

White Paper

The Need for Better Diversity Data in Clinical Trial Benchmarking and Feasibility



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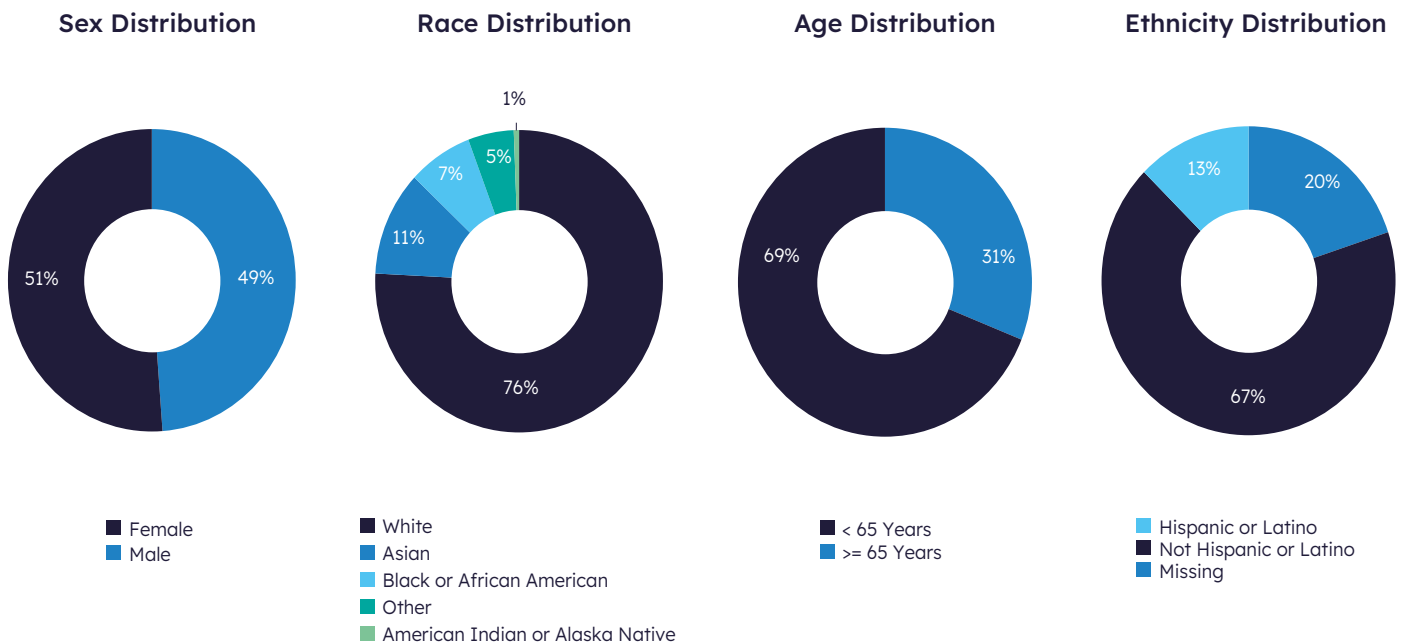
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Introduction

While the pharmaceutical industry as a whole acknowledges the need for greater diversity in clinical trials, there is ongoing debate as to the best approach. What life sciences professionals tend to agree on is the fact that representation in clinical trials does not align with the demographic makeup of the total population.

US census figures from 2021 show that ethnic and racial minorities comprised over 40% of the population. However, statistics from the US Food and Drug Administration (FDA) show that from 2015 to 2019, those groups were clearly underrepresented in clinical trials.¹

Figure 1. Drug Trials Snapshot (2015-2019) – Demographics of Trial Participation



Source: Food and Drug Administration

1. [2015-2019 Drug Trials Snapshots Summary Report \(fda.gov\)](https://www.fda.gov/oc/2020/08/2020-2019-drug-trials-snapshots-summary-report)

Regulatory Considerations

In the US, recent legislative proposals have been aimed at improving clinical trial diversity. The [Diverse and Equitable Participation in Clinical Trials \(DEPICT\) Act](#) requires sponsors to develop an action plan for ensuring diversity in clinical studies. The [Diversifying Investigations Via Equitable Research Studies For Everyone \(DIVERSE\) Trials Act](#) would reduce barriers to clinical trial participation by allowing sponsors to provide necessary equipment to subjects so they can participate remotely, or by paying ancillary costs of participation such as

transportation to and from the trial site.

[Draft guidance](#) issued in April 2022 by the FDA called on sponsors to develop plans for enrolling more participants from underrepresented racial and ethnic populations in the US into clinical trials. The 2023 ([Public Law 117-328](#)) omnibus spending bill enacted in December 2022 requires diversity action plans for the clinical trials used by the FDA to determine the safety and efficacy of drugs. It incorporates the DEPICT Act.

The action plan must meet certain requirements:

- 1 It must define a study's enrollment goals for underrepresented racial and ethnic participants, and these enrollment goals should be based, at least in part, on the trial's protocol objectives.
- 2 It should specify the study design features supporting analyses that will inform the safety and effectiveness of the medical product in the relevant racial and ethnic populations.
- 3 It should outline the sponsor's plan to collect data to explore the potential for differences in safety and/or effectiveness associated with race and ethnicity throughout the entire development life cycle of the medical product.
- 4 Sponsors are encouraged to leverage various data sources (e.g., published literature and real-world data) to set enrollment goals.

In the UK, comprehensive new [regulatory guidance](#) is in the works, designed to ensure that UK clinical trials are representative of the diversity of those who may benefit from the medicine. The guidance will outline how to achieve diversity in trials in a way that is proportionate and achieves the best results.

As of December 2022, Canadian regulators are requiring companies seeking marketing approval for drugs to submit verification of whether disaggregated data for sex, age, and race is in their clinical evidence. Health Canada

says this [regulatory mechanism](#) is “the first step in our larger goal of ensuring consistent representation of diverse populations in all clinical trials.” According to a Pink Sheet article², Health Canada said the data would allow it to:

- verify that clinical trial participants reflect the diversity of the types of people who will use the product
- analyze the safety and efficacy of health products by subpopulation, where feasible
- indicate where post-market monitoring might be needed to verify safety and efficacy within certain populations.

2. Pink Sheet, Oct. 6, 2022, “[Canada Addresses Diversity in Clinical Trials with New Rule for Drug Filings](#)”

Professional Obligations

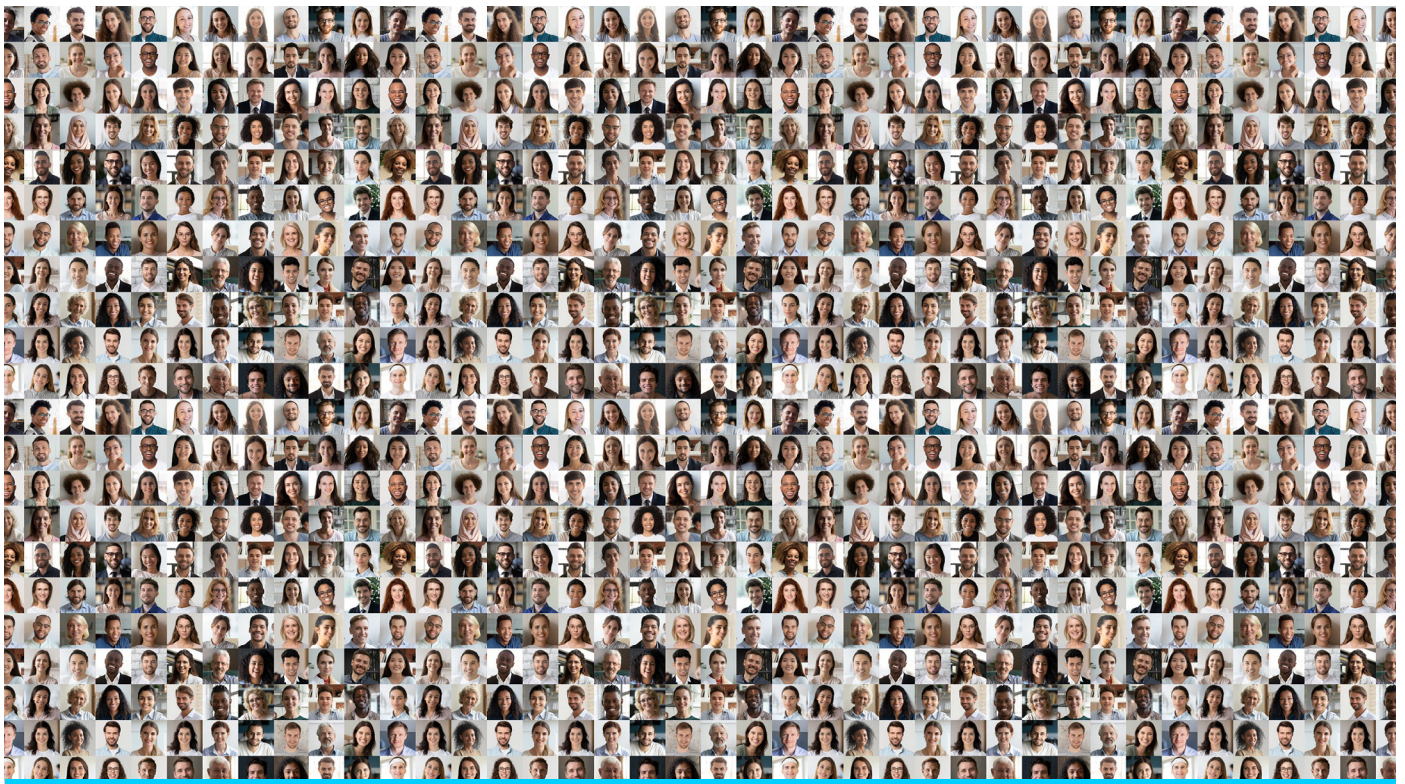
A patient's demographic characteristics can impact the efficacy of a drug. What works for one individual may not work for another. Age, gender, race, and other attributes — and the intersectionality of these attributes — can predispose a patient to certain diseases, and play a role in how a patient responds to treatment.

Likewise, the incidences and types of adverse effects may vary depending on demographic differences. Assuming that a drug is safe based on results from a clinical trial with all white male participants does a disservice to the public as well as the healthcare community.

To adequately address these disparities, not to mention meet FDA requirements, sponsors should have a trial diversity plan. A successful plan goes

beyond simply recruiting a diverse patient pool; it establishes endpoints and monitors them for variances along demographic lines. In addition, sponsors should ensure that inclusion/exclusion criteria do not exclude participants based on race and ethnicity. Of course, a trial diversity plan must also include a process and mechanisms in place to capture diversity data.

The [Clinical Trials Transformation Initiative](#) (CTTI), a public-private partnership designed to improve the quality and efficiency of clinical trials, recently unveiled new recommendations for increasing diversity in clinical trials. As part of CTTI's Diversity Project, experts and key stakeholders from across the clinical trials enterprise developed the recommendations, designed to ensure they are actionable, evidence-based, and consensus-driven.

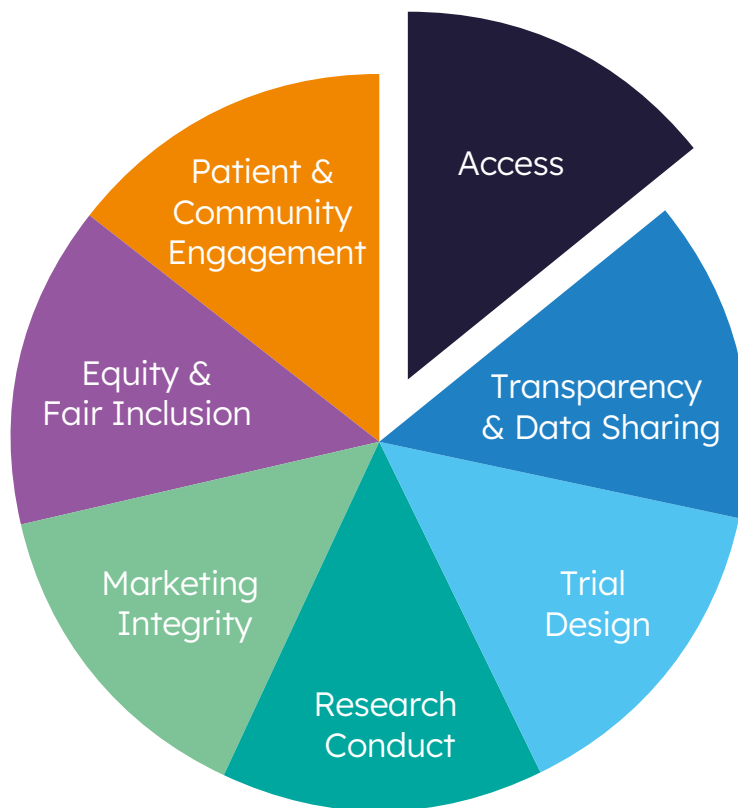


Ethical Imperatives

Lack of representation in clinical trials speaks to a larger issue of health equity and the gaps that exist in today's healthcare systems. It's a veritable Catch-22: Society's marginalized groups are also left on the sidelines when it comes to clinical research. In addition, there's an inherent lack of trust in the medical establishment among many in these groups, leading to a reluctance to participate in trials. It's a double whammy, with limited access to and understanding of clinical trials compounding the issue.

One initiative focusing on diversity in clinical trials is Bioethics International's [Good Pharma Scorecard](#) (GPS), with its new equity component. GPS ranks pharmaceutical companies on bioethics/social responsibility performance and governance, taking into account ethics and legal standards. Its measures evaluate the integrity of clinical trial designs, including diversity and fair inclusion.

Figure 2. GPS Social Responsibility Metrics



Source: Bioethics International

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Founder and president Jennifer Miller said one of the core reasons she formed Bioethics International is to build trust in the industry. According to a 2022 [Gallup poll](#), the healthcare industry had an overall 40% positive perception versus 25% for the pharmaceutical sector. And respondents to an earlier [Harris poll](#) perceived pharma as the least socially responsible sector in healthcare. The GPS has had a positive impact: Half of low-scoring large firms improve practices within 30 days of receiving a low GPS score, and industry median scores rise year after year on GPS measures.

Another lens through which to view trial inequities is the social determinants of health (SDoH). These are external factors that impact a person's health and quality of life: economic stability, access to and quality of education and healthcare, neighborhood and environment, and social and community context. Studies have shown that these factors influence up to 80% of health outcomes. Sponsors that take these determinants into consideration can better break down the barriers that might preclude certain groups of people from participating in clinical trials.

Beacon of Hope, established by Novartis and the Novartis US Foundation, is one community-based initiative designed to tackle the root causes of disparities in health and education. The 10-year collaboration is in conjunction with 26 historically Black colleges and universities (HBCUs) — including four HBCU medical schools — as well as Merck, Sanofi (winner of the 2023 Citeline Award for Champion of Diversity and Inclusion in Clinical Research), the National Medical Association, Thurgood Marshall College Fund, and Coursera. A prime focus area is to support research and validation of existing data standards that drive diagnosis, clinical trial endpoints, and population health policy.

Bristol Myers Squibb also is making inroads, and has earmarked \$150 million toward training

physicians and clinical trial investigators to work in diverse communities. In 2020, Takeda established two health equity-centered programs — the Center for Health Equity and Patient Affairs (HEPA), and the US Health Equity and Community Wellness division. One of HEPA's goals is to increase diversity in clinical trials.

As we will discuss below, the availability of demographic data — and using that data to inform future trials — is vital to improving representation and reducing inequities. With this data usage comes the responsibility of monitoring its use, particularly in terms of patient privacy when it comes to deidentified claims data. According to a [paper](#) by David Blumenthal and Cara James published in the *New England Journal of Medicine (NEJM)*, “federal policymakers should address comprehensively the many gaps in current privacy protections under existing laws and regulations.”



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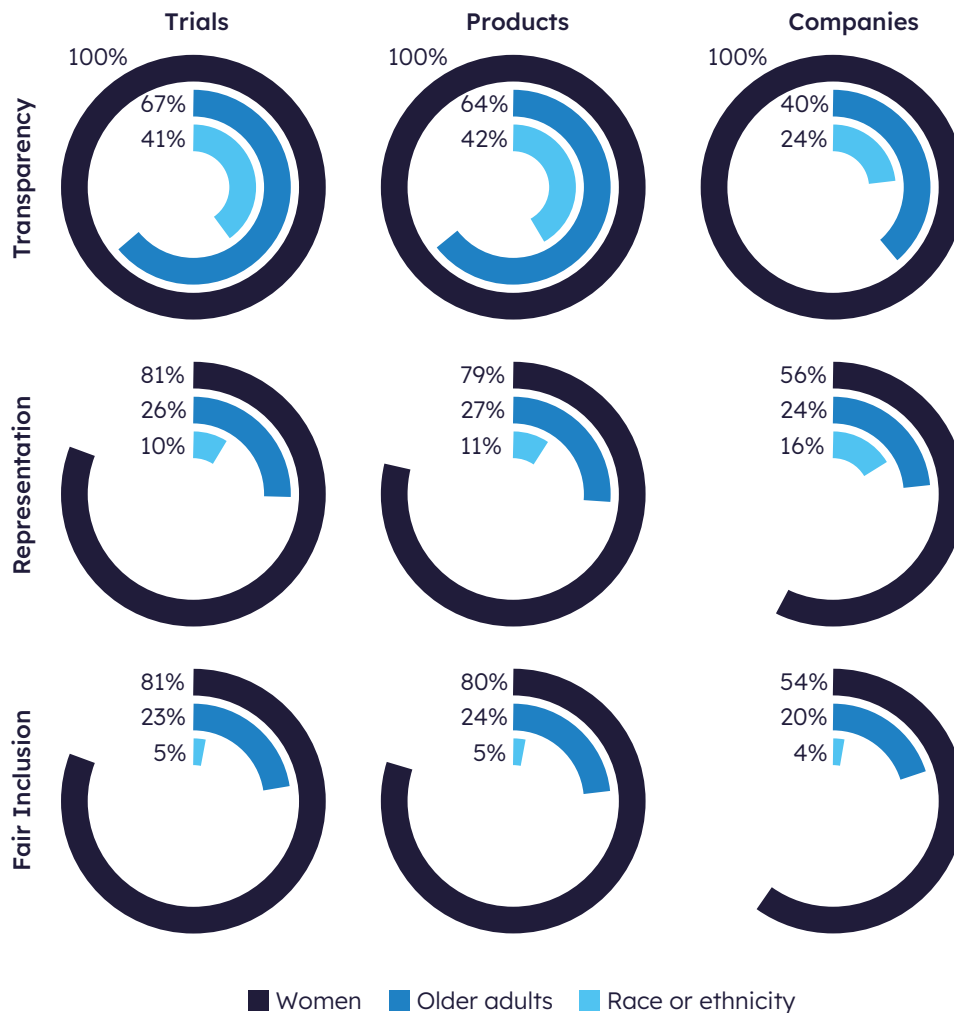
A Needle in a Haystack

Just as those from marginalized communities face multiple barriers to clinical trial participation, study sponsors face challenges in obtaining clinical trial diversity data. This data can provide a critical piece of the protocol puzzle when sponsors design clinical trials.

Bioethics International's Miller, an associate

professor at the Yale School of Medicine, is the primary investigator for the Yale University-Mayo Clinic Center of Excellence in Regulatory Science and Innovation (CERSI), a joint effort of Yale, Mayo Clinic, and the FDA. Its goals include creating an infrastructure for regulatory science knowledge generation, and conducting research to address key gaps in knowledge.

Figure 3. Proportion of trials, products, and companies receiving a 100% score on transparency, representation, and fair inclusion.*



*Measures for women, older adults, and racially and ethnically minoritized patients participating in clinical trials for novel oncology therapeutics approved by the FDA 2012-17

Source: [BMJ Medicine](#)

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In a separate study of novel oncology therapeutics, Miller and colleagues sought to develop a measure for fair inclusion in trials by assessing transparency and representation of enrolled women, older adults, and racially and ethnically minoritized patients. Miller said they focused on this disease area because it has the most robust demographic data and because it is a leading cause of death. She said the bulk of the data came from US Cancer Statistics, a Centers for Disease Control database with rigorous demographic data but not without its limitations. “Beyond oncology,” she noted, “it’s really hard to get any of that data.”

A [January 2023 study](#) revealed that, despite FDA recommendations, “many studies did not comply with reporting guidance of demographic characteristics. Failure to report race and ethnicity data was prevalent in US clinical trials conducted between 2008 and 2019.... Likewise, the inclusion of sexual and gender minorities in clinical trials is nearly nonexistent.”

It’s a vicious cycle: Sponsors need demographic data in order to make clinical trials more diverse, but they also need to disclose the data upfront. Disclosure teams should keep diversity in mind when submitting trials and reporting results to regulatory agencies, choosing categories such as age instead of “continuous” if categorization values are available. While choosing “continuous” is less time-intensive, spending a few more minutes to provide category information would enable diversity analysis.

When such demographic data points do exist, regulatory agencies must make them readily available, and sponsors need access in an efficient manner. Combing through databases can be a time-consuming endeavor. [A 2019 study](#) by the Tufts Center for the Study of Drug

Development revealed that a majority of life sciences companies use manual methods such as Microsoft Excel to integrate data. Utilizing technology that consolidates information from multiple databases can turn a monstrous manual task into a manageable one.

A distinction must be made between real-world data (RWD) and real-world evidence (RWE). The FDA defines RWD as “data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Examples of RWD include data derived from electronic health records, medical claims data, data from product or disease registries, and data gathered from other sources (such as digital health technologies)...” Other sources of RWD include billing data and patient-reported outcomes (PROs). Compared to data obtained via clinical trials, RWD sources typically include more diverse study populations.

The FDA defines RWE as “the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.” One way RWD can be used to promote clinical trial diversity is in modeling the impact of specific eligibility criteria on prospective participants so that more inclusive trial designs can be developed.

Mathematically, the more attributes known about a deidentified patient, the more likely that patient can be reidentified, creating exposure for civil and criminal penalties — plus the inevitable brand reputation impact. There is also a critical need to demonstrate that the incorporation of SDoH can improve patient outcomes, not disadvantage them. Unfortunately, many organizations are long on data use principles and short on mechanisms to ensure those principles are actually being followed.

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Diversity Data in Action

Diversity data have been “hard to get our hands on,” said Jameka Hill, Senior Director of Clinical Trial Health Equity at Moderna. These data elements simply were not reported, she noted, adding a touch of optimism, “We’re seeing a huge switch in the industry.” For sponsors like Moderna that want to be strategic, thoughtful, and successful up front, making diversity part of feasibility considerations and including diversity data points are key.

“We’re kind of like fingers crossed,” Hill said of efforts to expand diversity in clinical trials. However, for many studies, the research team is often seeking a very niche population, which complicates the matter. She said it is important to layer in inclusion/exclusion criteria that are not overly restrictive when looking to increase trial diversity.



Jameka Hill
Senior Director of Clinical Trial Health Equity at Moderna

She uses a nautical analogy to explain the importance of access to data in selecting trial sites to improve study diversity. “You can find your way to land on a boat if you sail a long time, but if you have a map you’ll get there much quicker. Citeline provides you with a map. I would encourage everyone to use this very untapped resource in the site selection process.”

Hill is referring to Citeline’s Sitetrove Diversity Module, the only solution that marries robust patient-level racial demographics from medical claims along with investigator gender data from the Centers for Medicare & Medicaid Services (CMS). These datasets are updated quarterly, providing sponsors with relevant demographics. She emphasized the need to have visibility into details that matter across the diversity spectrum — age, sex at birth, racial, and ethnic profiles — especially when it comes to health equity.

Trial sites must complete a quality assessment to be considered for Moderna studies. While many sites indicate they have access to diverse populations, Hill said this must be validated with other data sources such as census information, and diagnostic and ICD-10 coding. She is quick to note that just because a trial site is located in a diverse region, that doesn’t mean they serve those audiences. “There’s often a gap,” she said. She added that the demographics of the site staff and research staff are equally important to ensure that the site not only serves the community but represents the community.

“I think that data is crucial to diverse representation, but we can’t keep data in a silo,” said Hill. The data must be supplemented by site feedback. She credits sites for making a concerted effort, establishing relations with members of diverse communities. Because trust

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in the medical community — or lack thereof — is a big factor in trial participation among diverse populations, making these connections is essential.

Hill recognizes that much work remains to improve diversity in research. “There’s still a huge swath of populations that are completely underserved,” she said. “We need our sites,

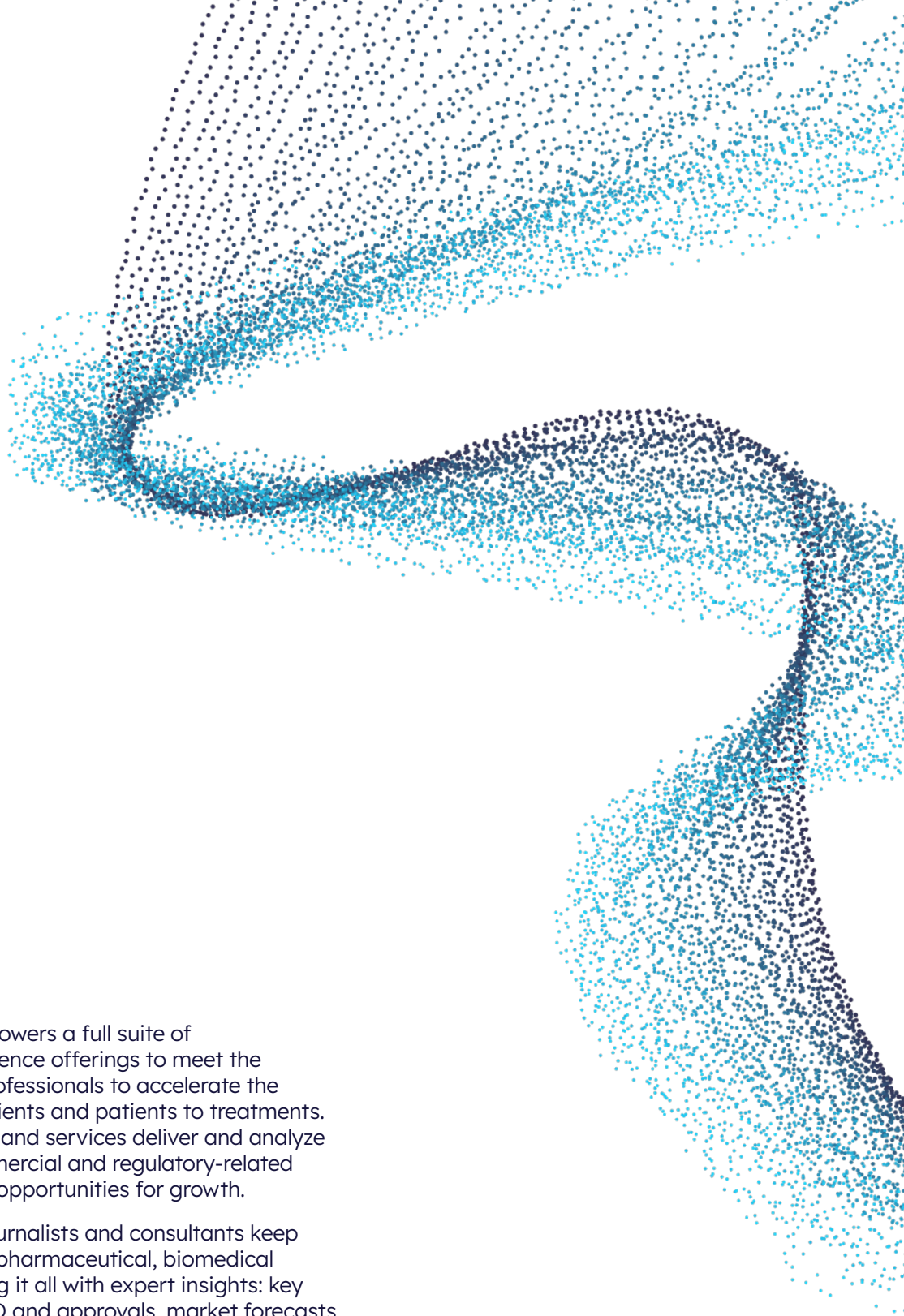
we need data. We also need community.” She added that this requires collaborations across all areas.

“I am interested to see where [clinical trial diversity] goes globally,” said Hill, “for the opportunity to understand where there are disparities in other populations and see where we can continue to evolve that.”

Conclusion

Diversity in clinical trials is most often looked at after the fact. That is, we look at diversity trends in terms of *completed* trials. In order to address the aforementioned regulatory, professional, and ethical aspects, diversity must be taken into consideration during a study’s planning and recruitment phases. Only then will the industry be able to reverse trends and make a true impact in representing all demographics in clinical research.





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