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Engaging the Community, Looking Inward: Meeting the Imperative of Diversity in Trials

By Theresa Defino

As the pandemic continues to grip the United States, bringing more illness and death to minorities in particular, and the nation reflects on a summer of unrest over racial injustice, the linked issues of lack of diversity among clinical trial participants and growing health disparities have come to the fore perhaps like no period in recent history.

For institutions and researchers alike, achieving diversity is no longer just a goal: especially for studies aimed at either treatment or vaccines for COVID-19, it has become an imperative. Fortunately for researchers and institutions, there are strategies, tools and ideas to assist with this challenge.

Among common themes: diversity begins at home. Experts say institutions should reflect on the number of their investigators who are members of the minority groups being studied and recommend all trial staff undergo cultural sensitivity training. Another key component of success is ensuring recruitment strategies aren't an afterthought; they must be built into every aspect of a trial, even before a protocol is designed. In addition real—and sustained—community engagement is essential.

In recent weeks, the Food and Drug Administration (FDA) has sought to bring attention to the issue, as has an institutional review board (IRB) firm. The Multi-Regional Clinical Trials (MRCT) Center of Brigham and Women's Hospital and Harvard has also made resources available to increase the diversity of trial participants.

MRCT's new report, "Achieving Diversity, Inclusion, and Equity In Clinical Research," was the subject of a Sept. 22 webinar sponsored by the FDA Office of Minority Health and Health Equity.[1] FDA representatives were among the members of a work group that helped draft MRCT's 341-page "guidance document," issued in August along with a 129-page "toolkit."[2] Other resources are available on a dedicated website, https://mrctcenter.org/diversity-in-clinical-trials.

FDA's office of minority health "is committed to reducing health disparities and improving health equity," said Richardae Araojo, FDA associate commissioner for minority health and the office director. She added that "a key priority for our office is working to advance the participation of racial and ethnic minority groups in clinical trials." The webinar was organized to "convene thought leaders and experts to educate and dialogue about the pressing issues that our communities face."

Other FDA officials in addition to Araojo were also involved, aided by a diversity workgroup that included representatives from NIH, universities, pharmaceutical firms, disease-specific patient organizations and foundations, among others. Work on the documents began in May 2017, long before the pandemic hit but fully informed by both racial disparities in health outcomes and lack of adequate representation in clinical trial enrollment.

The MRCT Center acted on the "urgency to publish" the report without some "finishing touches" in place, according to the authors. They were heeding the call because "the present focus on issues of diversity has

underscored the lack of diversity in clinical research" and the fact that "the COVID-19 pandemic has exposed the increased incidence and severity of disease on Black, Latinx, Pacific Islander, and some vulnerable populations. And yet, clinical trials directed to treat and prevent COVID-19 have underenrolled those that are disproportionately affected."

Impact of COVID-19 Is Uneven

During the webinar, Barbara Bierer, M.D., professor of medicine at Harvard Medical School and MRCT Center faculty director, explained that in trials, "underrepresentation of black or African American individuals, as well as Hispanic individuals, is not new."

Two important types of studies are especially problematic. According to 2015-2016 FDA data Bierer presented, Black/Africans composed just 2.5% of participants in cardiovascular studies and 2.7% in oncology trials. But data for the two-year period also showed that Black/Africans were "a full 24%" of enrollees in psychiatric drug trials. Although the exact reasons for higher minority enrollment are not known, "it gave us the clear indication that this is doable if one commits to it," said Bierer.

Although "there are many groups now really focused on providing and ensuring diverse representation in COVID-19 clinical trials," this has "been a challenge," she said.

COVID-19 Impact Is Uneven

But the need is undeniable. The overall incidence of COVID-19 is 38 per 10,000 people. But it jumps to 73 for Latinos, 62 for Blacks and 23 per 10,000 for whites, according to data Bierer shared. The mortality rate is also three-fold or higher for Blacks, Latinos and indigenous populations compared to whites, according to the information Bierer showed.

Bierer noted that it is "important to understand that race and ethnicity are not, in themselves, biological determinants" and "do not represent a certain biology that tracks with definition of race and ethnicity." As a result, "there's been some skepticism about why is it so important to bring a full representation of the populations into clinical trials if any clinical trial cannot be powered to understand differences amongst all these different sub groups."

Bierer added that "social determinants of health have a real impact" on biology, "but [are] also a matter of health equity, fairness, and public trust. If we don't look at diverse representation in clinical trials, we can't possibly understand those differences; we cannot understand the biology."

Having a diverse clinical trial workforce is also crucial and requires effort. Ensuring diversity among trial participants can't "wait until there is a sufficiently diverse workforce," said Bierer, adding, "we all must commit to building that workforce."

Investigators and staff "involved in the clinical trial enterprise should be trained in cultural competence and implicit bias," she added.

Trial sites should be scrutinized for their capacity—with data if possible—to enroll diverse participants. Additional efforts through data standards, "real-world data" and new methods of extracting data from analysis can help fill in gaps about subgroups, Bierer said.

Don't Just 'Fly In'

Other enrollment challenges include "lack of awareness [of] and access to clinical trials. The study design and

research procedures may be burdensome. The outcomes may not be relevant for [patients]," Bierer explained. Further, for participants, "payment is often delayed or nonexistent, and there is a sense of mistrust in the community," and trust is "fundamental to the work we do," she said.

"We think the first and one of the most important steps is a real commitment to patient and community engagement that supports diverse participation," said Bierer. This requires "forming relationships with the community and the patient base." Members of the community "should be in key leadership roles as advisers and as consultants to those that design the trials [and] be embedded in the work that goes forward," she said.

Actions should be taken so that "the patient perspective can influence research priorities"; that these individuals "feel empowered to express their opinions in a respected way"; and shared goals can be developed that ultimately would help "tailor the study design and conduct" and improve access, enrollment and retention, Bierer added.

She cautioned "it's important that these be sustained partnerships" and that "it's not that investigators fly into the community…and then disappear." When necessary, "trusted intermediaries between the academic staff and the community itself" are useful and will help "undergird all that we do [as part of] a transparent and trusting relationship."

The MRCT Center's toolkit includes a checklist for sponsors, clinical research organizations and others.[3]

While the workgroup's recommendations reflect "an aspirational effort," said Bierer, "there are many, many steps that we can take now and going forward in order to really make sustained change in the representation of diverse populations in clinical research. We appreciate that this is only the beginning of the journey there. Nevertheless, I think that each of us, by helping each other to be accountable using transparency, metrics, and discussion and research, we can figure out how to do a better job than we are doing now."

She said the MRCT intends to add more tools to the diversity web page and hold a series of webinars to discuss more details about specific recommendations.

Focus on Community Board, Patient Centricity

Many of the strategies that Bierer, and Luther Clark, M.D., deputy chief patient officer for Merck & Co. Inc., discussed during the FDA webinar were echoed by LaTasha Lee, vice president of clinical and social research and development for the National Minority Quality Forum. She was one of several speakers at a Sept. 23 webinar sponsored by WCG Inc., also on the topic of diversifying enrollment in clinical trials.[4]

Lee recommended the creation of community advisory boards, which she said can bring "diverse perspectives to conversations" and foster an understanding of "the needs of that community." Additionally, "If you do this structure right, those [boards] can actually inform your protocol, they can inform the design…inform your communications."

Like Bierer, Lee said institutions that lack diverse investigators should put the ones it does have "through cultural competency training," and should "employ strategies to support and train non-minority investigators on being connected to the communities in which they serve." For example, this could help them learn what words may have negative connotations among certain patient communities, she said, such as the use of the term "sicklers" among people with sickle cell disease.

As of September, there were "194 clinical trials in sickle cell disease currently recruiting" participants, Lee said, noting that the majority of clinical trials occur, especially in rare diseases like sickle cell disease, in major

academic centers. "And that's a problem, because we know when we're talking about diverse communities, major medical academic centers often present" a number of barriers, including location and a history of "past abuses," she said.

Lee described working with the ASH Research Collaborative, a nonprofit established by the American Society of Hematology in 2018 "to foster collaborative partnerships to accelerate progress in hematology, with the goal of improving the lives of people affected by blood diseases." Lee said she helped build the business plan for the collaborative, which included a comprehensive community engagement plan, use of a community advisory board composed of "trusted voices," and a "hub-and-spoke" model of clinical trial sites that included infusion clinics and other facilities and practices.

"Additionally, at each clinical trial unit, we had a dedicated research coordinator that was only focused on clinical trials in that particular consortium," Lee said. The consortium also "leveraged real-world data" from medical records "to inform what eligibility criteria in the study actually met a particular site."

The approach is one of "patient centricity," Lee said, which requires that "you start early" to "build a culture of research and engagement within that community. You find out what are the needs of that community," such as education. Then, educational materials would be "co-created" with the community, for example, she said. Patient-centered approaches "empower the community to make informed decisions about their care and their treatment."

Lee said she is also helping to launch the Minority and Rural Coronavirus Insights Study, which aims to enroll 5,000 individuals from several states and follow them for five years to examine the impact of COVID-19 on communities of color.

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1 U.S. Food and Drug Administration, "OMHHE Health Equity Lecture Series: Achieving Diversity, Inclusion, and Equity In Clinical Research," webinar, September 22, 2020, https://bit.ly/2SYhv5K.
2 "Diversity, Inclusion, and Equity in Clinical Trials," The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard, accessed October 19, 2020, https://bit.ly/2T7p9uD.
3 Theresa Defino, "Diverse Participant Engagement Strategies," *Report on Research Compliance* 17, no. 11 (November 2020).
4 WCG Inc., "Diversifying Clinical Trial Participation: Effective Strategies for Identifying and Recruiting Diverse Patient Participants," webinar, September 23, 2020, https://bit.ly/3kaTrIQ.