Continuing Pharmacy Education (CPE)

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Advancing Health Equity Through Clinical Trial Diversity & Inclusive Research: The Integral Role of Pharmacists

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Learning Objectives

- **REVIEW** key terms related to clinical trial diversity, inclusive research, and health equity
- **DESCRIBE** current FDA guidance and legal requirements related to improving participation of historically underrepresented racial and ethnic groups in clinical research
- **OUTLINE** trust-based frameworks for optimizing clinical trial diversity and outreach to historically underrepresented communities
- **RECOGNIZE** the role of pharmacists in advancing clinical trial diversity efforts, based on various practice settings: community, health system, industry

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Disclosure

I, Camille Pope, PharmD, RPh, am an employee at Acclinate, Inc

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Key Terms[1,2]

Diversity

Anything that **sets one apart from another**, including the full spectrum of human demographic differences as well as different ideas, backgrounds, and opinions

Inclusion

Implies a cultural and **environmental feeling of belonging and sense of uniqueness**; represents the extent to which one feels valued, respected, encouraged to fully participate

Equity

Fair treatment for all, while striving to identify and **eliminate inequities and barriers**

Health Equity

Everyone has a fair and just opportunity to be as healthy as possible; requires **removing obstacles** such as poverty, discrimination, and their consequences, and **eliminating health disparities** and determinants that adversely affect excluded or **marginalized groups**

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Why Is Applying A "Health Equity Lens" to Clinical Trials Important?[3,4]

It's the right thing to do for patients!
- Addresses key health disparities in historically underrepresented groups
- Improves access to life-prolonging medicines
- Representation in clinical trials should be reflective of real-world patient populations who actually use the drugs

Furthers understanding of how medicines work and answers scientific questions
- E.g., there may be differences in drug efficacy/safety based on biology and genetic make-up

Impacts timing of FDA approvals, availability of drugs, overall clinical development and business strategies
- E.g., potential for delayed/denied FDA drug approvals, based on lack of diversity in trials

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Lack of Diversity in Clinical Trials[5,6]

People of color make up ~42% of the U.S. population, but are often underrepresented in clinical trials

Black or African-American

13.4%
Of US Population
(Based on 2020 US Census)

8%
Of Trial Participants
(Based on 2020 FDA Drug Trials Snapshot)

Hispanic or Latino Origin

18.1%
Of US Population
(Based on 2020 US Census)

11%
Of Trial Participants
(Based on 2020 FDA Drug Trials Snapshot)

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Lack of Diversity in Clinical Trials (cont.)[7]

2022 FDA Drugs Snapshot

Average participation in clinical trials by subpopulation for 37 new drugs approved in 2022 (N=27,554)*

	White	Black/AA	Asian	Hispanic
Heart, Blood, Kidney, Endocrine	74.1%	3.6%	8.5%	13.1%
Autoimmune, Inflammatory, Lung	75.4%	5.3%	15.5%	10.2%
Infectious Disease	69.7%	22%	7%	23%
Neurological, Psychiatric	89%	3.7%	5.2%	6.7%
Cancers	78.1%	4%	11.5%	4.6%
Other	78.3%	8%	13%	12.5%

*Mean values are calculated based on demographic data reported per study ("NA" excluded); Combined percentages of all other races and ethnicities not shown adds up to 100% in the race and ethnicity categories, respectively

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FDA Draft Guidance – April 2022[8]

Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (OCE/CDER) Lela Fashoyin-Aje, 240-402-0285; (CBER) Office of Communication, Outreach, and Development, 800-835-4709, or 240-402-8010; or CDRHCliniacalEvidence@fda.hhs.gov.

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Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Minority Health and Health Equity (OMHHE)

[Date]
Clinical/Medical

Recommends development of a **"Race & Ethnicity Diversity Plan"** prior to starting pivotal trials intended for marketing submission

Submission of plan should occur to IND application, and discussion with FDA should occur no later than end of Phase 2 (for drug products)

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FDA Draft Guidance – April 2022 (cont.)[8]

Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Guidance for Industry

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[Date]
Clinical/Medical

Recommended Components of Diversity Plan:

- Overview of disease in underrepresented racial/ethnic populations in the US, including any differential data/findings
- Scope of development program, including expected geographic locations that may address inclusion
- Goals for enrolling underrepresented populations, based on demographics and background research
- Specific plan to enroll diverse populations --- detailed operational measures, including sustained community engagement plan and metrics
- Status of efforts, including plan for post-marketing data collection if initial diversity goals not met

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Food and Drug Omnibus Reform Act (FDORA) – December 2022 *Sections 3601-3604* [9,10]

Includes laws related to clinical trial diversity, modernization, and diversity action plans. Calls on FDA to:

- Require submission of diversity action plans for all Phase 3 clinical studies of new drugs or pivotal trials, as appropriate
- Update current diversity plan guidance by Dec 2023, with considerations for sponsors to incorporate data disaggregated by age group, sex, racial/ethnic demographic characteristics, and potentially geographic location and socioeconomic status
- Update current guidance to include considerations for public posting by sponsors of key information from diversity action plans on company websites, with regular reports to FDA regarding progress
- Host public workshops to enhance clinical trial diversity
- Issue an annual summary report on progress to improve clinical trial diversity

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What is Trust?[11]

Willingness of a party to be vulnerable to the actions of another party

- Expectation that the other will perform an action important to the trustor, regardless of ability to monitor or control that other party

Applies to clinical trial recruitment and retention, as there is inherent risk when deciding whether to participate

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Cognitive Trust vs. Affective Trust[12,13]

Cognitive Trust is based on:

logic, utility, rationality, competence, knowledge, evidence

vs.

Affective Trust is based on:

human emotions, social relations, personal goodwill, intrinsic value, genuine concern

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An "Integrated Model of Trust" for Clinical Trial Diversity[14]

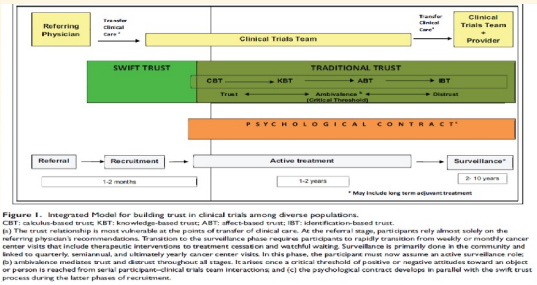

Figure 1. Integrated Model for building trust in clinical trials among diverse populations.
CBT: calculus-based trust; KBT: knowledge-based trust; ABT: affect-based trust; IBT: identification-based trust.
(a) The trust relationship is most vulnerable at the points of transfer of clinical care. At the referral stage, participants rely almost solely on the referring physician's recommendations. Transition to the surveillance phase requires participants to rapidly transition from weekly or monthly cancer center visits that include therapeutic interventions to treatment cessation and watchful waiting. Surveillance is primarily done in the community and linked to quarterly, semiannual, and ultimately yearly cancer center visits. In this phase, the participant must now assume an active surveillance role; (b) ambivalence mediates trust and distrust throughout all stages. It arises once a critical threshold of positive or negative attitudes toward an object or person is reached from serial participant–clinical trials team interactions; and (c) the psychological contract develops in parallel with the swift trust process during the latter phases of recruitment.

Integrated Model = Trust development that is framed through integrated clinical and business perspectives

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An "Affective Trust Framework" for Clinical Trial Diversity[15]

Inclusive Study Design
- Participant Selection
- Targeted Site Selection

Affective Community Engagement*
- Activation Points
- Cultural Communications

Trust-Enabling Technology
- Digital Engagement
- Artificial Intelligence/Machine Learning

*This should be a comprehensive strategy that starts before study kick-off, lasts the duration, and continues after study ends

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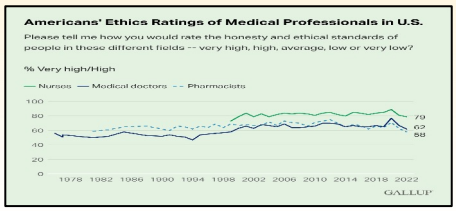
Pharmacists: Bridging the "Trust Gap"[16,17]

In 2022, pharmacists were ranked as the 3rd most trusted professionals in the US



Pharmacists are ideal partners for building trust within historically excluded populations, connecting patients to research opportunities, and conducting clinical trials

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Advantages to Involving Community Pharmacists in the Clinical Trial Process & Diversity Efforts[17-19]

Access to patients and patient information
- Convenient locations (within 5-10 miles of most US households) and regular contact with patients
- Can raise awareness of clinical trials, share study information, and identify potential participants
- Real-world evidence from pharmacy databases can inform more inclusive study protocol designs

Knowledge of the community
- Well-respected members of the community
- Understand the health needs and concerns of communities in which they live, serve, and work --- including social determinants of health (SDOH) that impact their patients
- Can develop and implement study recruitment strategies tailored to community needs

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Advantages to Involving Community Pharmacists in the Clinical Trial Process & Diversity Efforts (cont.)[17-19]

Facilitating communication
- Serve as a bridge or connector between research sponsors, principal investigators, study sites and community members
- Can provide culturally- and community-tailored information about research opportunities

Providing care
- Provide care to patients throughout study duration, including administration of medications and follow-up (i.e., in-person and/or leveraging virtual care models)

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Community Pharmacies & Decentralized Clinical Trials[19-21,26]

Decentralized Clinical Trial (DCT)*

A clinical trial where some or all trial-related activities occur at locations other than a traditional clinical trial site

- Locations "other than a traditional trial site" may be a participant's home or a local healthcare facility
- May be fully decentralized or hybrid
- May leverage in-person and/or telehealth capabilities, and digital health technologies

*DCTs are also addressed in an FDA draft guidance and in section 3606 of FDORA

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Community Pharmacies & Decentralized Clinical Trials (cont.)[19-21,26]

- Depending on study protocol, some activities may be conducted by healthcare providers (HCPs) close to the participant's home but not part of the trial personnel, as long as it aligns with HCP's clinical training. Conversely, some trial-related activities may require specifically trained trial staff
- **In a recent consumer panel survey conducted by a national pharmacy retail chain:**
  - **32% of respondents said "ability to participate in a trial through my local pharmacy" would make it easier to be in a study**
  - **56% of respondents said they've be willing to participate in a trial through a national pharmacy retail chain**

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Proposed Steps for Improving Clinical Trial Diversity through Community/Retail Pharmacists[18]

1) Identify pharmacies within locations/communities that have been historically underrepresented and excluded
1) Identify potential participants that match study protocol requirements
   - i.e., use of AI-enabled technology to assess de-identified pharmacy prescription databases to find patients
2) Initiate patient contact to determine interest in clinical trials
1) Perform initial inclusion/exclusion criteria assessment
   - e.g., administration of an IRB-approved questionnaire in-person or via telehealth
1) Refer patients meeting the criteria to the principal investigator for further screening
1) Monitor enrollment of historically underrepresented patients and adjust approach, as needed

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Challenges for Clinical Trial Programs at Community/Retail Pharmacies[19,20,22]

- Clinical trial oversight, data quality, and data privacy concerns --- could compromise integrity of study results
- Potential conflicts of interest, particularly with retail chains that have a financial stake in revenue generation (i.e., they are publicly held entities and may compromise patient safety or data quality for financial gain)
- Operational hurdles --- limited infrastructure and staffing to support trials
- Barriers to participation that cannot be addressed by the pharmacist (e.g., inconveniences stemming from poor protocol design, a sponsor's responsibility)
- Business challenges related to venturing into a new market area
  - At least 4 national pharmacy retail chains have created clinical trial units since 2021. However, one major chain recently confirmed closure of its unit by 2024, due to reassessment/realignment of "long-term strategic business priorities"

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Health-Systems Pharmacists (Research-Focused*)[23,24]

- **An essential member of the research team, in a role that goes beyond traditional dispensing of medications**
- **Several opportunities exist for impacting clinical trial diversity within role**

- Assists in background medication research on the study drug, including literature searches
- May write pharmacy section of study protocol (e.g., drug inventory, compounding, dispensing, record-keeping procedures)
- May write other protocol sections involving pharmacology, PK, drug exclusion criteria, adverse effects, and adherence monitoring
- May serve as a member of the institutional review board (IRB)

*Locations may be outpatient; primary "customers" are the principal study investigators

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Health-Systems Pharmacists (Research-Focused*) - cont. [23,24]

- Performs standard pharmacist tasks upon receipt of drug order for study medication from principal investigator
- Documents all processes and leads distribution of study drug including delivery to study location or patients' homes
- May meet face-to-face with patients during trial and afterward during transition-of-care period
- May collaborate with principal investigator on organization, analysis, and write-up of data related to study drug

*Locations may be outpatient; primary "customers" are the principal study investigators

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Industry Pharmacists & Clinical Trial Diversity[25,26]

- **Lack of trial diversity is not "just a Clinical Operations issue"**
- **Several opportunities exist for collaborating and impacting clinical trial diversity across various functions**

Clinical Development
- Study protocol development (including determination of population to be studied, diversity goals, and eligibility criteria)
- Selection of diverse principal investigators and advisory board participants
- Ensure proper data collection and interpretation
- Publish clinical study reports and manuscripts --- can ensure transparency of diversity data to external entities

Clinical Operations
- Diverse trial site and CRO selection/management (inclusive of training and monitoring)
- Other Clin Op responsibilities may include: site activation, screening and recruitment, study timeline management, study tracking regulatory/audit readiness…

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Industry Pharmacists & Clinical Trial Diversity (cont.)[25,26]

Regulatory Affairs
- Co-develop the clinical development and regulatory approval strategies/plans for trial diversity and communicate them to the FDA

Medical Affairs (Including Field Medical)
- Recommend new trial sites in racially/ethnically diverse geographic areas
- Identify up-and-coming racially/ethnically diverse key opinion leaders and investigators
- Regularly amplify reminders to sites re: importance of recruiting racially/ethnically diverse patients from their communities
- Bring insights re: opportunities and challenges with disease/trial education and diverse recruitment back to the clinical study team

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Industry Pharmacists & Clinical Trial Diversity (cont.)[25,26]

Patient Advocacy
- Facilitate connections with patient advocacy groups who focus on racially/ethnically diverse patients and complement community engagement efforts

Commercial/Marketing
- Enterprise business thinking --- leverage overall understanding of the business impact of reaching (or not reaching) trial diversity goals
- Conduct market research of real world-patient demographics by race, ethnicity and other subgroups (i.e., characterization of the "patient universe" or "patient funnel")

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Thank You!

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