# Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies
# Guidance for Industry

## *DRAFT GUIDANCE*

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**June 2024**
**Clinical/Medical**

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# Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. With the exception of certain portions of section VII, it does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

## I. INTRODUCTION

This guidance is intended to assist sponsors conducting certain clinical studies involving drugs,[2] biological products, and devices to meet requirements for the submission of Diversity Action Plans under section 505(z) and section 520(g)(9) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) as added by section 3601 of the Food and Drug Omnibus Reform Act of 2022 (FDORA).[3] Specifically, sections 505(z)(3) and 520(g)(9)(A) of the FD&C Act require that sponsors submit Diversity Action Plans for certain clinical studies in the form and manner specified by FDA in guidance. Diversity Action Plans are intended to increase enrollment of participants who are members of historically underrepresented populations in clinical studies to help improve the strength and generalizability of the evidence for the intended use population. Such plans must specify "the sponsor's goals for enrollment in [a] clinical study," "the sponsor's rationale for such goals", and include "an explanation of how the sponsor intends to meet those goals."[4] The Secretary is required to update or issue guidance to sponsors regarding the format and content of their Diversity Action Plan pertaining to clinical study enrollment goals "disaggregated by age group, sex[5], and racial and ethnic demographic characteristics of clinically

[1] This guidance has been prepared by the Oncology Center of Excellence (OCE) in collaboration with the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), the Center for Devices and Radiological Health (CDRH), the Office of Women's Health (OWH), and the Office of Minority Health and Health Equity (OMHHE) at the Food and Drug Administration.

[2] In this guidance, use of term "drug" refers to both human drugs approved under section 505 of the FD&C Act (21 U.S.C. 355) and biological products licensed under section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262) that are regulated as drugs.

[3] See the Food and Drug Omnibus Reform Act of 2022 (FDORA) included as part of the Consolidated Appropriations Act (December 2022) (P.L. 117-328).

[4] See section 505(z)(2) of the FD&C Act for drugs and section 520(g)(9)(B) of the FD&C Act for devices.

[5] See section 3602(a)(1) of FDORA. For the purposes of this guidance, "sex" is a biological construct based on anatomical, physiological, hormonal, and genetic (chromosomal) traits, and is generally assigned based on anatomy at birth typically categorized as male or female, but variations occur. Variations of sex refers to differences in sex development or intersex traits. See *Measuring Sex, Gender Identity, and Sexual* Orientation (2022). National Academies of Science, Engineering, and Medicine. Washington, DC: The National Academies Press.

relevant study populations."[6] Section 3604 of FDORA also requires that FDA annually submit to Congress, and publish on the Agency's website, a report that summarizes in the aggregate the Diversity Action Plans received and whether the clinical studies conducted met the demographic enrollment goals from the submitted Diversity Action Plans.

FDA is issuing this guidance to satisfy section 3602 of FDORA which requires that FDA update or issue guidance relating to the format and content of Diversity Action Plans required by sections 505(z) and 520(g)(9) of the FD&C Act.[7] This guidance describes the format and content of Diversity Action Plans, including the timing and process for submitting such plans by application or notification type. Additionally, this guidance describes the criteria and process by which FDA will evaluate sponsors' requests for waivers from section 505(z) or 520(g)(9) of the FD&C Act. This guidance also provides general recommendations for sponsors who may wish to publicly post key information regarding their Diversity Action Plans. This guidance replaces the draft guidance for industry titled *Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials* (April 2022). This guidance is not intended to address all issues related to the clinical development of medical products[8] such as the design of clinical studies, clinical study endpoints, or the data necessary to support a marketing submission; sponsors should refer to the appropriate FDA guidance documents for FDA recommendations on these matters.

Per section 3602(c) of FDORA, the requirements for Diversity Action Plans apply to clinical studies for which enrollment commences after 180 days from the publication of the final guidance. Because sponsors engage in study planning and implementing study activities prior to when enrollment commences, FDA does not expect a Diversity Action Plan to be submitted for clinical studies where the following circumstances are present:

- Clinical studies of drugs with protocols submitted within 180 days following the publication of the final guidance where enrollment is scheduled to begin 180 days after publication of the final guidance.
- Clinical studies of devices received by FDA in Investigational Device Exemption (IDE) applications within 180 days after publication of the final guidance.
- Clinical studies of devices that do not require an IDE application to be submitted to FDA that are approved by an institutional review board (IRB) or independent ethics committee (IEC) within 180 days after the date of publication of the final guidance.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidance describes the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of

[6] See section 3602(a) of FDORA. Goals for enrollment, as described below, are intended to improve the generalizability of study results and the potential detection of clinically important differences across populations (when present) by reflecting the patient population with the disease or condition in the US that is expected to use the medical product if approved, licensed, authorized, cleared, or classified.

[7] Section 3602(b) of FDORA.

[8] For the purposes of this guidance, use of term "medical product" refers to human drugs (including human biological products that are regulated as drugs) and devices.

the word *should* in Agency guidance's means that something is suggested or recommended, but not required.

An exception to this framework derives from the requirement in section 3601 of FDORA for FDA to specify in guidance, the form and manner for the submission of Diversity Action Plans. Accordingly, insofar as section VII of this document specifies the form and manner[9] for submission of a Diversity Action plan, it will have binding effect, once this guidance is finalized, as indicated by the use of the words, *must, shall,* or *required.*

## II. BACKGROUND

Clinical studies characterize the safety and effectiveness of medical products intended for the prevention, treatment, mitigation, cure, or diagnosis of many conditions or diseases. Some populations in the United States (U.S.) are frequently underrepresented[10] in biomedical research, including clinical studies, even when they bear a disproportionate burden for certain conditions or diseases relative to their proportional representation in the general population. There are myriad reasons for this, including but not limited to assumptions regarding the feasibility of enrolling a population in a clinical study that is representative of the intended use population and the impact on study timelines, and the lack of the prospective development and implementation of a strategy that helps ensure enrollment and retention of a clinical study population representative of the intended use population. Efficient development and approval/clearance of medical products is a highly desirable goal for the public, sponsors, and the FDA, underscoring the importance of prospectively defining the approach to generating data for a broader and more representative population early in the clinical development program.[11] Consistent implementation of actions to improve representativeness in clinical studies can support more equitable and timely access to medical discoveries and innovations, improve the generalizability of results across the intended patient populations, improve our understanding of the disease and/or medical product under study, and inform the safe and effective use of the medical product for all patients.

[9] FDA interprets the term "manner" in section 3601 of FDORA to include the process for submission of the Diversity Action Plans.

[10] Consistent with section 3602(a) of FDORA, this guidance focuses on underrepresented populations based on race, ethnicity, sex, and age group, but FDA notes that there are other underrepresented populations that sponsors may consider, such as pregnant or lactating individuals. *See* section 3602(a) of FDORA. Generally, for race and ethnicity, underrepresented populations may typically include participants who are Black or African Americans, Hispanic/Latinos, Indigenous and Native American, Asian, Native Hawaiian and Other Pacific Islanders, and other persons of color. Generally, for sex and age, underrepresented populations may typically include participants who are females and in the older adult and pediatric age groups, respectively. See, e.g., National Academies of Sciences, Engineering, and Medicine. 2022. *Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups*. Washington, DC: The National Academies Press. https://doi.org/10.17226/26479; Executive Order 14120, Advancing Women's Health Research and Innovation (89 FR 20095, March 18, 2024).

[11] Fashoyin-Aje L, Beaver J, Pazdur R. Promoting Inclusion of Members of Racial and Ethnic Minority Groups in Cancer Drug Development. JAMA Oncol. 2021 Oct 1;7(10):1445-1446 and, Fashoyin-Aje L, Tendler C, Lavery B, et al. Driving Diversity and Inclusion in Cancer Drug Development – Industry and Regulatory Perspectives, Current Practices, Opportunities, and Challenges. Clin Cancer Res. Jun 28, 2023.

FDA has issued several guidance documents to provide recommendations addressing measures to enroll representative populations with respect to specific demographic factors (e.g., race, ethnicity, sex, age group), and general measures that enhance diversity in clinical studies (e.g., broadening of eligibility criteria)[12,13] when scientifically appropriate, including in the post-approval setting.[14] Scientific experts and stakeholders have also provided recommendations on strategies to ensure diverse clinical study participation[15,16] and to improve evidence generation for the population for which the medical product is being developed. Such measures include starting with intention and deliberateness to achieve study population representativeness as part of the clinical and operational strategy.

In general, clinical study diversity helps ensure that clinical studies appropriately test the product in a representative sample of the product's intended use population. Factors to consider when setting enrollment goals include demographic characteristics (e.g., race, ethnicity, sex, age group[17]), clinical characteristics (e.g., presence of comorbidities, disease etiology), and other characteristics (e.g., access to standard preventive and diagnostic care, access to standard treatments of the clinically relevant population). FDA has published guidance with recommendations for the inclusion of certain populations (e.g., females, including individuals

[12] See the following guidance documents for industry: Draft guidance for industry *Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for FDA-Regulated Medical Products* (January 2024). In March 2024, the Office of Management and Budget (OMB) published a set of revisions to *Statistical Policy Directive No. 15: Standards for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity* to reflect new recommendations for race and ethnicity categories. FDA's draft guidance was issued prior to OMB's revisions. When finalizing the guidance, FDA intends to update the racial and ethnicity categories consistent with the revisions to OMB Policy Directive No. 15. When final, this guidance will represent FDA's current thinking on this topic. See also *Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs* (November 2020); and *Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies* (September 2017), and *Evaluation of Sex-Specific Data in Medical Device Clinical Studies* (August 2014).

[13] See series of guidance for industry regarding eligibility criteria for medical products regulated by CDER and CBER for the treatment of cancer including *Cancer Clinical Trial Eligibility Criteria: Brain Metastases* (July 2020), *Cancer Clinical Trial Eligibility Criteria: Patients with Organ Dysfunction or Prior or Concurrent Malignancies* (July 2020), *Cancer Clinical Trial Eligibility Criteria: Patients with HIV, Hepatitis B Virus, or Hepatitis C Virus Infections* (July 2020), *Cancer Clinical Trial Eligibility Criteria: Minimum Age Considerations for Inclusion of Pediatric Patients* (July 2020) and the Guidance for Industry *Male Breast Cancer: Developing Drugs for Treatment* (August 2020).

[14] See draft guidance for industry *Postmarketing Approaches to Obtain Data on Populations Underrepresented in Clinical Trials for Drugs and Biological Products* (August 2023). When final, this guidance will represent the FDA's current thinking on this topic.

[15] See Cancer Disparities Progress Report 2020: Achieving the bold vision of health equity for racial and ethnic minorities and other underserved populations. American Association for Cancer Research; ©2020. Available at https://cancerprogressreport.aacr.org/disparities/.

[16] National Academies of Sciences, Engineering, and Medicine. 2022. Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups. Washington, DC: The National Academies Press. https://doi.org/10.17226/26479.

[17] For the purposes of this guidance, age group representativeness refers to the inclusion of study participants from the entire age spectrum relevant to the disease or condition under study that the product is intended to treat.

who are pregnant and lactating; older adults; pediatric populations) in clinical studies.[18,19] Moreover, FDA regulations require Investigational New Drug (IND) application holders to include in their annual reports, among other things, the total number of subjects initially planned for inclusion in a clinical study and the number entered into the study to date, tabulated by race, gender, and age.[20] In addition, a new drug application (NDA) must present effectiveness and safety data by race, gender, and age and must identify any modifications of dose or dose interval needed for a specific subgroup.[21] For certain pediatric studies, FDA must take into account the adequate representation of children of ethnic and racial minorities.[22]

Consistent with section 3602(a) of FDORA, this guidance primarily focuses on Diversity Action Plans for the enrollment and retention of a clinically relevant study population, to help ensure adequate representativeness of study participants that reflect different age groups, sexes, and racial and ethnic demographic characteristics. However, FDA recognizes the broader issues regarding health disparities and differential access to health care and clinical studies that may occur based on other factors, including but not limited to geographic location, gender identity,[23,24] sexual orientation,[25] socioeconomic status (SES), physical and mental disabilities, pregnancy status,[26] lactation status, [27] and co-morbidity. As applicable, FDA encourages sponsors to consider such additional factors, which may support subgroup analyses, when developing Diversity Action Plan enrollment goals. For example, a sponsor developing a Diversity Action Plan that specifies enrollment goals disaggregated or tabulated by race, ethnicity, sex, and age group, should also consider the potential that pregnant or lactating individuals with the condition or disease may use the medical product.

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[18] See the following guidances for industry: *Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs* (July 1993), *Evaluation of Sex-Specific Data in Medical Device Clinical Studies* (August 2014), *Guideline for the Study of Drugs Likely to be Used in the Elderly* (November 1989), *E7 Studies in Support of Special Populations: Geriatrics Questions and Answers* (February 2012), *Providing Information about Pediatric Uses of Medical Devices* (May 2014), and *Premarket Assessment of Pediatric Medical Devices* (March 2014). See the following two draft guidances for industry: *Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials* (April 2018) and *Clinical Lactation Studies: Considerations for Study Design Guidance for Industry* (May 2019). When final, these guidances will represent the FDA's current thinking on these topics.

[19] See draft guidance for industry, sponsors, and IRBs *Ethical Considerations for Clinical Investigations of Medical Products Involving Children* (September 2022). When final, this guidance will represent the FDA's current thinking on this topic.

[20] See 21 CFR 312.33(a)(2). Note that we consider the term "gender" in this regulation to mean "sex."

[21] See 21 CFR 314.50(d)(5)(v) and (vi). Note that we consider the term "gender" in this regulation to mean "sex."

[22] See section 505A(d)(1)(A) of the FD&C Act.

[23] National Academies of Sciences, Engineering, and Medicine. 2020. Understanding the Well-Being of LGBTQI+ Populations. Washington, DC: The National Academies Press. https://doi.org/10.17226/25877.

[24] Alpert A, Brewer J, Adams S, Rivers L, Orta S, Blosnich J, Miedlich S, Kamen C, Dizon D, Pazdur R, Beaver J, Fashoyin-Aje L. Addressing Barriers to Clinical Trial Participation for Transgender People With Cancer to Improve Access and Generate Data. J Clin Oncol. 2022 Oct 27; JCO2201174.

[25] See footnote 23.

[26] See *Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)* available at Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) | NICHD - Eunice Kennedy Shriver National Institute of Child Health and Human Development (nih.gov) https://www.nichd.nih.gov/about/advisory/PRGLAC#:~:text=The%2021st%20Century%20Cures%20Act,back%20to%20the%20HHS%20Secretary.

[27] Ibid.

## III. CLINICAL STUDIES REQUIRING DIVERSITY ACTION PLANS

Under sections 505(z) and 520(g)(9) of the FD&C Act, submission of a Diversity Action Plan is required for certain clinical studies regarding drugs, biological products, and devices subject to sections 505, 515, 510(k), 513(f)(2), or 520(g) of the FD&C Act (21 U.S.C. 355; 360e; 360 (k); 360c(f)(2) and 360j(g)), or section 351(a) of the Public Health Service Act 19 (42 U.S.C. 262(a)).

For drugs, a Diversity Action Plan is required for a clinical investigation of a new drug that is a phase 3 study (as defined in 21 CFR 312.21), or as appropriate, another pivotal clinical study of a drug (other than a bioavailability or bioequivalence study).[28,29]

For devices, a Diversity Action Plan must be included in the Investigational Device Exemption (IDE) application for clinical studies of the device. An IDE application is required if the sponsor intends to use a significant risk (SR) device (as defined in 21 CFR 812.3(m)) in an investigation, intends to conduct an investigation that involves an exception from informed consent under 21 CFR 50.24, or if FDA notifies the sponsor that an application is required for an investigation.[30]

For devices for which an IDE application to FDA is not required, except for a device being studied as described in 21 CFR 812.2(c), section 520(g)(9)(A)(ii) requires sponsors to develop a Diversity Action Plan for any clinical study with respect to the device.[31] Diversity Action Plans for these devices must be submitted to FDA in any premarket notification, [32] request for classification,[33] or application for premarket approval[34] under section 510(k), 513(f)(2), or 515 of the FD&C Act, respectively.[35]

For devices, there are many types of clinical studies that may be conducted as part of the premarket process, representing different stages of device development and testing.[36] Additionally, not all device studies will require submission of an IDE application to FDA; for example, a study may be nonsignificant risk (NSR) and in compliance with 21 CFR 812.2(b)(1)(i) – (vii) or a study may be conducted completely outside the U.S. in such a way that

[28] See Section 505(z)(1) of the FD&C Act.
[29] 21 CFR 312.21(c) states that "Phase 3 studies are expanded controlled and uncontrolled trials."
[30] 21 CFR 812.20(a).
[31] Although medical device postmarketing clinical studies are outside the scope of this guidance, FDA considers diversity and representative patient enrollment to be important in postmarketing clinical studies of devices. We note that under sections 515, 519, and 522 of the FD&C Act, FDA has authority to require certain enrollment expectations for post-approval and postmarket surveillance studies.
[32] See 21 CFR 807.81.
[33] See section 513(f)(2) of the FD&C Act.
[34] See 21 CFR 814.20.
[35] In general, FDA believes that device studies that will require the submission of a Diversity Action Plan will be among those device clinical studies required to register via ClinicalTrials.gov under 42 CFR Part 11.
[36] For additional information on types of medical device studies, see guidance documents for industry and FDA staff *Design Considerations for Pivotal Clinical Investigations for Medical Devices* (November 2013) and *Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies* (October 2013).

submission of an IDE application is not needed.[37] FDA acknowledges that a Diversity Action Plan may not be particularly meaningful for certain device studies, such as for small studies conducted during the exploratory clinical stage. Notwithstanding this point, FDA expects sponsors to develop a Diversity Action Plan for a study that is intended to serve as the primary basis for FDA's evaluation of safety and effectiveness and benefit-risk determination. As such, while Section 520(g)(9) of the FD&C Act refers to clinical studies broadly, FDA does not intend to receive or review Diversity Action Plans for studies that are not designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use. A study that is exempt from the requirements of the IDE regulations under 21 CFR 812.2(c) does not require the development or submission to FDA of a Diversity Action Plan regardless of whether it is intended to serve as the primary basis for FDA's evaluation of safety and effectiveness and benefit-risk determination.

While sponsors are required to submit a Diversity Action Plan for the studies specified above, FDA strongly recommends that sponsors develop and implement a comprehensive diversity strategy across the entire clinical development program, including in early studies, when possible.

## IV. ADDRESSING RACE, ETHNICITY, SEX, AND AGE GROUP IN DIVERSITY ACTION PLANS

As described above, sections 505(z) and 520(g)(9) of the FD&C Act require that sponsors submit a Diversity Action Plan that specifies goals for clinical study enrollment, and FDORA states that such goals must be disaggregated by the race, ethnicity, sex, and age group demographic characteristics of the clinically relevant population.[38] When developing these goals, sponsors should consider the distribution of the intended use population according to these demographic characteristics.

Sponsors should consider whether certain demographic groups (e.g., older patients, pediatric patients, females, a particular race or ethnic group or combinations thereof) may have a different response to the medical product—either differential effectiveness or safety (e.g., based upon differential pharmacokinetics (PK), pharmacodynamics (PD), or due to possible differences in susceptibility to specific adverse events of concern for a drug or medical device), or due to differential presentation of the disease or condition. In some cases, it may be necessary to increase the proportional enrollment of a certain population in the clinical study to evaluate outcomes of interest or other clinically relevant factors in that group.

[37] See 83 FR 7366, Human Subject Protection: Acceptance of Data From Clinical Investigations for Medical Devices.

[38] Sections 505(z)(2) and 520(g)(9)(B) of the FD&C Act; see also section 3602 of FDORA.

Sponsors developing Diversity Action Plans should refer to other FDA guidance documents for additional recommendations relevant to sex and age considerations for clinical study enrollment.[39]

## V. CONTENT OF THE DIVERSITY ACTION PLAN

Under sections 505(z) and 520(g)(9) of the FD&C Act, a Diversity Action Plan must include:[40]

- the sponsor's goals for enrollment in the clinical study, disaggregated by race, ethnicity, sex, and age group of clinically relevant study populations,
- the sponsor's rationale for such goals, and,
- the sponsor's explanation of how the sponsor intends to meet such goals.

This section of the guidance describes the form and content of a Diversity Action Plan and provides recommendations that may be helpful in ensuring that the requirements of a Diversity Action Plan are met. While the requirements and recommendations described in this guidance are significantly aligned across drugs and devices, the types of submissions in which Diversity Action Plans must be provided, and timing of these submissions differ between drugs and devices under the FD&C Act. These different submission types may reflect different stages of the overall clinical development program for a medical product, and each type of submission is governed by unique statutory and regulatory requirements as well as different administrative considerations and review practices. As such, some of the requirements and recommendations for Diversity Action Plans differ for device submissions compared to drug submissions.

### A. Enrollment Goals

A Diversity Action Plan must include the sponsor's enrollment goals for a clinical study, disaggregated by the race, ethnicity, sex, and age group of the clinically relevant study population.[41] Sponsors must present their enrollment goals across subsets of the population with these demographic characteristics (e.g., for race: Asian, Black/African American, etc.). [42] These demographic characteristics are summarized in Table 1.

Generally, enrollment goals should be informed by the estimated prevalence or incidence of the disease or condition in the U.S. intended use population for which the medical product is being

[39] See the following guidances for industry: *Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs* (November 2020); *ICH E7: Guideline for Industry: Studies in Support the of Special Populations: Geriatrics*. (August 1994); *ICH E11 Clinical Investigation of Medicinal Products in the Pediatric Population* (December 2000); *ICH E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population* (April 2018); *ICH E7 Studies in Support of Special Populations: Geriatrics Questions and Answers* (March 2012); *Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials* (March 2019); *Inclusion of Older Adults in Cancer Clinical Trials* (March 2022). See also the draft guidance for industry *Geriatric Information in Human Prescription Drug and Biological Product Labeling* (September 2020); when final, this guidance will represent the FDA's current thinking on this topic.

[40] See footnote 6; see also sections 505(z)(2) and 520(g)(9)(B) of the FD&C Act.

[41] Sections 505(z)(2) and 520(g)(9)(B) of the FD&C Act; see also section 3602 of FDORA.

[42] See footnote 40.

studied. FDA recognizes that in some cases, increased enrollment (i.e., greater than proportional) of certain populations may be needed to elucidate potential clinically important differences in drug or medical device response between subsets of the study population. A rationale must be provided for the proposed enrollment goals, including when such goals may deviate from the estimated prevalence or incidence of a disease or condition in the intended use population.[43] Sponsors must provide in the Diversity Action Plan a description of the general approach and rationale,[44] which should include methodology used to derive target enrollment goals.

FDA recognizes that sponsors may, as part of their clinical development program, plan to conduct several clinical studies to support marketing authorization of a medical product that may be subject to Diversity Action Plan requirements. In such cases, the sponsor's enrollment goals specified in the Diversity Action Plan for each study should consider how individual clinical studies may fit into an overall clinical development program for the medical product (i.e., for a particular indication or intended use), and how such individual studies should help generate data representing the clinically relevant population's demographic characteristics consistent with the incidence or prevalence in the disease population for the program. In such a situation, the Diversity Action Plan for each clinical study should reflect a strategy that leads to an overall proportionate representation, even though individual clinical studies may not have proportionate representation.

FDA recognizes that certain development programs (e.g., rare diseases), may include a single, small pivotal study. Despite enrolling a representative population in that study, participant numbers may be small, potentially precluding the detection of any differences in safety and effectiveness across the study population, should they exist, or limiting the sponsor's ability to conduct a robust assessment of observed differences. However, consistent representative enrollment may provide opportunities for hypothesis generation and further study.

Whenever possible, sponsors should utilize appropriate available sources (e.g., certain registries that are reasonably expected to be demographically representative, publicly available epidemiological surveys, published literature, etc.) to obtain information about the estimated prevalence or incidence of the disease or condition across the affected population, by race, ethnicity, sex, and age group. When using non-publicly available sources (e.g., electronic health records, certain registries, or other privately held information sources) to derive incidence/prevalence estimates, sponsors should provide the rationale for the approach, a synopsis of the analysis used, and citations for the source(s) for these data.

The estimated prevalence or incidence of the disease or condition by demographic characteristics in the U.S. population for which the medical product is being investigated should generally inform enrollment goals. In certain situations, there may be limited or no data or information available to characterize the incidence and/or prevalence of the disease or condition, or the demographic characteristics of the intended population. In these circumstances, sponsors should consider the following or other approaches to setting enrollment goals, and should provide the rationale for the approach used:

[43] Sections 505(z)(2) and 520(g)(9)(B) of the FD&C Act.
[44] Sections 505(z)(2) and 520(g)(9)(B) of the FD&C Act.

- For a disease or condition where the prevalence/incidence and distribution in the population by demographic characteristics are known, there may be situations where for a subset of that disease or condition, this information is unavailable or has other limitations precluding its use for the purposes of goal setting. For example, there may be information regarding the distribution of the intended use population by the demographic characteristics of race, ethnicity, sex, and age group for cholangiocarcinoma, but such information may be unavailable for the subset of cholangiocarcinoma for which the medical product is intended, such as cholangiocarcinoma with an FGFR2 fusion. When evaluating a medical product in a such a subset of a disease or condition, it may be acceptable to use prevalence and incidence information for the broader disease and base enrollment on the demographic characteristics of that broader disease population (e.g., the enrollment goal for a study of FGFR2 mutated cholangiocarcinoma cancer could be based on prevalence or incidence information for cholangiocarcinoma).

- For a clinical study designed to investigate a medical product that is intended for a general use population (e.g., preventive vaccine), it may be acceptable to set enrollment goals based on general U.S. population demographics (i.e., U.S. census data).

- For a clinical study designed to investigate a medical product in a population for which there are limited or no data or information to characterize the demographic characteristics of the intended use population, it may be acceptable to set enrollment goals based on general U.S. population demographics (i.e., U.S. census data).

FDA recognizes the importance of global medical product development and supports the use of well-designed and conducted multi-regional clinical studies, when appropriate, to provide the evidence of safety and effectiveness for FDA-regulated medical products. Globally conducted clinical development programs should be designed with appropriate consideration given to differences in disease characteristics, medical practice, and available therapies when selecting foreign clinical sites and defining geographic regions. A Diversity Action Plan for a multi-national clinical study must describe participant enrollment goals for the entire study[45] and should not be limited to U.S.-enrolled participants. Additionally, the overall study design, including the selection of study sites, should account for the need to enroll a population representative of the U.S. intended use population as part of the overall medical product development program. FDA recognizes that the lack of uniformity across the globe in the use of population descriptors such as race and ethnicity may pose challenges when setting enrollment goals for international sites. For example, it may be challenging to identify corresponding populations defined on the basis of race or ethnicity when describing the affected population outside the U.S. and consequently, when setting enrollment goals for the clinical study. Sponsors should consider FDA guidance[46] when describing and presenting population race or ethnicity for the purposes of setting enrollment goals.

[45] See section 505(z)(2) and 520(g)(9)(B) of the FD&C Act.

[46] See draft guidance for industry *Collection of Race and Ethnicity Data in Clinical Trials and Clinical studies for FDA-Regulated Medical Products* (January 2024). When final this guidance will represent the FDA's current thinking on this topic. See also guidance for industry *Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies* (September 2017).

FDA recognizes that the distribution of the disease or condition across the clinically relevant population may differ by geographic region based on several factors, including but not limited to risk factors, screening practices, and available treatments, which may add complexity to enrollment goal setting. Sponsors should engage early with FDA review divisions to discuss how to address these factors in the Diversity Action Plan (See Sections VI and VII below for additional details on engagement with FDA).

In setting enrollment goals, sponsors may also consider characteristics such as geographic location and the SES of the population with the disease or condition in the intended use population if the available data suggest that these characteristics are expected to impact the outcomes under investigation in the study. As an example, geographic location and SES may affect enrollment and retention of the various subgroups of the population for a clinical study. The Diversity Action Plan should describe if and how these factors may have informed the sponsor's proposed enrollment goals. Additionally, early identification of barriers and implementation of strategies to mitigate such barriers should be described in the Diversity Action Plan.

**Table 1. Enrollment Goals Disaggregated by Race, Ethnicity, Sex, Age Group (Summary)**

| Enrollment goals must be disaggregated by:[47] |
|---|
| • Race (sponsors should list goals for each category according to FDA guidance for reporting race)[48]<br>• Ethnicity (sponsors should list goals for each category according to FDA guidance for reporting ethnicity)[49]<br>• Sex (sponsors should list goals for each category according to FDA guidance for reporting sex)[50]<br>• Age group (sponsors should list goals for clinically relevant age subsets according to FDA guidance)[51] |

### B. Rationale for Enrollment Goals

[47] Sections 505(z)(2) and 520(g)(9)(B) of the FD&C Act.; See also section 3602 of FDORA.
[48] See footnote 46.
[49] See footnote 46.
[50] See guidance for industry *Study of Sex Differences in the Clinical Evaluation of Drugs* (July 1993) and guidance for industry *Evaluation of Sex-Specific Data in Medical Device Clinical Studies* (August 2014).
[51] See the following guidances for industry *Inclusion of Older Adults in Cancer Clinical Trials* (March 2022) and *Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs* (November 2020). See also the draft guidance for industry *Geriatric Information in Human Prescription Drug and Biological Product Labeling* (September 2020). When final this guidance, will represent the FDA's current thinking on this topic. See also the guidances for industry *E7 Studies in Support of Special Populations: Geriatrics* (August 1994), *E7 Studies in Support of Special Populations: Geriatrics Questions and Answers* (March 2012), *E11 Clinical Investigation of Medicinal Products in the Pediatric Population* (December 2000), *E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population* (April 2018), *Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials* (March 2019), and *Pediatric Information Incorporated into Human Prescription Drug and Biological Product Labeling* (March 2019).

The Diversity Action Plan must include the sponsor's rationale for the enrollment goals.[52] To meet this statutory requirement, a sponsor's rationale must include sufficient information and analysis to explain how the sponsor determined its enrollment goals.[53] Thus, a sponsor's rationale for the enrollment goals should include:

- Background information necessary to understand the disease or condition for which the drug or device is being investigated, including an overview of the natural history of the disease or condition and risk factors, as well as prevalence and incidence estimates, if available.
- Any other background information that justifies the enrollment goals.
- If a sponsor plans to conduct several clinical studies to support a single marketing submission, the sponsor may opt to specify enrollment goals across the planned clinical studies. A sponsor's rationale for having different enrollment goals across planned studies must be included in the Diversity Action Plan;[54] the rationale provided should indicate how individual clinical studies are intended to contribute to the overall enrollment goals for the clinical development program for the medical product (i.e., for a particular indication or intended use).
- Additionally,
    - For drugs, the rationale should describe data and information that suggest a potential for differential safety and effectiveness of the investigational drug across the clinically relevant population such as possible differences in PK or pharmacodynamics (PD). Sponsors should also describe available data regarding differences in PK, PD, safety, or effectiveness (e.g., by sex, age, or by genetic variations which may be more prevalent in certain racial and ethnic populations that impact drug metabolism or susceptibility to adverse reactions)[55] in the Diversity Action Plan. Additionally, sponsors should describe, as applicable, the relevancy of other population-level or individual characteristics that available data suggest have an impact on the clinical outcomes (e.g., SES, geographic location, comorbidities). Sponsors should include citations for the sources of data and information (e.g., epidemiological databases, registries, etc.) upon which rationales for enrollment goals are based.
    - For devices, the rationale for enrollment goals should describe data and information about the potential for differential safety and effectiveness of the device across the clinically relevant populations. Sponsors should also describe available data regarding differences expected to impact safety or effectiveness (e.g., by sex, age or by genetic variations, which may be more prevalent in certain racial and ethnic populations that are expected to impact clinical outcomes or susceptibility to adverse events). Additionally, sponsors should describe, as applicable, the relevance of other population-level or individual

[52] Section 505(z)(2)(B) and 520(g)(9)(B)(ii).
[53] Section 505(z)(2)(B) and 520(g)(9)(B)(ii).
[54] Section 505(z)(2)(B) and 520(g)(9)(B)(ii).
[55] See guidance for industry *Clinical Pharmacogenomics: Premarket Evaluation in Early-Phase Clinical Studies and Recommendations for Labeling* (January 2013).

characteristics that available data suggest may have an impact on the clinical outcomes (e.g., SES, geographic location, comorbidities). Data on relevant factors for device performance (e.g., phenotypic, anatomical, technological, or biological factors) should be evaluated to characterize any differential effects across a diverse population by the relevant demographic characteristics. The rationale should describe how the sponsor considered the available information when setting the enrollment goals. For example, variations in skin pigmentation that may exist across a diverse population that can affect the performance of certain devices would be a relevant attribute to consider when describing the available data and information in the intended use population. Sponsors should include citations for the sources of data and information (e.g., epidemiological databases, registries, etc.) upon which rationales for enrollment goals are based.

### C. Measures to Meet Enrollment Goals

The Diversity Action Plan must include an explanation of how the sponsor plans to meet the specified enrollment goals.[56] To meet this requirement, the Diversity Action Plan should include a description of the enrollment and retention strategies for the study population. FDA recognizes that inequities in clinical study access and participation for certain populations occur within the context of broader health care inequities. While FDA recognizes the value of broad efforts to address healthcare systemic barriers that lead to disparities in clinical study participation rates across various populations (e.g., identification and training of diverse clinical trial investigators and staff, etc.), this section of the Diversity Action Plan should focus on specific measures that address the enrollment and retention of participants in the particular clinical study for which the Diversity Action Plan is developed. FDA encourages sponsors to consult patients and healthcare providers as part of the process for developing the Diversity Action Plan, including for considering enrollment and retention strategies. Examples of clinical study enrollment and retention strategies may include, but are not limited to the following[57]:

- Implementing sustained community engagement (e.g., through community advisory boards and navigators, community health workers, patient advocacy groups, local healthcare providers, community organizations, etc.).
- Providing cultural competency and proficiency training for clinical investigators and research staff may help facilitate the building of a trusting relationship with participants, provide a helpful resource for investigators and research staff on how to engage with participants with different backgrounds, help decrease biased communication and behavioral practices, and help avoid the use of cultural generalizations and stereotypes in interactions with participants.

[56] Sections 505(z)(2)(C) and 520(g)(9)(B)(iii) of the FD&C Act and section 3602(a)(1)(B) of FDORA.

[57] See also See also *Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs* (November 2020).

- Improving study participant awareness and knowledge of the clinical study (e.g., providing language assistance for persons with limited English proficiency[58]).
- Reducing participant burden (e.g., avoiding unnecessary study-related procedures, imaging, and laboratory tests; employing sites for procedures and laboratory tests that are convenient to the specific populations included in the enrollment goals; providing transportation assistance; providing dependent care; allowing flexible hours for study visits; reimbursement for costs incurred).
- Improving access to the clinical study by limiting clinical study exclusion criteria, selecting clinical study site locations that would facilitate enrollment of a representative study population (e.g., initiating the clinical study in sites that serve demographically diverse populations and that have prior experience enrolling diverse study participants in clinical studies), and considering the accessibility needs of persons with disabilities.
- Employing clinical study decentralization when appropriate.[59]

The Diversity Action Plan should also include a description of the sponsor's plan to monitor enrollment goals during the conduct of the clinical study to help ensure that goals are met. This measure can facilitate prompt intervention to address barriers to meeting enrollment goals. For example, the sponsor could consider specifying in the Diversity Action Plan the manner and frequency with which study enrollment will be monitored (e.g., when a certain proportion of the study population has been enrolled), and any measures that may be undertaken should the sponsor determine that the study is not on track to meet enrollment goals. Sponsors can also provide this information in submissions for Diversity Action Plan modifications and in briefing packages for meetings related to the clinical study.

## VI. TIMELINES FOR SUBMITTING DIVERSITY ACTION PLANS

Although a sponsor may discuss the Diversity Action Plan with FDA as soon as practicable during medical product development, sponsors must submit Diversity Action Plans for certain clinical studies for drugs and devices according to the following statutorily required timelines:

- For drugs, sponsors must submit the required Diversity Action Plan to the relevant IND application as soon as practicable but no later than the date on which the sponsor submits the protocol to FDA for the phase 3 study or, as appropriate, other pivotal study.[60]

[58] FDA strongly encourages stakeholders to ensure that study materials are accessible to individuals with limited English proficiency. To the extent an organization receives Federal financial assistance from the U.S. Department of Health and Human Services, Title VI of the Civil Rights Act of 1964 and its implementing regulations require the organization to take reasonable steps to provide meaningful access to its programs and activities by individuals with limited English proficiency. See 42 U.S.C. 2000d, et seq; 45 CFR part 80; see also Section 1557 of the Affordable Care Act, 42 U.S.C. 18116, which provides similar protections as those under Title VI in health programs and activities receiving Federal financial assistance.

[59] See draft guidance for industry, investigators, and other stakeholders *Decentralized Clinical Trials for Drugs, Biological Products, and Devices* (May 2023). When final, this guidance will represent the FDA's current thinking on this topic.

[60] Section 505(z)(3) of the FD&C Act.

Because FDA's review of and feedback on the Diversity Action Plan is most efficient if it occurs in the context of discussions regarding the trial design, study population selection, and other aspects of the clinical study, FDA recommends submission of the Diversity Action Plan when a sponsor is seeking feedback regarding the applicable clinical study for the drug (typically at the End-Of-Phase 2 meeting).

- For device clinical studies that require an IDE application to be submitted to FDA, the Diversity Action Plan must be included in the IDE application. Sponsors of certain studies for which submission of an IDE application is not required must develop a Diversity Action Plan to guide the development of any clinical study with respect to that device and must submit the Diversity Action Plan as part of the device's premarket notification (510(k)), PMA application, or De Novo classification request.[61] As discussed above, FDA expects there will be studies of certain devices for which FDA does not expect a Diversity Action Plan. When FDA's feedback on specific questions is necessary to guide product development and/or preparation of a submission before submitting a Diversity Action Plan in an IDE or a marketing submission, the sponsor should follow the Q-submission process for obtaining feedback or requesting a meeting with FDA (see section VII). A sponsor may include questions regarding the Diversity Action Plan in a Q-submission submitted to request feedback on questions related to design and conduct of a clinical study prior to its submission in an IDE application or prior to initiating a clinical study for which submission of an IDE application is not required.[62]

## VII. PROCEDURES FOR SUBMITTING THE DIVERSITY ACTION PLAN AND RECEIVING FEEDBACK

The process for submitting Diversity Action Plans will vary depending on the medical product type. This section describes the process for submitting a Diversity Action Plan for a clinical study of a drug or device and for receiving FDA feedback on the Diversity Action Plan.

To ensure that FDA can conduct a timely and efficient review of a Diversity Action Plan, sponsors should describe the required elements of the Diversity Action Plan clearly and concisely, with limited cross-referencing to previously submitted documents. In most cases, the Diversity Action Plan should be succinct, its length generally not exceeding 10 pages, excluding references.

**For Drugs:**

- The Diversity Action Plan must be submitted to the IND under which the applicable clinical study will be conducted.

- Sponsors should include relevant administrative information on the title page of the Diversity Action Plan including the drug name, IND number, proposed indication(s),

[61] A study that is exempt from the requirements of the IDE regulations under 21 CFR 812.2(c) does not require the development or submission to FDA of a Diversity Action Plan under section 520(g)(9)(A)(ii) of the FD&C Act.
[62] See the guidance for industry and FDA staff *Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program* (June 2023).

clinical study identification information (e.g., NCT number, title, study ID) and the Diversity Action Plan version number and date.

- The cover letter accompanying a Diversity Action Plan submission should alert FDA that the submission includes a Diversity Action Plan and denote whether the Diversity Action Plan is new or revised. Sponsors should indicate in the cover letter accompanying a new or revised Diversity Action Plan, "**DIVERSITY ACTION PLAN-Initial**" or "**DIVERSTY ACTION PLAN- Revised**," respectively, written in large, bolded type. If a partial waiver (see Section VIII below) has been granted for the clinical study that is the subject of the Diversity Action Plan, sponsors should alert FDA in the cover letter accompanying the Diversity Action Plan, and in the relevant section(s) in the Diversity Action Plan.

- Depending on the specifics for each clinical development program, the relevant Division in CDER or CBER may or may not provide feedback on the Diversity Action Plan. FDA feedback on a new or revised Diversity Action Plan may be at FDA's initiative or per the sponsor's specific request for feedback. Sponsors with specific questions regarding a planned or submitted Diversity Action Plan may include them as a topic for discussion in meetings with FDA.[63]

- Following submission of an initial Diversity Action Plan, a sponsor may, as appropriate, submit modifications to the Diversity Action Plan.[64] Such modifications may be based on feedback from the FDA or at the sponsor's own initiative. In such instances, the submission must include a copy of the Diversity Action Plan with changes tracked as well as a clean version. As part of the submission, sponsors must also include a "Summary of Modifications and Justification" section that outlines the modifications to the Diversity Action Plan and provide the rationale for such changes.

- For an IND that is required to be submitted in eCTD format, Diversity Action Plan submissions must be submitted in eCTD module 2.5, Clinical overview.[65]

- The status of the Diversity Action Plan submission and as appropriate, any discussions and correspondence with FDA regarding the Diversity Action Plan, including with respect to partial waiver requested or granted, should be included in the regulatory history for milestone meetings (i.e., in the meeting briefing document), as well as in marketing submissions.
- FDA regulations require IND sponsors to submit annual reports.[66] These annual reports must include for each study the total number of subjects entered into the study to date, tabulated by age group, gender, and race, among other information.[67] Sponsors should provide an update in their IND annual reports on their progress toward meeting Diversity

[63] See draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products* (September 2023). When final, this guidance will represent the FDA's current thinking on this topic.
[64] Section 505(z)(3) of the FD&C Act.
[65] For a discussion of eCTD submissions, see guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (February 2020).
[66] 21 CFR 312.33.
[67] 21 CFR 312.33(a)(2). Note that we consider the term "gender" in this regulation to mean "sex."

Action Plan enrollment goals. Sponsors should submit the Diversity Action Plan update in the annual report section pertaining to clinical study participant demographics. If such goals are not on track for being met at the conclusion of the study, the status report should include a description of the reason(s) the sponsor is not currently meeting or does not expect to meet enrollment goals and the sponsor's plan to mitigate such an outcome.

- In marketing application submissions, sponsors should provide a brief overview of the Diversity Action Plan pertaining to the phase 3 or other pivotal clinical study, an assessment of whether the Diversity Action Plan enrollment goals were met in the context of the relevant clinical study or the overall phase 3 development program, and as appropriate, an explanation of what measures may have contributed to the observed outcomes with respect to the enrollment goals. If a waiver from the requirement to submit a Diversity Action Plan has been granted, the sponsor should clearly indicate such in the marketing application submission and cite the correspondence granting the waiver. Sponsors should include information regarding the Diversity Action Plan in module eCTD 2.5 of the NDA or BLA submission.

**For Devices**

- FDA considers the Diversity Action Plan for a clinical study to be a constituent part of the overall process for generating clinical evidence for the subject device. As such, a sponsor may submit a pre-submission to request written feedback or a meeting with FDA regarding the Diversity Action Plan for a clinical study (See Section III for information on studies requiring submission of a Diversity Action Plan).[68]

- A Diversity Action Plan must be submitted as part of the IDE application for clinical studies of SR devices.[69]

- For device studies that require development of a Diversity Action Plan, but do not require an IDE (see Section III) the Diversity Action Plan must be submitted as part of a 510(k), PMA application, or De Novo classification request. While FDA encourages sponsors to seek Agency feedback when appropriate, consistent with existing approaches to developing clinical evidence, FDA anticipates that many Diversity Action Plans for studies not requiring submission of an IDE application may be developed without FDA's input. A pre-submission may be appropriate when FDA's feedback on specific questions is necessary to guide product development and/or submission preparation. For example, if submission of an IDE application is not required, a sponsor may opt to request FDA's feedback on the enrollment goals of the clinically relevant population for a proposed pivotal clinical study intended to support a particular intended use.

- The cover letter accompanying a submission that includes a Diversity Action Plan (e.g., an IDE application, marketing submission, or a Q-submission seeking feedback on a Diversity Action Plan) should alert FDA that the submission includes a Diversity Action Plan and, denote whether the Diversity Action Plan is new or revised. Sponsors should

[68] See guidance for industry and FDA staff, *Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program* (June 2023).

[69] Section 520(g)(9)(A)(i) of the FD&C Act.

state in the cover letter accompanying a new or revised Diversity Action Plan, "**DIVERSITY ACTION PLAN-Initial**" or "**DIVERSITY ACTION PLAN- Revised**," respectively, written in large, bolded type.

- Sponsors should include relevant administrative information on the title page of the Diversity Action Plan, including device name; sponsor contact information; relevant submission number(s) including as appropriate, IDEs, Q-submissions, and/or marketing submissions, proposed indication or indications for use statement, and intended use, clinical study identification information (e.g., NCT number, title, study ID), and the Diversity Action Plan version number and date.

- Following submission of an initial Diversity Action Plan, a sponsor may, as appropriate, submit modifications to the Diversity Action Plan. Such modifications may be based on feedback from the FDA or at the sponsor's own initiative. In such instances, the submission must include a copy of the Diversity Action Plan with changes tracked as well as a clean version. As part of the submission, sponsors must also include a "Summary of Modifications and Justification" section that outlines the modifications to the Diversity Action Plan and provides the rationale for such changes.

    - For modifications to the Diversity Action Plan for a SR study following approval of the IDE application under which an applicable SR medical device study will be conducted: FDA considers changes to the Diversity Action Plan included in an approved IDE to be similar to other types of changes made to the approved study. Such modifications may be in response to feedback from the FDA or at the sponsor's own initiative. In such instances, sponsors should follow the processes discussed in the guidance for industry and CDRH staff, *Changes or Modifications During the Conduct of a Clinical Investigation* (May 2001) which outlines FDA's implementation of 21 CFR 812.35, and discusses under what circumstances a change to an approved IDE application requires prior approval by FDA (i.e., through submission of an IDE supplement) and when such a change may be implemented with subsequent notice to the Agency (i.e., through a 5-day notice or annual report).

    - For modifications to the Diversity Action Plan for a study intended to support FDA's evaluation of a medical device and which does not require an IDE application: if the sponsor considers FDA's feedback on the modification to be necessary to guide product development and/or submission preparation, the sponsor should submit a pre-submission. FDA anticipates that most modifications to a Diversity Action Plan for studies that do not require an IDE will not require feedback from the Agency.

- Marketing submissions, IDE applications, and requests for feedback or meetings should include a summary of any discussions and correspondence with FDA regarding a relevant Diversity Action Plan, including with respect to any waiver requests (see Section VIII). If a waiver has been granted for any requirements discussed in this guidance, the sponsor should clearly indicate such in the cover letter of the submission and should provide a copy of FDA's correspondence granting the waiver.

- As part of periodic reporting requirements under applicable FDA regulations (e.g., IDE annual reports),[70] sponsors should include an update to FDA on their progress toward meeting Diversity Action Plan enrollment goals. If such goals are not being met or are not expected to be met at the conclusion of the study, the status report should include a description of the reason(s) why the sponsor is not currently meeting and/or does not expect to meet enrollment goals and the sponsor's plan to mitigate such an outcome.

- In marketing submissions that contain clinical data from studies conducted under an approved IDE application submitted to FDA, sponsors should provide a brief overview of the Diversity Action Plan pertaining to the relevant clinical studies that generated data to support the marketing submission. Sponsors should also provide an assessment of whether the Diversity Action Plan enrollment goals were met in the context of the applicable study or the development program and, as appropriate, an explanation of what measures may have contributed to the observed outcomes with respect to the enrollment goals.

- In marketing submissions for which the device study did not require an approved IDE application and was not exempt from IDE requirements under 21 CFR 812.2(c), sponsors must provide the Diversity Action Plan for the study. In addition to the information described in Section V above, sponsors should also include an assessment of whether the Diversity Action Plan enrollment goals were met in the context of the relevant clinical study or the development program and, as appropriate, an explanation of what measures may have contributed to the observed outcomes with respect to the enrollment goals.

- In circumstances where a Diversity Action Plan is required to support marketing authorization, FDA recommends that sponsors provide a clear and concise description of the Diversity Action Plan for inclusion in the public-facing summary documents (e.g., De Novo Summary, 510(k) Summary, PMA Summary of Safety and Effectiveness (SSED)).

## VIII. REQUESTING DIVERSITY ACTION PLAN WAIVERS

FDA anticipates that submission of a Diversity Action Plan as discussed in this guidance will be possible in most cases. However, under section 505(z)(4) and section 520(g)(9)(C) of the FD&C Act (as amended by section 3601 of FDORA), FDA may waive the requirement to submit a Diversity Action Plan, or any part thereof, either on the Agency's initiative or at a sponsor's request if certain criteria are met.[71] While the appropriateness of a waiver is a case-specific determination and will depend on factors relevant to a specific development program, FDA will evaluate whether any of the following statutory criteria are satisfied when considering whether a waiver is appropriate:[72]

**a.** A waiver is necessary based on what is known or what can be determined about the prevalence or incidence in the U.S. of the disease or condition for which the new drug or

[70] See 21 CFR 812.150(b)(5).
[71] Sections 505(z)(4)(A) and 520(g)(9)(C).
[72] Sections 505(z)(4)(A) and 520(g)(9)(C).

device is under development (including in terms of the patient population that may use the drug or device).

**b.** Conducting a clinical investigation in accordance with a Diversity Action Plan would otherwise be impracticable; or,

**c.** A waiver is necessary to protect public health during a public health emergency.

FDA may grant a waiver from the requirement to submit a Diversity Action Plan (full waiver) or a waiver for any requirement of a Diversity Action Plan (partial waiver).[73] Given the importance of increasing enrollment of historically underrepresented populations in clinical research, including in clinical studies of drugs and devices, in order to detect potential differences in product performance and improve the generalizability of the results full or partial waivers from the requirements around the submission of a Diversity Action Plan will only be granted in rare instances. If FDA determines that the statutory criteria for granting a waiver are met and that granting a waiver on the Agency's initiative is appropriate, such as the need to protect public health during a public health emergency, FDA will notify interested parties through appropriate channels. For example, to the extent permitted under applicable disclosure law, FDA may consider public communications and/or post relevant information on FDA's website regarding the decision to issue the waiver. Sponsors should consider the following in determining whether to submit a request for a full or partial waiver:

- FDA generally does not intend to waive the requirement to submit a Diversity Action Plans even if the disease or condition under study is relatively homogenous with respect to race, ethnicity, sex, or age group. If supported by relevant data and information, sponsors should indicate in their rationale supporting their enrollment goals why the targeted population is homogenous.

- FDA is required to issue a written response granting or denying a waiver request within 60-days of receiving such request.[74] As such, sponsors should submit requests for a waiver (if warranted) as early as feasible, and no later than 60 days before the Diversity Action Plan is required for submission. FDA strongly encourages sponsors to discuss plans to request a waiver early in the planning stages of the clinical study or clinical development program. Sponsors should request a waiver early enough to allow sufficient time for preparation and submission of the Diversity Action Plan as required, should FDA deny the waiver request. Sponsors should not submit waiver requests less than 60 days before the Diversity Action Plan is required.

- As noted above, sponsors may decide to include different enrollment goals across multiple planned phase 3 or other pivotal studies. FDA recognizes that under these circumstances, the enrollment goals for each individual study may not be fully reflective of the enrollment goals across all studies. In these cases, sponsors should not seek a waiver for each study. Rather, in their Diversity Action Plans, sponsors should specify how the enrollment goals are expected to be met across the development program and provide a rationale for the enrollment goals for a specific study.

[73] See sections 505(z)(4)(A) and 520(g)(9)(C)(i) of the FD&C Act.

[74] See sections 505(z)(4)(B) for drugs and 520(g)(9)(C)(ii) for devices.

- For drugs, a waiver request should be submitted electronically to the IND, in **eCTD module 1.12.5, Request for a waiver** and should be submitted to the IND application under which the clinical study that is subject to the requirement of a Diversity Action Plan will be conducted. The accompanying cover letter should include "**DIVERSITY ACTION PLAN- Waiver Request**" written in large, bolded type. The waiver request submission should include the following information: IND number, applicable clinical study name or identification number and a justification for the waiver request, including relevant data and information.

- For devices, a waiver request should be submitted as a standalone submission with an accompanying cover letter that includes "**DIVERSITY ACTION PLAN- Waiver Request**" written in large, bolded type. The waiver request should include the following information: submission number(s) if available, information about the device including a device description and proposed intended use, the applicable clinical study, the type of marketing submission that the clinical study is intended to support, and a justification for the waiver request, including relevant data and information.

## IX. SPONSOR PUBLIC POSTING OF KEY INFORMATION FROM DIVERSITY ACTION PLANS

FDA strongly encourages sponsors to share strategies for meeting Diversity Action Plan enrollment goals with the public. To further promote transparency, sponsors may consider publicly posting on their website key information from their Diversity Action Plans, namely their clinical study enrollment goals disaggregated by race, ethnicity, sex, and age group, and a brief description of the measures taken to achieve the stated goals. For medical products or uses that are not approved, licensed, cleared, or classified, such key information should be available in the same location as other content regarding such products (e.g., on the "pipeline" page of a sponsor's website). Although sponsors can post such key information at any time, while the study is still open for recruitment, sponsors may wish to consider:

- Linking from such a posting to a recruitment website for the trial or to a commonly used repository for clinical trial information, or
- Linking to the sponsor's website posting from a recruitment website for the trial or from a commonly used repository for clinical trial information because patients and the public may be searching for clinical studies in clinical trial databases such as ClinicalTrials.gov.[75]

FDA recommends the use of consumer-friendly language when sharing key information from Diversity Action Plans.

[75] To add a link on ClinicalTrials.gov to the key information from a Diversity Action Plan posted on the sponsor's website, responsible parties should use the *Available Individual Participant Data (IPD) and Supporting Information* data element. Patients, providers, and other members of the public could subsequently search for study records displaying these links on ClinicalTrials.gov by using the *AvailIPDType* field name.

# APPENDICES

## APPENDIX 1: ELEMENTS OF A DIVERSITY ACTION PLAN[76] (SUMMARY)

The cover letter accompanying a submission that includes a Diversity Action Plan (DAP) should alert the FDA that the submission includes a DAP and denote whether the DAP is new or modified. Indicate in the cover letter accompanying a new or revised DAP, "**DIVERSITY ACTION PLAN-Initial**" or "**DIVERSTY ACTION PLAN- Revised**," respectively, written in large, bolded type. If a partial waiver has been granted, the sponsor should clearly indicate this in the cover letter of the submission and, should provide a copy of the FDA's correspondence granting the waiver. The DAP should contain a clear and concise description of the required elements of the DAP, with limited cross-referencing of previously submitted documents to facilitate review. In most cases the DAP should be succinct, its length generally not exceeding 10 pages, excluding references.

**TITLE PAGE**

The title page of the DAP should include relevant administrative information.

- Medical product name.
- IND/IDE number (if applicable), and/or other relevant submission information (e.g., to identify previous Q-submissions or marketing submissions for the medical device).
- Proposed indication or indications for use statement and intended use.
- Clinical study identification information (e.g., NCT number, title, study ID).
- **DAP version number and date**

**ENROLLMENT GOALS**

Enrollment goals must be disaggregated by:[77]

- Race (sponsors should list goals for each category according to FDA guidance for reporting race)[78]
- Ethnicity (sponsor should list goals for each category according to FDA guidance for reporting ethnicity)[79]
- Sex (sponsors should list goals for each category according to FDA guidance for reporting sex)[80]
- Age group (sponsors should list goals for clinically relevant age subsets according to FDA guidance)[81]

**RATIONALE FOR ENROLLMENT GOALS**

Diversity Action Plans must include a rationale for the enrollment goals. To meet this statutory requirement, a sponsor's rationale must include sufficient information and analysis to explain how the sponsor determined its enrollment goals. Thus, a sponsor's rationale for enrollment goals should include information necessary to understand the disease or condition including natural history, risk factors, etc. If conducting several clinical studies to support a single marketing submission and opting to specify enrollment goals across the planned clinical studies, sponsor must indicate how the individual clinical studies are intended to contribute to the stated enrollment goals.

Additionally,

- **For drugs the rationale should include:**

[76] This Appendix is intended to summarize the elements of a Diversity Action Plan; sponsors should refer to the detailed description provided in the main text of the guidance for information on the content and format of the Diversity Action Plan.

[77] Sections 505(z)(2) and 520(g)(9)(B) of the FD&C Act; see also section 3602 of FDORA.

[78] See the draft guidance for industry and FDA staff *Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for FDA-Regulated Medical Products* and the guidance *Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies* (September 2017).

[79] See footnote 78.

[80] See guidance for industry *Study of Sex Differences in the Clinical Evaluation of Drugs* (July 1993) and guidance for industry *Evaluation of Sex-Specific Data in Medical Device Clinical Studies* (August 2014).

[81] See the following guidances for industry *Inclusion of Older Adults in Cancer Clinical Trials* (March 2022) and *Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs* (November 2020). See also the draft guidance for industry *Geriatric Information in Human Prescription Drug and Biological Product Labeling* (September 2020). When final this guidance, will represent the FDA's current thinking on this topic. See also the guidances for industry *E7 Studies in Support of Special Populations: Geriatrics* (August 1994), *E7 Studies in Support of Special Populations: Geriatrics Questions and Answers* (March 2012), *E11 Clinical Investigation of Medicinal Products in the Pediatric Population* (December 2000), *E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population* (April 2018), *Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials* (March 2019), and *Pediatric Information Incorporated into Human Prescription Drug and Biological Product Labeling* (March 2019).

  - Data and information that describe the potential for differential safety and effectiveness of the investigational drug across the clinically relevant population (e.g., differences in pharmacokinetics [PK]/ [pharmacodynamics [PD]).
  - Data regarding genetic differences in PK, PD, safety, or effectiveness (e.g., genetic variations, which may vary based on ancestry, that impact drug metabolism or susceptibility to adverse reactions).
  - As applicable, the relevancy of other population-level or individual characteristics that available data suggest have an impact on the clinical outcomes (e.g., socioeconomic status, geographic location, comorbidities).
- **For medical devices the rationale should include:**
  - Data and information that describe the potential for differential safety and effectiveness of the device across the clinically relevant populations.
  - Available data regarding genetic differences that may impact safety or effectiveness (e.g., genetic variations, which may vary based on ancestry, that are expected to impact clinical outcomes or susceptibility to adverse events).
  - Data on relevant factors for device performance (e.g., phenotypic, anatomical, technological, or biological factors) should be evaluated to characterize any differential effects across a diverse population by the relevant demographic characteristics; The rationale should describe how the sponsor considered the available information when setting the enrollment goals.
  - As applicable, the relevance of other population-level or individual characteristics that available data suggest may have an impact on the clinical outcomes (e.g., socioeconomic status, geographic location, comorbidities).

The DAP should include citations for the sources of data and information upon which the enrollment goals are based.

**MEASURES TO MEET ENROLLMENT GOALS**

The DAP must include an explanation of how the sponsor plans to meet the specified enrollment goals.[82]

- The DAP should include a description of the enrollment and retention strategies for the study population (focus is on measures that address diversity and representativeness of participants enrolled in a specific clinical study).[83]
- The DAP should include a description of the plan to monitor enrollment goals during the conduct of the clinical study to ensure that goals are met.

[82] Section 3602(a)(1)(B) of FDORA.

[83] Section 3602(a)(1)(B) of FDORA.