Abstract

This paper presents an overview of recent U.S. regulatory and industry efforts to expand clinical trial participation from minority and ethnically diverse groups. The influence of pharmacogenetics and pharmacogenomics, health literacy, and the rising influence of the patient voice in clinical development are discussed. This paper concludes with suggestions for practical ways the research community can focus efforts and collaborate to close the diversity gaps in clinical research.

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Diversity in Clinical Trials: Important Gaps to Fill

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I. Introduction

Expanding on a constellation of recent efforts to improve diversity in clinical trials, in April 2022, the FDA issued a draft guidance entitled, *Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials*. Providing instructions for content and format, the latest guidance requires sponsors to develop a Race and Ethnicity Diversity Plan to support an adequate representation of participants from underrepresented racial and ethnic populations in any clinical trial conducted as part of an NDA or BLA marketing submission. [1] While still in draft, trial sponsors can start preparing now for the adoption of this guidance to ensure broader representation in future clinical trial populations.

This guidance follows years of well-documented evidence that clinical trials are not representative of the diversity in the U.S. population and often don't represent the disease population the investigational product is intended to treat. When considering the disproportionate burden for certain diseases among racial and ethnic minorities and the decades of clinical research findings that reveal "significant differences among racial and ethnic groups in the metabolism, clinical effectiveness, and side-effect profiles of many clinically important drugs," [2] explicit regulation must address these diversity gaps to safeguard and advance public health.

Based on 2020 U.S. census figures, nearly 40% of the population belongs to a racial or ethnic minority. [3] In contrast, clinical trial populations tend to be more homogenous.

African Americans make up approximately 3% of clinical trial participants while representing 12-14% of the US population. Another disparity exists among Hispanics, who represent 18% of the U.S. population but less than 8% of clinical trial participants. [4] **In contrast, Whites account for approximately 58% of the total U.S. population and make up 83.3% of clinical trial participants.** [5,6]

Barriers to research participation from minority sub-groups are believed to stem from a general lack of awareness of opportunities, as well as concerns about past medical research misconduct among vulnerable populations. [7]

Against a history of unethical biomedical research practices and forced participation, the FDA has focused on informed consent policies. Unfortunately, until recently, the focus on informed consent has superseded the publication of guidance that seeks to ensure the even distribution of disease populations and promote equal opportunities for participation. [3]

While drug sponsors have long felt pressure from many converging forces to expand the heterogeneity of clinical trials, including scientific advances, social responsibility expectations as well as shifting demographics of the consumer health public, **clinical trial diversity has shifted from a nice-to-have to a must-have.** [8]

1. FDA guidance: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diversity-plans-improve-enrollment-participants-underrepresented-racial-and-ethnic-populations

2. Journal Natl Med Assoc. 2002; 94:1-16

3. 2020 U.S. Population More Racially, Ethnically Diverse Than in 2010 (census.gov)

4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8057389/

5. Oh, S, et al., 2015. Diversity in Clinical and Biomedical Research. A Promise Yet to be Fulfilled. Plos Medicine. Available at: http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001918

6. U.S. Census Bureau; National Institutes of Health, Tufts CSDD, 2010.

7. http://www.fda.gov/ForConsumers/ByAudience/MinorityHealth/default.htm

II. Why it Matters – Beyond Diversity for Diversity's Sake

Regulatory communications have been clear to emphasize that FDA actions to expand clinical trial inclusion seek to address real-world disease population heterogeneity and variability in drug response. Left unchallenged, these known gaps can lead to ineffective medicines as well as more adverse events for significant subgroups of a disease population. These gaps can also further exacerbate disparities in health outcomes among racial and ethnic groups. [9]

On a general level, it is well known that age, gender, and concomitant medications impact drug metabolism. Beyond these basic considerations, research consistently demonstrates that genetics, environment, and psychosocial factors determine differences in drug response among racial and ethnic groups. These three factors influence drug effects both individually and symbiotically. However, most research in this area has focused on genetic factors due to the strength of their reproducibility over the other two factors.

Genetic polymorphisms in specific drug metabolism genes alter enzyme-level activity by reduction, elimination, or enhancement, leading to differential rates of elimination of the drug metabolized.

Pharmacogenetic research in drug response variability among subpopulations has been limited to a few therapeutic areas, namely cardiovascular and central nervous systems. Within these two areas, different racial, ethnic, and geographical groups have shown to be poor metabolizers of many common drugs, including anti-arrhythmic agents, antidepressants, beta-blockers, neuroleptics, and opioids.

Common examples cited include the differential responses of African American and White patients to beta-blockers, ACE inhibitors, and diuretics used for the treatment of hypertension. For the treatment of blood pressure, Chinese populations respond differently to the beta-blocker propranolol than Whites. Asian populations typically require lower dosages than white populations of a variety of different hypertension and psychotropic drugs, including lithium and antidepressants. [10]

A lesser-known example involves adverse events associated with antipsychotic drugs among subgroups of Azkenazi Jews, specifically those presenting clusters of human lymphocyte antigen (HLA) typings (45). This subpopulation is associated with a substantially increased risk of clozapine-induced agranulocytosis. [11]

Other significant ethnic differences that have been noted in drug response include psychotropics for the treatment of general anxiety as well as beta2 agonists, inhaled corticosteroids, and leukotriene antagonists for the control of asthma.

While pharmacogenetic research is now used more frequently to support drug selection and guide accurate dosing in drugs, the use of genotyping to identify variations in drug response is a limited but rapidly emerging field. The use of pharmacogenetics in communities of color is even more limited. Ultimately, drug developers must keep pace with these advancements because clinical trials have an ethical obligation to reflect the population most vulnerable to the condition or disease probed by the trial. [12]

8. https://www.pharmavoice.com/news/FDA-guidance-clinical-trials-diversity/623429/

9. U.S. Food and Drug Administration Report: FDA Action Plan to Enhance the Collection and Availability of Demographic Subgroup data. August 2014. Available at: http://www.fda.gov/downloads/RegulatoryInformation/Legislation/SignificantAmendmentstotheFDCAct/FDASIA/UCM410474.pdf

10. Burroughs, V, Maxey, R, Levy, R. Racial And Ethnic Differences In Response To Medicines: Towards Individualized Pharmaceutical Treatment, Journal of the National Medical Association, Vol 94, No 10 (Suppl) October 2002

11. Lin, K, Poland, R, Ethnicity, Culture, and Psychopharmacology. 2000. Available at: http://www.acnp.org/g4/GN401000184/CH180.html)

As more empowered patients seek clinical trials as a treatment option, the expansion of genomic testing for diagnostic or predictive purposes creates a meaningful path for more informed decision-making about risk monitoring and medical interventions while reinforcing the urgent need for more inclusive research. “Recognition that clinical trials are another tool to help improve and/or extend life is growing, so patient expectations are not just focused on finding a clinical trial, it’s about finding one that’s right for them while contributing to the future of personalized medicine, advises Matt Maxwell, Chief Patient Experience Officer at Alcanza Clinical Research.

III. What the Diversity Plan Should Contain

The draft guidance outlines a framework with content requirements for diversity plans. Five categories within the recommended framework include:

- an overview of the disease or condition
- scope of the product development program
- goals for enrollment of underrepresented racial and ethnic participants
- action plan for diverse participant enrollment and retention
- status of enrollment goals

Overview of the disease or condition

The plan should begin with an assessment of data on the progression and treatment of the disease or condition across racial and ethnic populations for which the investigational product is intended to treat and any data that indicates the potential for the investigational product to have differential safety and effectiveness associate with underrepresented racial or ethnic populations in the U.S.

Scope of the product development program

The product development program scope includes the planned trials or studies that will support the investigational product’s safety, effectiveness, and optimal dosage in a future marketing submission. The content should include a description of the study design, target trial population, eligibility criteria, endpoints, and planned geographic site locations. Discussion should address how these trial components address the inclusion of underrepresented racial and ethnic populations.

When there are data that indicate that the product may perform differentially based on factors related to race or ethnicity (e.g., pulse oximeters’ performance in populations based on skin pigmentation - have low accuracy in measuring oxygen saturation in darker skin and are three times as likely to miss low oxygen levels in Black patients compared to White patients.) [13] the plan should specify the study design features that will inform the safety and effectiveness of the product in the relevant populations.

Additionally, FDA encourages the early collection of pharmacokinetic, pharmacodynamic, and pharmacogenomic data from a diverse population to inform analyses of drug exposure and response, which should be included in this section.

Importantly, the plan should address how the sponsor will collect data to explore the potential for differences in safety and/or effectiveness associated with race and ethnicity throughout the entire development lifecycle of the product, beyond pivotal trials necessary for submission.

12. Belle, D, Singh, H. Genetic Factors in Drug Metabolism. Am Fam Physician. 2008 Jun 1;77(11):1553-1560http://www.aafp.org/afp/2008/0601/p1553.html

Goals for enrollment of underrepresented racial and ethnic participants

This section focuses on the definition of specific racial and ethnic populations and justification of trial enrollment projections based on assessments provided in Section 1, Overview of the disease population. **Enrollment goals should be based on disease epidemiology and other known information that may impact health outcomes across racial and ethnic groups. If the disease burden is higher in specific underrepresented groups, it may be necessary to enroll more than proportional participation from those groups to help illustrate important differences.**

Action plan for diverse participant enrollment and retention

Trial feasibility, recruitment, and trial operation plans feature prominently in this section, as sponsors must describe how they will enroll and retain target underrepresented populations, what metrics will be used to track performance and what contingency actions will be taken if goals are not met. "How" strategies include site location and access, with an emphasis on reducing participation burdens, such as transportation assistance, disability accommodations, language assistance, and other methods to make trial participation easier. Strategies also include sustained community engagement, requiring the sponsor to describe work with community advisory boards or leaders and or local patient advocacy and healthcare providers. The third element of strategy relates to trial conduct and efforts taken to reduce known burdens such as frequency of visits and/or duration of individual visits. Any planned efforts to offset clinic visits with home nursing, telehealth, or the use of local lab providers should be described in this section. In addition to trial operation specifics, sponsors must outline the planned use to characterize safety, efficacy, and optimal dosage

Status of enrollment goals

If, despite "best efforts", enrollment goals are not met, sponsors should be prepared to discuss a plan and provide justification for collecting data in the post-approval setting.

FDA encourages sponsors to submit plans early in clinical development and no later than when seeking regulatory feedback for Phase III trials, which typically occurs during an End of Phase II meeting with FDA representatives.

IV. Changing the Clinical Trial Research Framework

Incorporating more diversity into an intricately layered research value chain is "a both straightforward complex process." "The roadmap is clear, but organizations have to be willing to put in the effort and invest in fundamental changes to our clinical research framework to reach underrepresented communities who stand to benefit the most from clinical trial participation," stated Carlos Orantes, CEO of Alcanza Clinical Research.

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In practical terms, that means expanding clinical research beyond its metropolitan base into smaller cities and more rural areas and finding ways to support small investigator sites, family medical practices, and community care facilities with research enablement through technology, team support, and regulatory knowledge. It also means expanding research team diversity.

13. https://www.kff.org/racial-equity-and-health-policy/issue-brief/use-of-race-in-clinical-diagnosis-and-decision-making-overview-and-implications/

Although many well-intentioned efforts are underway to expand research, through collaboration with patient advocacy groups, research-naïve medical practices, and other efforts, "we're a long way away from sustainable impact," declared Orantes. "We need to think bigger about partnerships, education, and community engagement."

As a starting point, **diversity and inclusion considerations need to take place earlier in the process,** just as patient involvement in early-stage drug development is helping to better define and characterize the disease population, allow for a deeper understanding of the patient journey, and aid in the development of research protocols that ensure greater relevance, credibility, and feasibility. [14] **This shift will require a fundamentally different approach to planning and collaboration with research stakeholders, which often takes place during the protocol design of later-phase clinical trials.**

Patient advocacy and community-building strategies are a key component of diversity and inclusion considerations, especially patient engagement for disease areas that are known to have disproportionate representation from underrepresented populations.

As strategies need to be disease-specific and intentional for specific communities, direction on the how, when, and who to reach out to for clinical trial opportunities will be informed by pre-engagement exploration with patient advocacy and community groups.

Implementation of the diversity guidance will also impact the scope and timing of clinical trial feasibility. "Moving aspects of these planning activities forward in the development process will promote deeper and more collaborative relationships with sites, especially those who can build bridges with local patients and physician groups," Orantes argued.

Investigator site assessments that focus on access to diverse patient populations should also explore mechanisms to increase access and convenience among these populations. "Perceptions of convenience can vary across different patient groups and communities, so it's important to explore what support can facilitate participation and promote retention," said Matt Maxwell. "Education may be equally as important as other perceived conveniences, such as transportation assistance, flexible hours, or the ability to complete some assessments remotely."

Moving research beyond academic centers and large investigator site networks has other operational implications. "The industry needs to think about typical burdens imposed on a site and how we can bring more flexibility into research delivery without sacrificing consistency or compliance," said Maxwell. "Most importantly, sites that specialize in disease areas with underrepresented populations need early access to protocols. They need more input into eligibility criteria and educational materials that will help connect with impacted patients, especially in situations with low health literacy."

Preparation for more inclusive trials is one of many forces that is re-shaping the clinical research landscape. This trend, along with the combined impact from the lessons of COVID, expanding public engagement, and increased research complexity, will make the industry less fragmented and more collaborative in the future, predicts industry influencer Ken Getz, but he also argues for tighter integration of regulatory initiatives and industry efforts to impact patient engagement and inclusion. [15]

14. Hoos, A, et al. Partnering with Patients in the Development and Lifecycle of Medicines: A Call for Action. Therapeutic Innovation & Regulatory Science. 2015

V. Expanding Public Health Literacy

Improving health literacy is widely recognized as a critical first step to removing barriers to clinical trial participation. Described as a "population-level problem of enormous proportion" by the U.S. Department of Health and Human Services, it has been a national priority for more than a decade. However, this effort is a massive undertaking, requiring collaboration and coordination across government agencies, major health organizations, industry, nonprofits, and community-based organizations.

Health literacy refers to a person's ability to "obtain, process and use health information" and requires knowledge of current health topics, the healthcare system, disease prevention, and management. Optimal health literacy means that adults can perform "complex and challenging" activities, such as integration, synthesis, and analysis of complex information, key tasks required for seeking and evaluating clinical trial participation opportunities. [16]

While low health literacy can affect people of all ages, races, incomes, and educational levels and is widespread among the adult population, low health literacy is more pronounced in elderly adults, racial and ethnic minorities, people with low education and income levels, as well as non-native language speakers, and people with poor health. In addition, low health literacy is negatively associated with self-reported health, preventive services, and management of chronic conditions. [17]

The U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion issued the National Action Plan to Improve Health Literacy in 2010. Acknowledging that no single organization can improve health literacy on a national scale on its own, the plan was intended for use as a framework for health professionals, public and private sector organizations, and communities to adapt and customize for their own needs. Key tenets of this comprehensive plan addressed the development and dissemination of communications, health care delivery, standards-based health education, health literacy best practices, and interventions in addition to local outreach for adult education.

Some of the strategies recommended to support seven goals related to improving health literacy were later adopted in efforts to expand clinical trial awareness and participation. The plan devoted significant consideration to communication matters. Select key recommendations included:

Communication Development: Central to the improvement of health literacy is the use of information incorporating simple and non-technical language and information design principles to aid understanding. Adoption of the user-centered design was urged, with the involvement of representatives from the target audience in the design and testing of all communication materials. Co-creation is essential to community engagement and the established practice of inclusive research.

15. Imaging the Future State of Clinical Research https://www.wcgclinical.com/wp-content/uploads/2022/03/clinical-trials-in-the-era-of-covid-19-part-7.pdf

16. U.S. Department of Health and Human Services. 2000. Healthy People 2010. Washington, DC.In National Library of Medicine Current Bibliographies in Medicine: Health Literacy. Selden CR, Zorn M, Ratzan SC, Parker RM, Editors. NLM Pub. No. CBM 2000-1. Bethesda, MD: National Institutes of Health, U.S. Department of Health and Human Services.

17. National Center for Education Statistics. 2006. The Health Literacy of America's Adults: Results From the 2003 National Assessment of Adult Literacy. Washington, DC: U.S. Department of Education

Communication Dissemination:

- Best practices include the use of language, formats, and channels most relevant to the target population. Alternatives to traditional written information formats include video, graphical display, and formal health communication skills training for health care professionals.
- Targeted approaches, designed for the preferences and/or needs of specific groups of people, can be effective for outreach and adherence for people with low health literacy.
- Cross-sector partnerships with groups responsible for delivering health services (including philanthropic, non-profit, and professional organizations) help ensure culturally and linguistically relevant information. Partnerships are considered an optimal channel to accelerate progress and create sustainable efforts.
- Technology, including social media, help expand patients' access to health care teams and information, especially "electronic health tools which can deliver health information and services at the time, in the place, and in the multiple formats people need and want."
- Along with content, formats and channels should be tested with target groups for acceptability and cultural appropriateness. [18]

There's plenty of evidence to suggest that the industry is steadily improving the effectiveness of educational and instructional materials through the adoption of these health literacy principles. Although there is still room for improvement, most large biopharmaceutical organizations require the use of these principles in the creation of all patient-facing materials; a practice that has also been adopted by communication agencies, patient recruitment firms, and contract research organizations in clinical trial education as well as recruitment and retention efforts.

VI. Site-Level Considerations

As biopharmaceutical organizations pursue intentional strategies to make medicine more representative, they can look to investigator sites as the best resource to create collaborative and sustainable relationships with the communities they serve.

"Every community is unique," said Maxwell, "but there are best practices for asking what challenges they have and what you can do to help, followed by active listening as part of pre-engagement. When the time comes for disease awareness and clinical trial education, co-creation should be a top priority to build trust and address them in a culturally relevant way. The details matter – and key questions to ask include *Does the language resonate? Are the photos representative of similar people and the right symptoms? Are activities of the target population represented?*

Education is equally important. Sites can tap into their physician, nurse, research coordinator, and other healthcare team knowledge to host educational, free screening, and diagnostic tests in underrepresented communities.

It's also becoming more common for many sites to have an in-house community outreach team member whose role includes finding new ways to connect with community leaders, small practices, and non-traditional sites. Community-building is arguably more important than clinical trial recruitment advertising. Sponsors who invest in trial-specific advertising without budgeting for community-building activities are not likely to connect with these patient groups.

18. U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. (2010). National Action Plan to Improve Health Literacy. Washington, DC

The diversity of the site team is mission-critical to expanding participant diversity. When minority patients receive treatment from healthcare professionals who look like them, a growing body of evidence shows improvement in medication adherence, shared decision-making, and health literacy, as well as reduced implicit bias from physicians. [19]

VII. Looking Forward

The recent proliferation of industry efforts focused on diversity and inclusion has raised awareness of health inequities and the public health consequences of narrow inclusion. The complex issue of systematic and consistent implementation will likely remain for decades to come.

Although still in its infancy, the number of new drug applications with targeted therapies continues to increase each year. In the near future, advances in pharmacogenetics and pharmacogenomics may continue to uncover significant information about cross-racial differences in the actions of new and existing drugs.

Research collaboration is gradually improving, aided in part by scientific advances, rising operational complexity, and the urgent need for more diverse patients that coincides with the rise of patient demand for unmet medical needs, quality of life preferences, and individualized medicine.

Efforts to improve diversity among clinical research team is also gradually improving, but significant work remains. The industry must amplify and accelerate clinical research education and mentorship opportunities to enhance clinical research in minority and underrepresented populations.

Ultimately, biopharmaceutical organizations and the wider research community must focus on continuous improvement. Meaningful progress requires continual exploration and commitment to change.

19. https://www.ajmc.com/view/improving-diversity-in-clinical-trials-how-early-stage-investigators-are-reaching-underserved-populations

VIII. Appendix: Regulatory Initiatives – Four Decades of Progress

The FDA has responded in a variety of ways to raise awareness of racial and ethnic disparities in clinical trials and promote more inclusive clinical trial participation. Following growing FDA concern in the 1980s over differences in safety and efficacy among population subgroups, select regulatory initiatives over the past three decades include:

- 1985: In the first regulation of its kind, the analysis of population subsets was required to support dosing modifications for specific subgroups in 21 CRF 314.50. [20]
- 1988: Regulatory guidance (Guideline for the Format and Content of the Clinical and Statistical Sections of New Drug Applications) reinforced the importance of conducting population subset analyses on safety and efficacy from clinical study data submitted in NDAs. It included race and ethnicity as key population subsets. [21]
- 1993: Regulatory guidance (Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs) recommended gender analysis of clinical study data specifically aimed at evaluating pharmacokinetic data from women. Additional guidance (New Drug Evaluation Guidance Document: Refusal to File) provided the rationale for the use of the refusal-to-file option if specific analyses for populations subsets of the overall disease population were not provided. In the same year, the FDA also abandoned its traditional practice of barring women of child-bearing potential from Phase I trials. [22]
- 1998: The Demographic Rule required IND holders to identify and categorize clinical trial participants by age, race, and gender and required NDA sponsors to include safety and efficacy data for demographic subgroups. [23]
- 1999: The International Conference on Harmonization (ICH) published guidance (E5 Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data) allowing data collected in one region of the world to be used in the drug approval process of another region. It also provided a "framework for evaluating medicines with regard to their sensitivity to ethnic factors." [24] Follow-up E7 guidance specifically urged the inclusion of patients older than 75. [25]
- 2005: Guidance (Guidance on Collection of Race and Ethnicity Data in Clinical Trials) called for the standardization of race and ethnicity data collection in clinical trials to ensure consistency in demographic subset analyses and facilitate the evaluation of differential effects of drug response in terms of safety and efficacy among population subgroups. The guidance document also established uniform categories of defining racial and ethnic subgroups based on sociocultural considerations. Minimum choices for ethnicity categories included:
    - Hispanic or Latino
    - Not Hispanic or Latino

In studies for which race and ethnicity information is collected separately, minimum choices included:

- American Indian or Alaska Native
- Asian (reflecting origins from India to Japan)
- Black or African American
- White (reflecting origins from Europe, the Middle East, or North Africa)

20. 21 CFR 314.50(d)(5)(v)
21. http://www.fda.gov/downloads/Drugs/.../Guidances/UCM071665.pdf
22. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126835.pdf
23. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm126396.pdf
24. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm126396.pdf
25. http:www.ich.org

Importantly, the guidance also recommended including contextual information on disease prevalence and plans to address the potential underrepresentation of subgroups part of the overall disease population. [26]

- 2005: FDA approved BiDil, a heart failure drug specifically targeted to Black patients. [27]
- 2012:Following increased public calls to improve minority clinical trial participation, the FDA was granted authority by Congress in the Food and Drug Administration Safety and Innovation Act (FDASIA), to evaluate the inclusion and analysis of demographic subgroups in clinical trials, and report on the findings and take action. [28]
- 2011: The FDA Office of Minority Health was established as part of the Affordable Care Act of 2010 with a mission to reduce ethnic and racial health disparities. [29] In addition to serving in an advisory role to the FDA Commissioner on minority health and health disparities, the office provides "leadership and direction in identifying agency actions that can help reduce disparities." This includes the dissemination of information and communication to the public about research opportunities. [30]
- 2014: The FDA published a three-point action plan designed to improve "the completeness and quality of demographic subgroup data collection, reporting, and analysis (quality); identify barriers to subgroup enrollment in clinical trials and employing strategies to encourage greater participation (participation); and make demographic subgroup data more available and transparent (transparency).
- 2015: The FDA launched Drug Trials Snapshots, a website designed for the public that provides demographic breakdowns of clinical trial participants for all approved drugs as a tool to help consumers evaluate the risks and benefits of specific medications. As part of a follow-up action from the 2014 plan to make demographic data more available and transparent, information includes differences in the benefits and side effects among sex, race, and age groups. [31]
- 2016: Guidance entitled *Collection of Race and Ethnicity Data in Clinical Trials* outlined how to collect and present race and ethnicity data in submissions to the FDA and recommended that sponsors develop and submit a plan to address the inclusion of clinically relevant populations for discussion to the agency.
- 2017. The guidance entitled Evaluation and Reporting of Age, Race, and Ethnicity-Specific Data in Medical Device Clinical Studies provided FDA's expectations for evaluating and reporting age, race, and ethnicity data in clinical studies involving medical devices.
- 2020. FDA finalized Enhancing the Diversity of Clinical Trial Populations guidance. This focused on expanding clinical trial eligibility criteria in later phase trials to better reflect the patient population likely to use the drug in clinical practice and better characterize the broader benefit-risk profile.
- 2022. FDA issued draft guidance requiring trial sponsors to submit a Race and Ethnicity Diversity Plan to support the adequate representation of participants from underrepresented racial and ethnic populations in clinical trials conducted as part of an NDA or BLA marketing submission.

26. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm126396.pdf

27. https://www.law.uh.edu/healthlaw/perspectives/(RS)BiDil.pdf

28.http://www.fda.gov/downloads/RegulatoryInformation/Legislation/SignificantAmendmentstotheFDCAct/FDASIA/UCM410474.pdf

29. Patient Protection and Affordable Care Act, Pub. L. No.111-148, section 10334(as codified in 42 U.S.C. § 300u-6

30. http://www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM304661.pdf

31. http://www.fda.gov/Drugs/NewsEvents/ucm424178.htm

Figure 1. The chart below, an example of the information available in Drug Trials Snapshots, depicts the trial demographics for ADDYI, a treatment for hypoactive sexual desire disorder in pre-menopausal women. The drug, approved in August 2015, involved 4 clinical trials of 3099 women with low sexual desire disorder. The trials were conducted in the United States, Canada, and Europe.

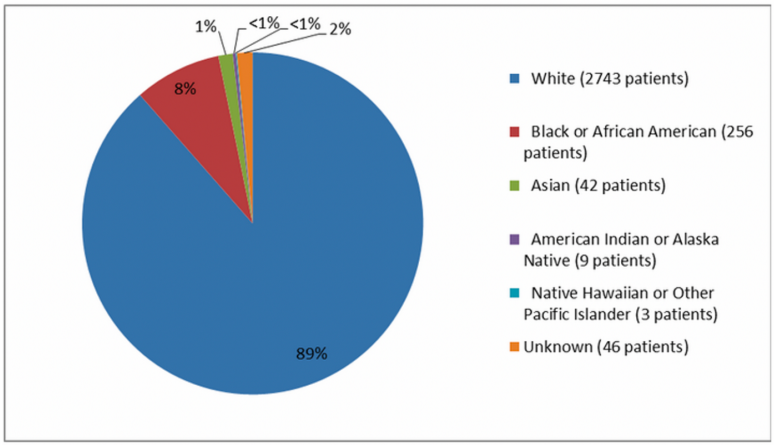

Figure 2. Summary of the percentage of women and African Americans who participated in clinical trials for select cardiovascular drugs.

Snapshots on Cardiovascular Drugs

BRAND NAME	INDICATION	WOMEN	African Americans
UPTRAVI	Pulmonary arterial hypertension	80%	2%
REPATHA	Hypercholesterolemia (HoFH)	50%	5%
SAVAYSA	Reduce risk of pulmonary embolism in VTE patients	43%	3.6%
PRALUENT	Hyperlipidemia	40%	4%
SAVAYSA	Reduce the risk of stroke in a Afib patients	38%	1.3%
KENGREAL	Blood thinner following heart procedure	28%	3%
CORLANOR	Heart failure	24%	1.2%
ENTRESTO	Heart failure	22%	5%
AVERAGE		41%	3.1%