A Non-Representative Sample: Racial and Ethnic Diversity in Clinical Trials of FDA-Approved Drugs

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Background

The Food and Drug Administration (FDA) recently released two draft guidance documents on patient representation in clinical trials; the first guidance, aimed at improving enrollment of diverse trial populations, recommends broadening eligibility criteria and adopting more inclusive enrollment practices, and requires that manufacturers submit a diversity plan as part of the regulatory process.[1] The second guidance includes recommendations on post-marketing approaches (e.g., study design, recruitment, statistical considerations) to obtain data in under-represented populations.[2] In parallel, the Institute for Clinical and Economic Review (ICER) published a value framework that prioritizes patient diversity, assigning a "representation score" to each demographic category specifically for the trial's US patient population.[3] In light of these evolving requirements, we sought to assess the current state of patient representation in clinical trials.

Objectives

The objective of this study was to examine racial and ethnic diversity among patients enrolled in pivotal trials of FDA-approved drugs compared with the US population.

Methods

- Demographic data were extracted from pivotal trials for all New Drug and Biologic License Applications approved by the FDA from January 2017 through December 2022.
- Patient demographics were assessed as a median percentage across trials and compared to US Census Bureau 2022 population estimates.
  - Additional subgroup analyses were conducted by therapeutic area (per ICD-10 classification).
  - Race and ethnicity data were reported separately (e.g., a patient could be categorized as both white and Hispanic/Latino).

Table 1. Overview of FDA Approvals (2017-2022)

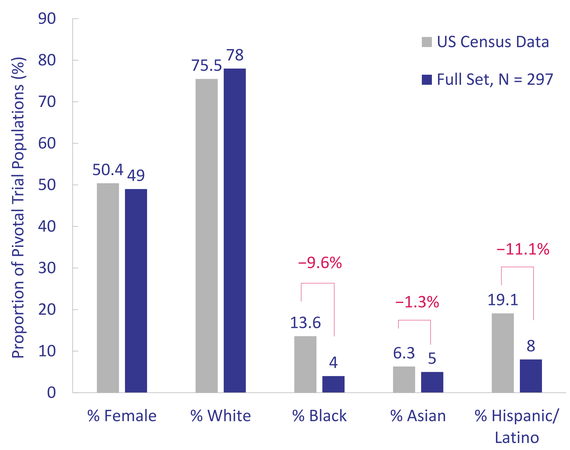
Year	Approvals (n)	Therapies (n)	NDA (n)	BLA (n)
2017				
Orphan	**18**	18	13	5
Non-orphan	**28**	28	21	7
2018				
Orphan	**34**	34	22	12
Non-orphan	**26**	25	21	5
2019				
Orphan	**20**	20	16	4
Non-orphan	**27**	27	21	6
2020				
Orphan	**31**	31	22	9
Non-orphan	**22**	22	18	4
2021				
Orphan	**26**	26	19	7
Non-orphan	**25**	24	18	7
2022				
Orphan	**21**	20	10	11
Non-orphan	**18**	17	12	6

BLA = Biologics License Application; FDA = Food and Drug Administration; NDA = New Drug Application

Results

- There were a total of 297 FDA approvals between 2017 and 2022, encompassing 293 therapies (Table 1).
- Most therapies were indicated for treatment of neoplasms, followed by nervous system disorders, endocrine disorders, and infectious diseases (Figure 1).
- Black, Asian, and Hispanic/Latino participants were notably underrepresented, comprising a median 4%, 5%, and 8% of pivotal trial populations, respectively, vs 13.6%, 6.3%, and 19.1% of the US population (Figure 2).
- These trends varied little over the time period evaluated, aside from a small uptick in Asian representation (from 3% to 7%; Figure 3).

Figure 2. Pivotal Trial Diversity for FDA-approved Drugs (2017-2022)



FDA = Food and Drug Administration
Differences shown in red are absolute percentage point differences.

Demographics by therapeutic area

- When demographics were assessed by therapeutic area, Black (2% to 5%) and Hispanic/Latino patients (3.5% to 9%) were underrepresented in nearly all categories, with the notable exception of infectious disease (18% and 15%, respectively), most commonly HIV (Figure 4).
  - Asian patients were underrepresented (2.5% to 4%) in approvals for endocrine and nervous system diseases but were well-represented in blood disorder approvals (9.2%).
  - White patients were particularly overrepresented in endocrine and skin disorders (85% and 84%, respectively).
- Female patients tended to be underrepresented in trials of skin and infectious diseases, while overrepresented in trials of nervous system and blood disorders.

Impact of US patient enrollment

- Diversity limitations are frequently attributed to ex-US patient populations; however, 60% of approvals with a majority-US population (n=102) enrolled a white population higher than the national average (75%).

Figure 1. FDA Approvals by Therapeutic Area (2017-2022)

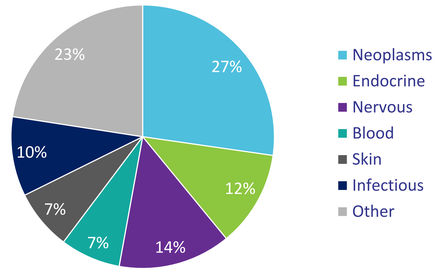


Figure 3. Pivotal Trial Diversity Trends over Time

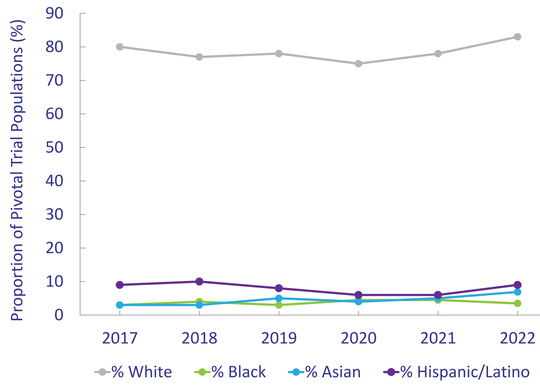


Figure 4. Pivotal Trial Diversity Trends by Therapeutic Area

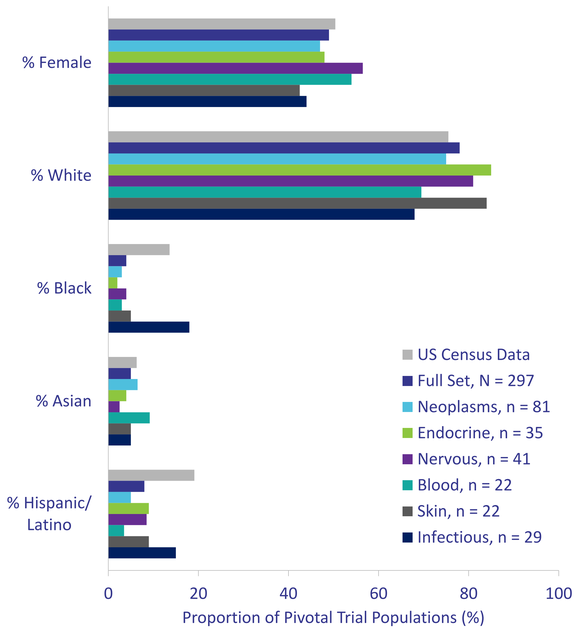
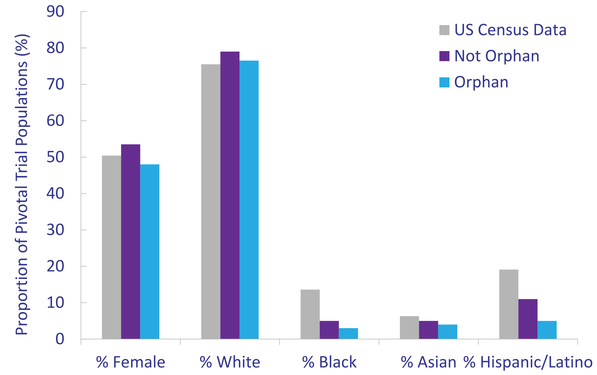


Figure 5. Pivotal Trial Diversity for Orphan vs Non-orphan Indications



Orphan drugs

- Among orphan drug approvals (n=146), Black, Asian, and Hispanic/Latino patients were further underrepresented compared with non-orphan indications (n=151; Figure 5).

FDA response to insufficiently diverse trial populations

- In the subset of approvals with ≥90% white participants (n=64), most FDA reviews (59%) noted this lack of diversity, with only 27% described as consistent with the target patient population.
- Moreover, three recent reviews of oncology drugs cited insufficient diversity as the rationale for requiring a post-marketing commitment.

Conclusions

- Black and Hispanic/Latino patients are underrepresented in pivotal trials across nearly all therapeutic areas, with no improvement over the 5 years evaluated. Representation was particularly poor in oncology and hematology trials.
- FDA is increasingly scrutinizing pivotal trial diversity as part of the regulatory process, and issuing post-marketing commitments to verify clinical benefit in a representative patient population.
- Given recent emphasis on diversity by both FDA and ICER, manufacturers should anticipate increased focus on representation in regulatory and reimbursement decisions, and adapt their clinical development programs accordingly. Potential approaches for manufacturers may include diversity-targeted site selection, mobile sites, and decentralized trials, as well as proactively planning for diversity-focused postmarketing studies.

References

1. FDA 2020. "Enhancing the Diversity of Clinical Trial Populations-Eligibility Criteria, Enrollment Practices, and Trial Designs; Guidance for Industry. Draft Guidance.
2. FDA 2023. "Postmarketing Approaches to Obtain Data on Populations Underrepresented in Clinical Trials for Drugs and Biological Products." Draft Guidance.
3. ICER 2023. Value Assessment Framework.

Disclosures/Acknowledgments

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