DAP MODEL

Diversity Action Plan

Introduction

This document was adapted from the MRCT Center's Recruitment Strategy Document[1] to align with the FDA draft guidance Diversity Plans to Improve Enrollment of Participants From Underrepresented Racial and Ethnic Populations in Clinical Trials'[2] (here termed the "Diversity Action Plan" or DAP, as a model). This document is intended to ensure that all stakeholders, including sponsors, CROs, institutions, sites, investigators, and their study staff are prepared to consider diverse participation in a clinical trial program. This document will be updated upon the release of the final FDA guidance document.

By necessity, the draft DAP does not give sufficient weight to multiple strategies that will contribute to diverse participant participation. For instance, long-term, sustainable partnerships with communities and community organizations (e.g., community providers, faith-based institutions, employer groups, patient advocacy organizations, and others) help institutions, sponsors, sites, and study teams build trust and enhance access to clinical trials. Investment in clinical research infrastructure should be coupled with investment in education, innovation, and training of a diverse workforce. We provide resources elsewhere for those considerations.[3]

It is important for any sponsor, CRO, or other organization to ensure that strategies to increase inclusion and diverse representation in clinical research are integrated and communicated throughout the organization, centralized in review and oversight, and able to leverage experience to improve future work.

Developing a comprehensive Diversity Action Plan (DAP) is integral to fostering inclusivity and equity in clinical trials. This entails providing a fair opportunity for participation in research, along with ensuring a fair opportunity to derive benefits from the research, acknowledging that these benefits may take various forms. This model outlines key considerations for sponsors to establish enrollment goals, focusing on race/ethnicity, age, sex/gender of participants, early in the clinical development process. The Plan is designed to enhance the understanding of any potential differential safety or effectiveness associated with different populations in the context of drug development. There is an emphasis on the collection of diverse pharmacokinetic (PK), pharmacodynamic (PD), and pharmacogenomic data, facilitating analyses that inform drug exposure and response.

[1] MRCT Center, available at: https://mrctcenter.org/diversity-in-clinical-research/wp-content/uploads/sites/8/2021/03/13-Recruitment-Strategy-Document.pdf (Accessed December, 2023). Note that additional suggestions and tools are provided in the Recruitment Strategy Document. Please consult that resource for further helpful resources.

[2] US Food and Drug Administration. Diversity Plans to Improve Enrollment of Participants From Underrepresented Racial and Ethnic Populations in Clinical Trials. Accessed online, June 2022. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diversity-plans-improve-enrollment-participants-underrepresented-racial-and-ethnic-populations

[3] See MRCT Center Diversity, Inclusion, and Equity in Clinical Research. Available at: https://mrctcenter.org/diversity-in-clinical-research/.

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This document begins with the objectives of the Diversity Action Plan, going beyond the FDA's draft guidance to offer a global perspective. Sponsors are encouraged to specify the intended regions and countries participating in the trial and document proposed approaches to tackle barriers to diverse, inclusive, and equitable recruitment in countries beyond the US, although this information may not necessarily be required for FDA submission. Additionally, the document will elaborate on the FDA's five recommended sections within the draft guidance.

It is crucial to consider a phased approach in the development of the Diversity Action Plan (DAP), progressing from a U.S.-centric strategy to a global one that acknowledges the unique needs, priorities, and populations in each country. Recognizing that a uniform approach may prove insufficient, it becomes imperative to formulate strategies tailored to the specific requirements of local studies. This involves a focus on diversity priorities, equity, and the reduction of barriers. The alignment with the ethical principles outlined in the *roadmap* is proposed to ensure a more nuanced and inclusive global approach. The DAP is designed to be a global, dynamic, and evolving document, maintaining relevance amid the ever-changing landscape of clinical trials.

Objective

- Summarize the objective of the diversity plan, including disease epidemiology and a description of how diverse and/or underrepresented populations are considered.
- Clarify whether the scope of the DAP is focused by therapeutic area, study, or product.
- Describe the plan to identify countries and sites to meet the intended recruitment and enrollment goals.
- Include relevant information on the safety and efficacy of the treatment or intervention being investigated and the population of interest.
- If no data exist that indicate the impact of race and/or ethnicity or other demographic or non-demographic variables on safety or effectiveness, enrollment should nonetheless reflect the epidemiology of the disease.

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[This is intended to serve as a guide. All sections should be revised, as necessary, to reflect the specific objectives and challenges of a given protocol)

Sponsor Logo	Other Logos

Clinical Trial Representation /Diversity Action Plan

Study Title
Protocol #(s)
NCT #(s)
IND #(s)
Version #

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ABBREVIATIONS

Version History

Revision	Date	Author(s)	Description

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1. Overview of the Disease/Condition

Provide a comprehensive depiction of the disease or condition under investigation, intending to provide (1) information on demographic factors (e.g., race/ ethnicity, geography [region/country, rural/urban location], age, sex, gender identity, sexual orientation, disability status, socioeconomic status, pregnancy and lactation status, comorbidities, other) that are related to differences in risk factors, disease burden, or outcomes, (2) provide an overview of the disease/condition in each of the identified population(s) and (3) outline the incidence and mortality rates in each group. This section is intended to describe the real-world patient population, by subgroup, and by country for the disease or condition being studied, and not specifically for the investigational product or product development program. Cover the following key components:

I. Disease/Condition Incidence & Prevalence

- **Incidence, prevalence, and/or character of the disease or condition:** Give an overview of the disease's occurrence, encompassing its incidence (frequency of new cases), prevalence (total cases), and/or character (e.g., severity, temporal differences in progression, etc.) across (a) the overall population, (b) distinct racial and ethnic minority subgroups, and (c) other subgroups with relevant disparities as known.
    - For overall population: describe data sources used to collect information on incidence and prevalence of the disease or condition:
        - In the US
        - In other regions or countries, if relevant
    - For distinct racial and ethnic minority populations: describe data sources used to collect information on incidence, prevalence, and character of the disease or condition, and completeness of those data. Include a brief description of data gaps. Include information based on data from the US and from other regions and countries.
    - For other subgroups (e.g., sex/gender/sexual orientation, age, geography, disability, veteran status, etc.): describe data sources used to collect information on incidence, prevalence, and character of the disease or condition, and completeness of those data. Include information based on data from the US and from other regions and countries (as relevant and available).
    - Summarize data to provide an assessment of the current understanding of subpopulation differences in the disease or condition in the US and outside the US.

- **Differences in Pathophysiology:** Using disparities by subgroup identified above, provide an in-depth discussion of differences in the disease's underlying biological mechanisms, and correlative and/or causative factors, across different subpopulations, if known.

- **Differences in Prevention, Screening, or Diagnostic Approaches:** Present an account of the differences in methodologies employed for diagnosing the disease, encompassing the range of tests, evaluations, and tools used for identification, as well as differences in screening or prevention strategies by subpopulation and/or geography, if known.
- **Differences in Treatment Strategies:** Offer insights into differences in the existing strategies used for treating the disease, by subpopulation and/or geography, if known.

II. Participant/Patient Disease Profile

- Outline the patient profile/study population, including disease prevalence, references to the demographics including but not limited to age, sex, gender identity, sexual orientation, race, ethnicity, ancestry, and non-demographic factors such as social determinants of health, co-morbidities, medications, the diagnosis pathway, treating physician's treatment options, etc. Consider these in relation to the study question.

2. Scope of Medical Product Development Program

This section describes the medical product development program, prior and planned trials that will support the planned marketing submission(s). Include subpopulations (e.g., race, ethnicity, geography [region/country, rural/urban location], age, sex, gender identity, sexual orientation, disability status, socioeconomic status, pregnancy and lactation status, comorbidities, other, as relevant) and mention of the planned Pediatric Investigations Plan if available.

Document the intended patient population(s) for the product. Explain differences in the plan compared to the real-world patient population affected by the disease or condition. Include overview of the study design, study population, and eligibility criteria, endpoints, and the expected geographic locations of the studies. Discuss how the study will address inclusion of underrepresented racial and ethnic populations and other relevant subpopulations. As applicable, summarize any differences in clinical pharmacology studies (PK /PD data, pharmacogenomics) associated with subpopulations (e.g., race, ethnicity, sex, age, ability, comorbidity) and/or other relevant information.

I. Product Development Program

- Outline the overall product development plan and planned product indication.
- Describe prior pre-clinical and clinical studies that specifically provide any evidence of product differences by subpopulation. Include a summary of prior pharmacokinetic/pharmacodynamic (PK/PD) and pharmacogenomic studies in different subpopulations that have been done that provide evidence of similarity or differences in safety or efficacy across those subpopulations.

- Describe how this current study fits into the overall product development plan. Describe any concurrent studies that overlap and/or may provide insights into this study and the proposed DAP.
- Summarize planned future studies that will support the marketing application, including geographic locations of the studies, and how these future clinical trials or studies will contribute to the safety and efficacy of the IP in different subpopulations and to an understanding of subpopulation differences, if any.

II. Summary of Clinical Studies Included in This Diversity Action Plan

- Briefly outline the overall study questions, designs, including study eligibility criteria.
- Describe how the study question reflects the needs of diverse populations or subgroups and the input of patients and/or local communities within the different countries the study is being conducted (if applicable).
- Describe how healthcare provider, patient, participant and/or community input was sought, collected, and included in the design of the study, selection of outcomes and endpoints, and population-specific insights (e.g., recruitment approaches, review of participant-facing materials).
    - Include a description of the variety of demographic representation of the individuals and groups from whom that input was sought.
- When applicable, describe the detailed operational measures that will be implemented to enroll and retain underrepresented populations in the planned study(ies) and the planned use of data to characterize the safety, efficacy, and optimal dosage in these participants. when applicable.
- Summarize the plan to assess subpopulation variance of screen failure rates, enrollment, retention, side effect, and efficacy.

** Please note that certain aspects will likely be centrally managed, such as outcomes and endpoints, while others will require country and site-specific attention, like recruitment approaches and reviews of participant-facing materials*

3. Goals for Enrollment of Underrepresented Participants

In this section, provide justification for the planned enrollment goals of participants from racial and ethnic subpopulations, and other subpopulations, as relevant to the real-world patient population affected by the disease or condition. Here, describe the goals for enrollment of subpopulations, based on the epidemiology of the disease or condition and/or based on identified subpopulation differences. These goals are most effectively established when incorporated into the development program with early engagement with the FDA. This ensures alignment between sponsors and the FDA on these "goals," emphasizing that they are not intended as mere minimum quotas.

Include plans for adaptation of the trial or enrichment of certain subpopulations that may be needed to identify potentially important differences.

I.Study Plans

- Describe and justify the planned enrollment goals of the intended participant populations, including under-represented populations, based on epidemiology of the disease or condition in the U.S. and other countries.
- Justify any eligibility criteria that result in exclusion of underrepresented populations. Include the ethical or scientific basis for such criteria, and upon what data the criteria were based.
    - If applicable, describe how eligibility criteria will be adapted and amended over the course of the trial, consistent with demonstration of safety, to result in a study population that accurately reflects the population affected by the condition.
    - If adaptive eligibility criteria are not anticipated, explain why not, and how the information will be collected and analyzed after the trial concludes.

4. Specific Plan of Action to Enroll and Retain Diverse Participants

In this section, the region, country and site, selection process are specified, including how the feasibility assessment is conducted to optimize the likelihood of success in recruitment, enrollment, and retention of representative participants. The methods to identify, assess, and validate sites with access to and experience with the intended study populations are described.
In addition, the recruitment and retention strategies are detailed, including special tactics, services, modifications, and accommodations that will be provided, as well as other methods to reduce participant burden and optimize retention. Patient, patient advocacy, and community engagement plans, and outreach to local and community healthcare providers, as outlined above.

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I. Selected Countries and Planned Projections

- Include a list of potential country sites and participants with the planned activation schedule as available
- Describe the process for selecting these regions, countries, and sites in study planning and the feasibility assessment performed.
- Provide the percentage of participants that will be enrolled from the US and from each region and/or country outside the US, and for each country, the percentages of participants by demographic variable and extending that analysis to other subpopulations relevant to epidemiology of the disease or condition or to the safety and efficacy of the product itself.
    - Consider whether over-enrollment of certain subpopulations is necessary to gather important data on safety or efficacy for those subpopulations.
    - Describe how and how frequently enrollment, and enrollment by subpopulation will be monitored over the course of the study.
    - Explain how under-enrollment will be identified, communicated, and mitigated as the study progresses.
    - List the intended countries which will have sites that will participate in the clinical trial/program:
        - Country 1
        - Country 2
        - Country 3…

      Describe how and why the countries were chosen and the kind of population represented based on the epidemiology of the disease.
- For each country, provide the intended country plan to the extent possible, and complete the table as the study progresses. This can vary from country to country.

Country	Randomization Target (N)	Total Number of Sites	Monthly Randomizatior Rate per Site (P/S/M)	Over Enrollment Allowance (%)	Screen failure ratio (% screen fail)	Sites Actively Screening (%)	Target First Site Initiated (Date)	# of days until 25% Sites Active	# of days until 50% Sites Active	# of days until 90% Sites Active	First Patient Screened (FPI) (Date)

II. Site Capacity Profile

- Describe the feasibility assessment process that has or will be performed to select regions, countries, and sites specific to the disease or condition that is being studied.
    - Describe criteria for site selection to maximize potential to enroll intended subpopulations.
    - Use a data-driven approach to support the intentional identification of sites that support the enrollment of diverse populations-sites that have historically supported enrollment and those that could potentially support enrollment. Outline data sources and planned analyses.
    - Describe any geophysical mapping that has been performed to optimize the likelihood of site recruitment of the intended subpopulations relevant to the disease or condition.
        - Include data on satellite sites or partner organizations (e.g., community health centers) that may be relevant to recruitment and retention.
- If feasible to the study, flexible options should be listed to ease access to a clinical trial/research study for those who may have time or logistical challenges. This includes the possibility of virtual visits, after-hour/weekend hours, and/or using local labs or home visits may reduce recruitment and retention barriers. Accommodations to enable people with disabilities access to research are essential and are required by law in the U.S.
    - Include information on other measures that have been or will be introduced to reduce participant burden (e.g., provision of reimbursement, compensation, transportation, food, childcare, eldercare).
    - Describe how the number or frequency of procedures has been minimized to reduce burden, and whether the site(s) align and agree.
- As practicable, outline the site profile, including patient capacity, staffing/resourcing, language assistance, translation services, specialty type (if any), special needs/reasonable equipment modifications for persons with disabilities, social environment safety of the site for vulnerable populations such as sexual and gender minorities (SGM) and others.
- Describe whether and how the diversity of the study site workforce (e.g., principal investigators, study staff, patient navigators) will be assessed.
- Describe whether and how the experience in recruitment and retention of participants from the intended subpopulations by the site, PI, and study staff will be considered.
- Describe permissible remote or decentralized elements (e.g., local imaging facilities and laboratories, remote or in-home visits, telehealth, electronic data capture, electronic patient reported outcomes, etc.) that further reduce participant burden, whether participants will be able to choose whether to use those decentralized elements, and whether sites are able to implement these changes.
    - Ensure that selected sites have processes and procedures in place to implement the planned study modifications, accommodations, and flexibilities.

- Describe what community engagement efforts, if any will be utilized to support sites in engaging the targeted communities of the desired patient population

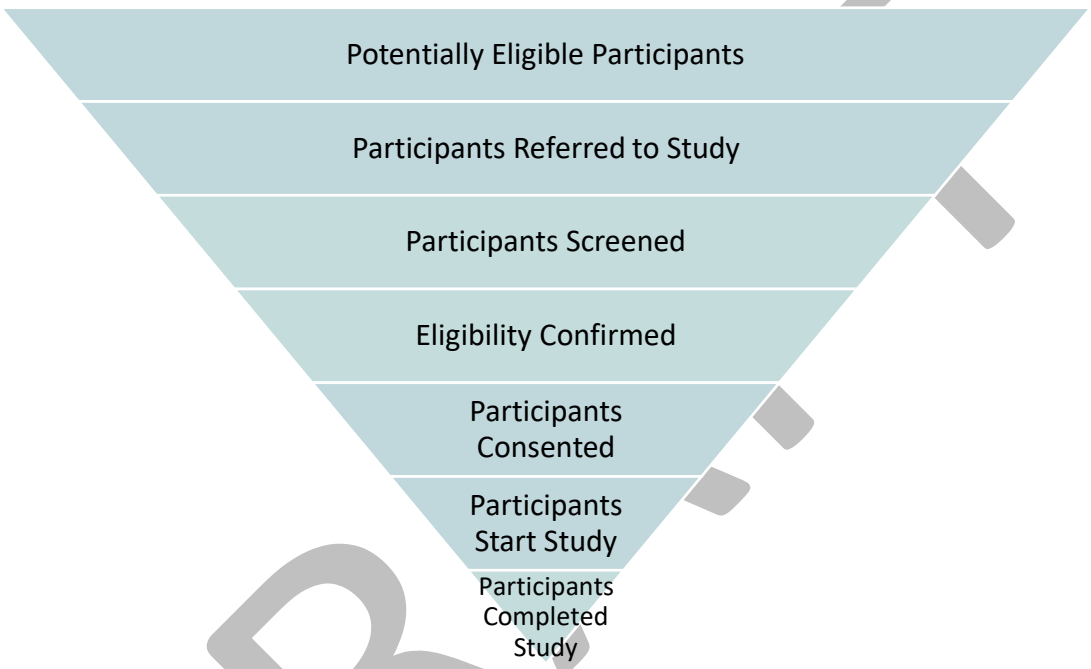
III. Recruitment and Retention Strategies

- Describe community engagement activities and partnerships that will enable education, awareness, and access amongst desired populations, including advisory boards, advocacy organizations, community healthcare workers, and providers.
- Provide a high-level overview of primary and secondary participant recruitment and retention strategies. What specific approaches and techniques will be used to access and engage intended populations?
- Describe healthcare provider materials, outreach, and plans for dissemination. Simplify referral and intake processes.
- Describe patient/participant recruitment materials that are or will be developed and how they are going to be used.
    - Describe any patient, participant, or community review of those materials.
    - Explain whether and when the patient/participant recruitment materials will be translated and into which languages, and whether modifications to the materials will be made for inclusion of people with disabilities.
    - Describe process for dissemination to the intended populations to optimize relevant patient populations will have access to the materials.
    - Describe efforts to simplify referral and intake processes, including the provision of patient navigators and/or linguistically and culturally appropriate interpreters.
    - Include specific activities planned that address barriers to participation for any of the intended study populations.
        - Identify sustained community engagement efforts and community partnerships by sponsor and/or site.
        - Describe planned patient, patient advocacy, and community engagement activities that may increase access, referrals, and recruitment of relevant subpopulations.
        - Include outreach to community healthcare providers, referral networks, and others, and whether contract vendors will be used.
            - Identify method of outreach (e.g., email, webinars, in-person or virtual meetings)
        - Describe how principal and site investigators and their study teams have been engaged and/or trained to fulfill the goals of broad and diverse participant recruitment.
        - Describe any specialized technology that will be used.

IV. Recruitment Projections

- Detail both study-specific target numbers by subpopulation – age, sex, race, ethnicity, etc. Recognize that not every site needs to enroll a target number of diverse or underrepresented patients, but the overall study should.

[Sample recruitment planning table]



** Note that in a multi-country study, under-representation will come in different forms. This works for factors such as age (children/older adults) and biological sex but may not for the many social/cultural factors that may influence patient experience/outcomes, but which vary within and between countries.*

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PLANNED	Ethnic Categories									
	Not Hispanic or Latino			Hispanic or Latino			Ethnicity Unknown / Not Reported			
Racial Categories	Female at birth	Male at birth	Unknown / Not Reported	Female at birth	Male at birth	Unknown / Not Reported	Female at birth	Male at birth	Unknown / Not Reported	**Total**
American Indian / Alaska Native										
Asian										
Native Hawaiian or Other Pacific Islander										
Black or African American										
White										
More than One Race										
Unknown or Not Reported										
TOTAL										

Please note that this table is an example, and the categories can be modified as appropriate. It is derived from the current OMB categories and can be changed as appropriate. If you are conducting Sexual Orientation and Gender Identity (SOGI)research, there are additional considerations. What is meant by 'sex' in this document is biological sex at birth, but other categories may need to be included if intersex individuals' part of the participant population of interest.

5. Status of Meeting Enrollment Goals

In this section, how recruitment and retention will be monitored, and suggested action steps for mitigation if recruitment or retention are under target, are explained. Risk and contingency management plans are considered.

I. Recruitment Monitoring and Mitigation Plan

- Detail how and how often tracking, review, and analyses of recruitment and enrollment numbers will be ascertained.
    - Include age, sex/gender, race/ethnicity, disability, and other categories as relevant.
    - Include specific oversight of site performance against site-specific recruitment commitments.
    - Collect information from sites on recruitment persistent barriers, unforeseen challenges, and, equally, successful strategies.
    - Provide suggested mitigation strategies if recruitment and enrollment are under target compared to anticipated plans.
- Provide information on how each site, country, and region will be monitored and by whom. Include information on whether there are dedicated sponsor or sponsor designees assigned to the region, country, or site for support.

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II. Retention Monitoring and Mitigation Plan

- Describe how and how often tracking, review, and analyses of enrolled participants and study follow-up will be performed.
    - Include age, sex/gender, disability, and other categories as relevant.
    - Include specific oversight of site performance against site-specific retention commitments.
    - Collect information from sites on retention persistent barriers, unforeseen challenges, and, equally, successful strategies.
    - Provide methods that will be used to monitor retention (i.e., patient navigators or ambassadors; frequency and style of follow-up reminders) and provide suggested action steps for mitigation if retention is under target.
        - Consider schedule of escalating interventions if site-specific recruitment does not improve with implementation of mitigating strategies.
    - Include information on whether and how often rates of screen failure, enrollment, drop-out, and lost-to-follow up will be performed on subpopulations.

III. Risk and Contingency Management

- Outline the risks associated with this study in terms of recruitment timelines and milestones, and list the contingency strategies, triggers, and the action plan, annotating any differences in:
    - US sites, investigators, and study staff
    - In other region and countries
- Specifically outline triggers for pauses in enrollment by site and/or by subpopulation, for dynamic adjustments of site subpopulation commitments, and/or for addition of new sites.

V. Data Analysis

Here, a plan and justification for collecting data in the post-marketing setting if enrollment goals are not met should be outlined. Learnings from the process should be retained and adjustments made to future diversity action plans.

- Outline what would trigger a post-approval study for further collection of subpopulation data (post-approval requirements and/or post-approval commitments studies).
- Collect real-world data to enhance understanding of product effects in diverse patient populations.
- Perform pos hoc analysis of performance on diversity metric and memorialize lessons learned

