Achieving Diversity, Inclusion, Equity In Clinical Research

Barbara E. Bierer, MD
Professor of Medicine, Harvard Medical School
Faculty Director, MRCT Center of BWH & Harvard
bbierer@bwh.harvard.edu

Luther T. Clark, MD
Deputy Chief Patient Officer
Merck & Co., Inc
luther.clark@merck.com
The views and findings expressed in this document are those of the authors and do not imply endorsement or reflect the views or policies of the U.S. Food and Drug Administration or the affiliated organization or entity of any member who contributed to this work. Individuals have served in their individual capacity.

The MRCT Center is supported by voluntary contributions (www.MRCTCenter.org) and grants.
Our Vision

Improve the integrity, safety, and rigor of global clinical trials.

Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.
**Coronavirus cases per 10,000 people**

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Cases per 10,000 people</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>23</td>
</tr>
<tr>
<td>All</td>
<td>38</td>
</tr>
<tr>
<td>Black</td>
<td>62</td>
</tr>
<tr>
<td>Latino</td>
<td>73</td>
</tr>
</tbody>
</table>

**Adjusted for age, race and ethnicity widens the gap in mortality compared to Whites**

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Fold Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>3.4</td>
</tr>
<tr>
<td>Latino</td>
<td>3.3</td>
</tr>
<tr>
<td>Indigenous</td>
<td>3.3</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>2.9</td>
</tr>
<tr>
<td>Asian</td>
<td>1.3</td>
</tr>
</tbody>
</table>

*The New York Times*
July 5, 2020

*Fold increase*

September 15, 2020
https://www.apmresearchlab.org/covid/deaths-by-race
Racial Disproportionality in Covid Clinical Trials
Daniel B. Chastain, Pharm.D., Sharmo P. Osae, Pharm.D., Andrés F. Herazo-Martínez, M.D., Carlos Franco-Paredes, M.D., M.P.H., Joanna S. Chastain, Pharm.D., and Henry N. Young, Ph.D.

COVID-19 disparities: An urgent call for race reporting and representation in clinical research
Hala T. Borno a,b, Sylvia Zhang a, Scarlett Gomez b

Researchers call out lack of diversity in COVID-19 clinical trials
Mary Chris Jaklevec, MSJ
https://jamanetwork.com/journals/jama/fullarticle/2769611
Drug Trial Snapshots: Summaries

Participation of Black or African American individuals in clinical trials for oncology, cardiology, and psychiatry

2015-2016

Cardiovascular Disease
N = 92,329
2.50% 1,415
97.50% 55,118

Oncology
N = 7,691
2.74% 211
97.26% 7,480

Psychiatry
N = 5,810
24.18% 1,405
75.82% 4,405

https://www.fda.gov/media/106725/download

22 September 2020
FDA-hosted Launch

©MRCT Center

mrctcenter.org/diversity-in-clinical-trials/
Background

- Clinical trials are needed to develop new treatments and new vaccines.
- Participants in trials should reflect the population affected by the disease, or those intended to utilize the intervention.
- We should not assume that all individuals respond similarly to interventions.
- Underrepresentation in clinical trials of Black, Latinx, Asian, Native American, and other underserved populations—as well as women and individuals at either end of the age spectrum—is not new, and persists in both industry and academic trials, and across therapeutic areas.
- Race and ethnicity are not a biological determinants, but social determinants of health have a real impact on real biology.
- Diverse representation in clinical trials is not simply a matter of biology, but a matter of health equity, fairness, and public trust.
Leadership

- RADM Richardae Araojo, PharmD, MS, U.S. FDA
- Barbara E. Bierer, MD, MRCT Center
- Luther T. Clark, MD, Merck & Co., Inc.
- Milena Lolic, MD, U.S. FDA
- David H. Strauss, MD, Columbia University
- Sarah White, MPH, MRCT Center

MRCT Center staff:
- Carmen Aldinger, PhD, MPH
- Hayat Ahmed, MS
- Laura Meloney, MS, MPH
- Joshua Smith-Sreen, MBE

And the invaluable contributions of >50 workgroup members, representing:

- Patients, Patient Advocates
- Academia
- Pharmaceutical companies
- CROs
- Non-profit organizations
- Trade associations
- Government agencies
- Research institutes

Each serving in their individual capacity.
Maria Apostolaros, PhRMA
Abhijit Bapat*, Novartis
Stacey Bledsoe*, Eli Lilly and Company
Shari Bodnoff*, Novartis
Racquel Bruton, Biogen
Elizabeth Cahn, Cancer Connection
Li Chen, Amgen
Patrick Cullinan, Takeda, currently BlueBird Bio
Liza Dawson*, National Institutes of Health (NIH)
Maria De Leon*, Parkinson’s Foundation
Theresa Devins, Boehringer Ingelheim, currently Regeneron Pharmaceuticals
Anthony Edmonds, Takeda
Rhona Facile, Clinical Data Interchange Standards Consortium (CDISC)
Rachel Fones, IQVIA
Laura Gordon*, Institute for Advanced Clinical Trials for Children (iACT)
Anya Harry, GlaxoSmithKline (GSK)
Melissa Heidelberg, Genentech/ A Member of the Roche Group
Quita Highsmith, Genentech/ A Member of the Roche Group
Sharareh Hosseinzadeh, Novartis
Lloryn Hubbard*, Genentech/ A Member of the Roche Group
Anne Marie Inglis*, GlaxoSmithKline (GSK), currently Mallinckrodt Pharmaceuticals
Aarthi B. Iyer*, Kinetiq, now Advarra
Becky Johnson*, IQVIA
Tesheia Johnson, Yale School of Medicine
Jonathan Jackson*, Massachusetts General Hospital
Marcia Levenstein, Vivli
Roberto Lewis, Columbia University
Eldrin Lewis, Brigham and Women’s Hospital, currently Stanford University
Jianchang Lin*, Takeda
Erin Muhlbradt, National Cancer Institute (NCI)
Isabela Niculae*, Biogen
Latha Palaniappan, Stanford University
Claude Petit, Boehringer Ingelheim
Claire Pigula*, Biogen
Melissa Poindexter*, Advances in Health
Nicole Richie, Genentech/ A Member of the Roche Group
Bryant (Abel) Riera*, Population Council
Suzanne M. Rivera, Case Western Reserve University
Frank W. Rockhold, Duke University
Ricardo Rojo*, Pfizer
Rosanne Rotondo*, Novartis
Fabian Sandoval, Emerson Clinical Research Institute
Richard Sax*, IQVIA
Hollie Schmidt, Accelerated Cure Project for Multiple Sclerosis
Karlin Schroeder, Parkinson’s Foundation
Mary Scroggins*, Pinkie Hugs
Jessica Scott*, Takeda
Lana Skirboll, Sanofi
Steven Snapinn, Seattle-Quilcene Biostatistics
Stacey Springs*, Harvard Medical School
Sara Tadesse-Bell, Genentech/ A Member of the Roche Group
Ann Taylor*, Columbia University
Paul Underwood, Boston Scientific
Junyang Wang, Food and Drug Administration (FDA)
Robert Winn*, University of Illinois
Gerren Wilson*, Genentech/ A Member of the Roche Group
Crispin Woolston, Sanofi
Honghui Zhou*, Johnson & Johnson

*involvement limited in time
Achieving Diversity, Inclusion, and Equity in Clinical Research

Guidance and Toolkit Released 6 August 2020

mrctcenter.org/diversity-in-clinical-trials
A broad definition of diversity

- Race
- Ethnicity
- Sex
- Gender
- Ancestry
- Age
- Social Determinants of Health
- Environmental factors
- Genetics
- Co-morbidities
- Concurrent medications
- Other

Intersectionality:
- Dimensions of diversity are not independent variables
In the end, an individual is being treated
Sections of the Guidance Document

• Preface
• Part A – Building the Case
• Part B – Background, Ethical Principles, and Regulatory Directives
• Part C – Broadening Engagement
• Part D – Data Standards and Analysis
• Part E – Study Design, Conduct, and Implementation
• Part F – Stakeholder Commitments and the Future
• Part G – Appendix

Toolkit
Features of the Guidance Document

- Multi-stakeholder contributions and consensus
- Practical and actionable recommendations
- Accountability section considers how each stakeholder can change the paradigm
- Toolkit provides adaptable resources not easily found elsewhere
Barriers: Every stakeholder has responsibility

**Sponsors/Institutions/Sites/Regulators**
- Lack of engagement
- Lack of diverse workforce
- Trial time and cost
- Variable regulatory expectations

**Data Collection/Data Analysis**
- Lack of data standards
- Data collection and reporting variable
- Analyses inconsistent

**Investigators/Referring Physicians/Staff**
- Uncertain scientific utility of inclusion
- Eligibility criteria limiting
- Site feasibility inaccurate
- Inadequate staffing and time constraints
- Recruitment and retention challenges
- Lack of cultural competence and diverse staff

**Patients/Advocates/Communities**
- Lack of awareness
- Lack of access
- Study design and research procedures burdensome
- Outcomes of uncertain value
- Logistics of trial conduct
- Payment and other concerns
- Mistrust
Patient and community engagement support diverse participation

Forming Relationships
The patient and community to be in key leadership roles, as advisors, and as consultants

Training and Support
Patient perspective to influence research priorities and questions

Shared Goals
Seek input to tailor study design and conduct to improve access, enrollment, and retention

Sustained partnerships
Build Trust

©MRCT Center

mRCTCenter.org/diversity-in-clinical-trials/
Participant’s Clinical Trial Journey

Early Interventions
- Awareness
- Access
- Recruitment
- Screening

Study Conduct
- Informed consent: Participant on study
- On study: Additional testing Randomization
- Participant Last visit: End of study treatment
- Follow-up period
- End of trial LPLV

End of Study, Data Analysis, and Reporting
- Data Lock
- Data Analysis Complete And Reporting

Patient and Community Engagement
- Education & Health Literacy
- Feasibility Assessment
- Eligibility Criteria

Study Design
- Informed consent simplification
- Logistical issues
- Decentralized trials
- Payment, transportation, childcare, etc.

Standardized data collection
- Post-trial access to medicines
- Return of results
- Referring physician engagement

Data standards
- Data analysis
- Results reporting
- Community outreach
Product Development Pathway

**DIVERSITY CONSIDERATIONS BY CLINICAL DEVELOPMENT LEVEL**

- **Pre-clinical**: Research evaluation of possible metabolic or biologic elements to mechanism of action (MOA), heterogeneity of effect (HOE – efficacy or safety outcomes, pharmacokinetically, pharmacodynamically)
- **Plan early clinical trials**: Evaluate or validate assumptions made during pre-clinical research.
- **Engage regulators**: Based on early data to establish pathway to address gaps or explore specific indications and opportunities.
- **Conduct trials**: Designed to characterize biologically relevant diversity issues. If none identified, ensure access and social justice aspects of diversity are in place.
- **Conduct post-approval studies and leverage RWE**: To bolster evidence base and explore under-represented diverse populations.

**STUDY LEVEL DIVERSITY CONSIDERATIONS**

**Organizational Diversity Competence and Capacity Considerations**

- Workforce Development
- Cultural competency
- Resources, human and financial
- Infrastructure
- Accountability

©MRCT Center

22 September 2020

FDA-hosted Launch

mrctcenter.org/diversity-in-clinical-trials/
Opportunities: What can we do?

**Trial Design**
- Characterize target population based on epidemiology, disease burden and demographics
- Engage patient population to maximize recruitment and retention strategies and minimize burden of trial

**Site Selection**
- Determine access to potential target population to guide country, region, and site selection
- Use data-driven strategies
- Determine the feasibility of enrollment figures for target subpopulations in partnership with site(s)

**Site Support & Communication**
- Communicate targets for enrollment including demographic projections
- Assist sites with local recruitment plan and outreach activities
- Assess and support each site’s cultural readiness
- Provide diversity training to Investigators and site staff

**Accountability**
- Ensure recruitment strategy is informed by patient preferences
- Connect with referral networks in the community, including organizations directly involved with target population
- Monitor and communicate site progress, address and adjust with site as needed
Key Sponsor Opportunities & Future Actions

- Patient and Community Awareness, Access, Engagement, and Participation; Trust, Trustworthiness
- Workforce Diversity
- Eligibility and Study Design
- Logistics and Flexibility
- Data Standards and Analyses
- Innovation
- Genetics
- Diversity in data sources and databases; RWE
Accountability in Partnership

Holding ourselves and one another accountable

- Metrics
- Transparency
- Dialogue
The work ahead

• What can each of us do now?
  • One step at a time towards change
• Targeted recommendations for special populations
• Additional tools and resources
• Need for local, national, and international focus going forward
• Committing to inclusion is our first step.

“...the real work of change is done year by year, month by month, and day by day, by all of us, by each of us...”

mrctcenter.org/diversity-in-clinical-trials
Leaning in: *Practical Approaches to improving diversity in Clinical trials*

<table>
<thead>
<tr>
<th>Webinar Topic</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community awareness, access, knowledge</td>
<td>October 14, 2020</td>
</tr>
<tr>
<td>Workforce Development</td>
<td>October 28, 2020</td>
</tr>
<tr>
<td>Study Design, Eligibility, Site Selection &amp; Feasibility</td>
<td>November 11, 2020</td>
</tr>
<tr>
<td>Study Conduct (Recruitment, Retention)</td>
<td>December 9, 2020</td>
</tr>
<tr>
<td>Data Standards and Analysis</td>
<td>January 13, 2021</td>
</tr>
<tr>
<td>Stakeholder Roles and Responsibilities</td>
<td>January 27, 2021</td>
</tr>
<tr>
<td>Role of Data in Diversity: Genetics &amp; RWD</td>
<td>February 10, 2021</td>
</tr>
</tbody>
</table>

*Leaning in webinars will be held Wednesdays 11 AM -12 noon ET*
Discussion and Questions