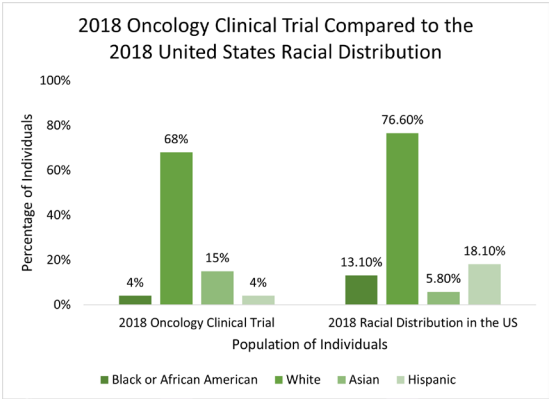
The Draft Guidance also contains recommendations for identifying the scientific issues to be discussed in a Race and Ethnic Diversity Plan. These recommendations appear perfectly adequate and logical, although scientific colleagues may argue it over emphasizes the relationship of race and disease—we will leave such concerns to the scientific experts.

However, the Draft Guidance does not address or acknowledge several significant challenges.

First, it does not address the substantial task of enrolling diverse populations in clinical trials. In our many discussions with clients since the release of the Draft Guidance, we have heard consistent concerns: implementation is not simple, and it is not done quickly. As the following charts demonstrate, the participation in trials by persons of color fluctuates but remains well below the actual racial and ethnic distribution in the United States.



Reference: 2015-2020 "Drug Trials Snapshot Summary Reports" US Food & Drug Administration



Reference: Vose J. "Minority Enrollment to Clinical Trials: Road to Increased Access" NLM 3/15/21

A second, equally important concern is that the Draft Guidance does not consider the trickle-down effect the recommended actions will have on the community—including local clinics, hospitals, community cancer centers, and Federally Qualified Health Centers (FQHCs). Implementation of these actions will stress the infrastructure, educational capacity, and finances of these entities.

For example, although as much as 90% of cancer patients are treated in a community oncology setting, most trials occur at academic centers, making them only accessible to the remaining 10% of the patients. Patients must have an interest in trials, locate an appropriate trial, and qualify for the trial—then they must adjust their work and life schedules in order to travel to these centers for care. Disproportionately, patients of color have not been afforded the resources of time, money, and family and social support needed to engage in this process. In short, diversity in oncology trials is highly impacted by where those trials are offered. The lack of attention to providing information and care in the patient's spoken language and relevance to cultural background may present additional barriers to this process and trial participation.

Conducting clinical trials at community oncology sites could greatly reduce or even remove the obstacles these patients face; and indeed, community oncology continues to increase participation in trials with varying degrees of success. As recently described by three FDA officials and a diversity thought leader, the key to scaling these efforts in a sustainable way will be the engagement of community clinicians. These providers already have well-established, trusting relationships with their patients—of all colors—and can facilitate open and honest discussions about the benefits and risks of trial participation.

Unfortunately, multiple barriers impede clinicians' involvement in trials, including a lack of time and compensation for discussing trials with their patients, lack of recognition for referring patients to trials, and lack of the training, support, and resources that the clinicians need to participate in research. Increasing opportunities for involvement in trials for clinicians of diverse populations is critical. Overcoming these barriers with training, funding, and logistical support could enhance the role of community clinicians in clinical trials, increase the number of community sites conducting such trials and, in turn, increase the diversity of the patient populations that enroll in them.

Additionally, as some community sites have already noted, conducting more trials creates additional challenges, unrelated to diversity issues *per se*. Such challenges include difficulty in recruiting, retaining, and training clinical trial staff, collecting and managing the significant amount of data required for trials, and challenges in managing and storing increasingly complex cancer treatments. These issues could also be addressed with training, in addition to financial and logistical support.

Third, the Draft Guidance does little to acknowledge medical mistrust that exists in some communities—particularly communities of color—or the bridge-building and education that is still needed to overcome these barriers. Some companies have made modest progress to address these concerns by, for example, revising and expanding trial eligibility criteria, streamlining informed consent documents, and building relationships within community settings versus defaulting to large, academic centers for a majority of trials. Still, this largely incremental progress has not done enough to ensure that broad and diverse populations will participate.

Finally, and importantly, industry, with greater regularity, is approaching disease-specific patient advocacy organizations to help with trial recruitment, including recruitment of diverse patients. Most of these organizations believe in trial education and recruitment, but do not want to be viewed as "headhunters" for the biopharmaceutical industry. These organizations want to educate patients about trials, teach patients how to find trials, provide trial navigation, and even invest in building and maintaining databases of trials; for the most part, however, they would not wish to be responsible for recruiting patients, nor compensated by industry directly or from clinical research organizations (CROs) for doing so. We fear this Draft Guidance may exacerbate this type of request to patient organizations.

Increasingly, the biopharmaceutical industry is reaching out to organizations that focus on segments of society that have been traditionally stigmatized in healthcare, such as Black men and women, LGBTQ+ communities, Native Americans, and rural health communities. These organizations have much to offer, but we risk recreating the problem—long understood by patient advocates—of each company approaching these organizations with the same requests for supporting their efforts in trial development and recruitment. To us, this model seems unsustainable and may quickly exhaust the community of advocates and patients who will be inundated with requests for help. No single organization, no matter how dedicated to the historically excluded populations it supports, can meet the needs of the entire industry.

While these issues can seem daunting, they are both quantifiable and surmountable and could potentially be overcome with greater collaboration and investment across the entire community that cares about drug development and diversity.

Our Recommendations

Overall, we need a better, comprehensive, and coordinated approach across government, non-profit, and private sectors to address this issue. Ensuring diversity in clinical trials is essential and requires new thinking, bold ideas, and an uncommon commitment to cooperation across the sector. We see successful enactment of the Draft Guidance resting on three key pillars where Patient Engagement and Advocacy can play a significant role: (1) fostering collaboration within the non-competitive space; (2) building capacity for community sites; and (3) crafting deep and meaningful relationships of trust in patient communities.

1. **Fostering collaboration within the non-competitive space**. The Draft Guidance affects every company's clinical development program, and strong, successful programs are informed by patient input every step of the way. Each clinical trial has nuances that require specific types of patient and advocate input. Still, some commonalities exist in the ways that underserved populations have experienced the healthcare system, and creative solutions have worked previously to educate and support patients in trial participation.

   We can envision building an association of advisory boards supported by and available to multiple companies simultaneously. Rather than each company sourcing its own advisory boards, this association would provide shared advice, solutions, and input to commonly identified issues

affecting all companies as they work on meeting the requirements in the FDA Guidance, once finalized.

One type of board would be advisory councils comprised of the leading advocacy organizations focused on healthy equity issues. These councils would be longitudinal in nature. Companies would contract with them, and they would be available throughout the contract period for advice on relevant topics in the non-competitive space, such as educating on medical mistrust and successful ways of addressing it, sharing creative strategies proven to work to support diverse participation in clinical trials, and ensuring companies gain real understanding of these communities and their needs.

A second board type would focus on DEI/HE programs in specific therapeutic areas for the purpose of input on clinical trial protocols, raising awareness of a disease, reviewing marketing materials, and more.

Both types of boards would avoid the duplication of each company approaching the same groups to ask the same questions. Instead, these boards could develop a series of topics that are of interest to companies and conduct company-sponsored roundtable meetings in which sponsors could engage in dialog with the board regarding those topics.

2. **Building capacity for community sites**. As noted earlier, barriers to trial development and recruitment in historically excluded community settings exist and require investment in practical and logistical solutions in order to support Draft Guidance goals. A number of companies have made important financial investments to build expertise in the next generation of trial managers in these communities, but the individual efforts of any one company will not be adequate to address the systematic problems. Community settings may be inundated with expectations that cannot be easily fulfilled.

   Fortunately, we have good models for addressing systematic problems. In 1999, for example, the Institute of Medicine published the report *To Err is Human: Building a Safer Health System*. The paper determined that close to 100,000 patients in the US died from medical errors each year. This led to a demand for more accountable care and better communication to address the needs for improvement in clinical care management, the capture of data for continuity of care, and the definition of measures to monitor costs and quality of care. From that demand, governmental action was taken to provide financial incentives to support and coordinate efforts to improve healthcare through the adoption of health information technology (HIT) and the development of a nationwide health information exchange (HIE). Objectives for the “meaningful use” of these technologies were established to outline what providers must achieve to participate in the Electronic Health Record (EHR) Incentive Programs.

   Ensuring diversity in clinical trials requires no less of an effort. While we are not suggesting we wait for the US government to act, we are suggesting that a similar financial incentive structure involving a public-private partnership could provide the infrastructure needed for trial sites in communities traditionally left behind to be successful. Entities such as biopharmaceutical trade organizations could join forces with leading healthcare think tanks to develop a comprehensive plan to support these needs in underserved areas. This should include developing the next generation of leaders in the diversity space and promoting diversity in investigators.

3. **Crafting deep and meaningful relationships of trust within patient communities**. Progress will not be made until we understand, acknowledge, and respect the lived experiences of individuals who have systematically been discriminated against, offered lesser treatments or no treatment at all, and who, as a result, have feared clinical trials rather than understand them as

potential opportunities for hope. These issues will only be solved with a concerted effort to engender trust, which begins by building relationships that are not based on the need to demonstrate trial recruitment numbers. This begins with companies forging and investing in lasting partnerships in communities, irrespective of filling a trial quota. Patient advocacy organizations and biopharmaceutical companies frequently work on co-creating solutions that are of mutual benefit. These efforts can be expanded to include community organizations outside of the usual sources.

VOZ Advisors has the good fortune of working with clients who understand these matters and who know that ensuring trial participation of diverse populations is not only the right thing to do, but also the right business decision. We applaud the FDA for taking this step with the Draft Guidance and establishing additional useful resources, such as its initiative on clinical trial diversity. We invite the healthcare community at large, in particular Patient Advocacy and Engagement executives, to rise to the challenge by acknowledging the critical issues, and we hope our thoughts will spur positive actions to rectify a long-standing inequity in clinical trial participation.

We would love to hear your thoughts. Please direct any questions or comments to Misha Mathur at mmathur@vozadvisors.com.

You can tune in to our webinars and podcast series*:*

- Understanding the FDA Draft Guidance on Improving Diversity in Clinical Trials: A discussion of considerations in developing and submitting the recommended race and ethnicity diversity plan
- FDA Draft Guidance on Diversity in Clinical Trials: Charting a Path Forward through Patient Advocacy & Engagement
- *Raising Our Voices for Health Equity*