DIVERSITY IN CLINICAL TRIALS: LIFE SCIENCES INITIATIVES AND CHALLENGES IN LIGHT OF THE FDA's LATEST GUIDANCE

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INTRODUCTION

This paper is a follow up to *Diversity in Clinical Trials Participation: A Life Sciences Perspective,* focused on examining the perspectives of former clinical trial participants, clinical trial coordinators and principal investigators, to better comprehend the actions being taken to promote inclusivity and diversity in clinical trials.

To date, life sciences' efforts towards driving equitable healthcare have centered around access to care, early identification and prevention. Meanwhile, less attention has been given to the impact of homogenous trial populations. Clinical trial diversity continues to be one of the greatest challenges pharmaceutical and biotech companies face in ensuring the delivery of medicines that are effective for all people.

Efforts to improve racial and ethnic diversity in trials have increased in the last decade, however disparities remain. Over 40% of the United States (U.S.) population is currently comprised of ethnic and racial minorities[1], often only 5 to 10% of clinical trial participants represent any minority population. This disparity is striking and exposes the non-white population to harm as a result of an uncomfortable gap of knowledge around what is effective and ineffective (or even dangerous) in minority patients.

This research actively examined and explored what initiatives are being undertaken at the corporate level to improve the diversity of trials, the effectiveness of those initiatives and the impact of the FDA's guidance to improve diversity now and in the future.

OBJECTIVES

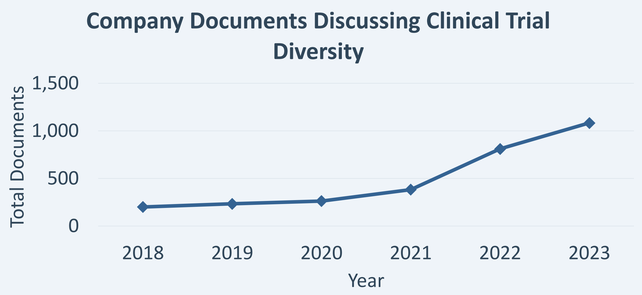
- Follow-up on previous research with former trial participants to understand the perspective of the pharmaceutical company on their efforts to recruit and retain minority trial participants
- Understand what initiatives are being undertaken at the corporate level to improve diversity of trials
- Characterize the effectiveness of current diversity initiatives for clinical trials
- Understand the expected impact of FDA guidance on improving trial diversity
- Provide recommendations for the future of DEI in clinical trials in light of FDA guidance

METHODS

- Secondary research was conducted to review company documents and presentations to assess the state of current activities and investment towards trial diversity
  - Documents were included for the time period of 2018 to 2023
  - Relevance and mentions were assessed by keyword searches for combinations of "clinical trials" and "diversity" and synonyms
  - Only primary companies were included in the overall trend analysis
- Following our literature review, primary market research was conducted via semi-structured qualitative interview methodology
  - One-on-one 45-minute telephone interviews were conducted with pharma and biotech executives in charge of clinical trial diversity initiative design and/or execution across the US
  - The sample included 15 executives from small to large pharma and biotech companies who have served as a clinical trial diversity leaders within their organization for at least one year

RESULTS

Figure 1 | Overall Company Mentions of Clinical Trial Diversity



- Since 2018, clinical trial diversity has seen increasing representation in company documents and communication – with significant jumps in 2022 and 2023.
- Companies have provided increasing coverage on their initiatives and investment in environmental, social and governance reporting and investor presentations as well as at medical conferences.

Table 1 | Key Activities Reported by Pharma in Public Documents

Collaboration	➢ Working to establish Clinical Trial Diversity Centers of Excellence ➢ Collaboration across groups to expand diverse participation in trials ➢ Strategic collaborations with non-profits to advance health equity in core therapeutic areas
Strategic Realignment	➢ Revising processes and systems to capture and analyze demographic parameters such as patient race and ethnicity ➢ Committing to designing clinical trials that reflect the racial and ethnic diversity of the communities they serve ➢ Establishing diversity goals based on disease epidemiology
Investment	➢ Contributing to industry partnerships advancing diversity initiatives ➢ Developing and testing diversity measurement tools ➢ Building community-based partnerships in underserved communities

- While the FDA guidelines have not gone into full effect, it appears that many companies are proactively implementing strategies to ensure compliance.
- However, overall secondary analysis identified a gap in the current reporting of actual efforts. Companies have increased discussion and focus on DEI efforts and investment but have yet to provide tangible reporting on outcomes.

Figure 2 | Company Commitment to Trial Diversity Varies Greatly

"We actually wrote in our clinical trial protocol that we will enroll x number of patients of African American origin, x number of patients of Hispanic origin, etc. It forces you to really make a serious effort in enrolling those patients." – Director of Clinical Development, 2023

"We do not set a certain quota or certain percentage of the study population that we proactively say we will need to enroll based on the race. I don't really see any practical initiatives being put in place." – Senior Physician Clinical Development, 2023

- The lack of uniformity in diversity initiatives amongst Pharma companies shows that the impact of the guidance will be variable. Additionally, companies who are not prepared to address the tenets of the guidance may be met with challenges that delay getting their products to market

Table 2 | Barriers to Pharma Attaining Clinical Trial Diversity

Limited human and financial capital	➢ Limited human and financial capital hinder the ability to effectively execute improvements in trial diversity activities ➢ A cost benefit analysis must be considered, which can often lead to funds being diverted away from diversity initiatives ➢ Accordingly, diversity is prioritized in trials where the disease has a disproportionate impact on a specific minority group
Other Priorities	➢ For some companies trial diversity is a top priority, while others are just starting to formally organize teams and initiatives around trial diversity

- Ongoing barriers to ensuring clinical trial diversity are often familiar to pharmaceutical organizations and executives, however additional steps are needed to address them
- Organizations must be conscious of socioeconomic barriers, language and cultural barriers, and general skepticism from diverse groups and work to address each challenge

Table 3 | Recommended Tactics to Improve

Willingness to Take Less Experienced Trial Clinicians	➢ Respondents mentioned including more minority PIs will help improve trial diversity, but that may come at the cost of taking less / inexperienced clinical researchers
Make CROs Accountable	➢ CROs are a driving force behind trial execution, so requiring CROS to have diversity plans will help ensure trials have a balanced mix of participants
Be Flexible	➢ Flexibility in inclusion criteria and modes of patient follow up will be necessary to ensure minority groups can be included given challenge with transportation, personal and work commitments and the general mistrust that many minorities have for pharma companies

- This research found that some CROs have diverse teams that brainstorm ways to increase recruitment and participation from hard-to-reach patient demographics, but others still are not excellent on delivering with tactics to recruit diverse respondents
- With the role CROs play with respect to trial planning and recruitment it will be important for them to aid with initiatives moving forward

Table 4 | Anticipated Challenges with FDA Guidance

Pharmacokinetic – Pharmacodynamic Data	➢ Limited PK/PD data available in many less common disease states within ethnic groups ➢ Studies tend to be smaller and less representative of the general population ➢ Primary and Secondary endpoints are usually primary focus of trial, rather than exploratory endpoints
Enrollment Goals	➢ Limited pathophysiology data within ethnic groups to ensure participants match study needs ➢ Implementation of education and community engagement
Repercussions	➢ Delays in acceptance of clinical trial by the FDA ➢ Issues or delays with drug approval

- Difficulties in obtaining pharmacokinetic-pharmacodynamic (PK/PD) data and make summarizations for underrepresented populations difficult especially in rare diseases
- In more common conditions such as diabetes, obesity and heart disease PK/PD data is easier to obtain for minority populations

DISCUSSION & CONCLUSION

Discussion

What are pharma companies doing today?

- Companies have provided increasing coverage on their initiatives and investment by clearing defining diverse enrollment expectations in trial protocols, choosing trial sites in areas known for strong minority populations, collaborating with Patient Advocacy Groups, and providing equitable resources to get to and from trial sites

What is the impact of the FDA guidance so far?

- Amongst pharma employees, familiarity with impending FDA guidance varied depending on whether company's leadership made adherence to guidance a priority; companies who have started to prioritize diversity remain outliers
- While companies appear focused on DEI activities, tangible outcomes remain hazy due to lack of clear metrics and transparency
- The largest barrier cited by 100% of executives was resources, both human and financial; executives also expect difficulties in obtaining pharmacodynamic data, implementing strategies to engage diverse populations, meeting enrollment goals, and lack of clarity around potential repercussions for not making efforts to meet diversity and inclusion goals

Future Recommendations:

- Dedicating more resources to on-the-ground, targeted activities that have the greatest potential to attract minority groups of interest into trials (festivals, churches, etc.)
- Hold CROs to a higher standard for what they can do to ensure minority recruitment; make this a key criteria in CRO selection

Conclusions

- The FDA has attempted to enhance diversity in clinical trials by introducing guidelines and promoting transparency and accountability
- Current guidelines' lack of clarity and absence of specific penalties for non-compliance may lead to varying levels of adherence
- Community led interventions will play a significant role in building the trust, connection, and engagement within minority communities to partake in clinical research

REFERENCES

1. *Diversity in Clinical Trials Participation: A Life Sciences Perspective*
2. FDA Draft Guidance – Diversity Plans to Improve Enrollment… Docket FDA-2021-D-0789
3. AlphaSense

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Disclosures: