U.S. FOOD & DRUG ADMINISTRATION

Center for Devices and Radiological Health

Discussion Paper: Health Equity For Medical Devices

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Disclaimer: This paper is for discussion purposes only and is not draft or final guidance. It is meant to facilitate early input from groups and individuals outside the Agency. The Agency intends to use such input in developing future guidance. As such, this document is not intended to convey any current policy regarding health equity and the Food and Drug Administration's (FDA) evaluation of medical device clinical studies.

I. Introduction

Disparities in health care and health outcomes occur across many demographic, socio-economic, geographic, and biological dimensions. Addressing these disparities is integral to improving the overall quality of life and health outcomes for all people within the United States (US). The FDA's Center for Devices and Radiological Health (CDRH) is committed to advancing health equity by working toward assuring that all patients have timely access to safe, effective, and high-quality medical devices and safe radiation-emitting products. CDRH is providing this discussion paper to receive public input on advancing health equity in the context of medical devices.

The health equity concepts described in this discussion paper are informed by various resources. For example, Executive Order 13985[1] calls for "a comprehensive approach to advancing equity for all, including people of color and others who have been historically underserved, marginalized, and adversely affected by persistent poverty and inequality." It also defines "equity" as "consistent and systematic fair, just, and impartial treatment of all individuals, including individuals who belong to underserved communities that have been denied such treatment, such as Black, Latino, and Indigenous and Native American persons, Asian Americans and Pacific Islanders and other persons of color; members of religious minorities; lesbian, gay, bisexual, transgender, and queer (LGBTQ+) persons; persons with disabilities; persons who live in rural areas; and persons otherwise adversely affected by persistent poverty or inequality." Similarly, the Department of Health and Human Services (HHS) Healthy People 2030 Framework[2] defines "equity" as "a society in which all people can achieve their full potential for health and well-being across the lifespan" and the Centers for Disease Control and Prevention (CDC) defines "health equity" as "the state in which everyone has a fair and just opportunity to attain their highest level of health."[3]

FDA recognizes the urgent public health need for innovative technologies that help to reduce barriers to achieving health equity and that help to improve health outcomes across diverse populations. As part of CDRH's 2022 to 2025 Strategic Priority to Advance Health Equity,[4] CDRH has committed to:

- Facilitate availability of and access to medical technologies for all populations;
- Empower people to make informed decisions regarding their healthcare;
- Support innovation of novel and existing technologies that address health inequities; and

[1] See Executive Order 13985 on Advancing Racial Equity and Support for Underserved Communities Through the Federal Government, 86 FR 7009 (January 20, 2021).
[2] For more information, please see the HHS website on Healthy People 2030 Framework.
[3] For more information, please see the CDC website on What is Health Equity.
[4] For more information on the Strategic Priority to Advance Health Equity, please see FDA website on CDRH Strategic Priorities and Updates.

- Reduce barriers to increase participation by diverse populations in evidence generation.

As part of these Strategic Priorities, CDRH has committed to developing "a framework for when a device should be evaluated in diverse populations to support marketing authorization."[5] Medical devices are intended for the prevention, treatment, or diagnosis of many diseases and conditions that impact the US population, including those that are serious and life-threatening and for which a satisfactory method of prevention, diagnosis or treatment may not exist. Clinical studies often play a critical role in understanding the safety and effectiveness of new medical devices in the populations that are intended to use them. Further, in some cases, access to clinical studies may also be an aspect of a participant's clinical care. Given the diversity of the United States population, medical device clinical studies should be designed to adequately represent the population that is intended to use the device so that the information generated from the study can provide a more complete understanding of device performance across populations.[6] FDA's oversight of medical devices includes evaluation of the benefits, risks, safety, and effectiveness of a device for its intended use before it can be legally marketed in the United States. Increasing the diversity of study cohorts to ensure that a study adequately represents the intended use population may help to generate information on how individuals with different backgrounds, lived experiences, and clinically important characteristics (such as comorbidities) may be affected by medical devices.

In this discussion paper, we describe factors that may be important for sponsors and other relevant parties as they develop medical device clinical studies. The factors and considerations were developed through interactions with external stakeholders[7] and this discussion paper provides FDA's initial thoughts for early public input. This document also includes questions on which we seek feedback from the public. However, this document is not intended to propose or implement a regulatory policy. This document is intended to stimulate discussion to inform further policy development in accordance with good guidance practices.

As noted above, we have included questions seeking public input and feedback. FDA also welcomes general comments and suggestions outside the posed questions. Please submit your feedback to the questions throughout this discussion paper and other general comments or suggestions to https://www.regulations.gov, Docket No. FDA-2024-N-3616 by October 4, 2024. If you submit feedback to the questions specified below, please identify question numbers, as applicable. Please also review the instructions for submitting comments that are included as an attachment on https://www.regulations.gov.

II. Approach

Although premarket authorization of a specific device does not always require clinical data, many decisions do require information that can only be derived from clinical studies to support authorization. We acknowledge that the process for generating clinical data, regardless of the source, can be complex. As such, this discussion paper focuses on a few important considerations that may be relevant for FDA's evaluation of clinical evidence. The discussion paper first discusses factors that may help sponsors and investigators during the design and development of study objectives and a clinical study plan. Second, the discussion paper

[5] For more information on the Strategic Priority to Advance Health Equity, please see FDA website on CDRH Strategic Priorities and Updates.
[6] See 21 CFR 860.7(f)(1)(ii).
[7] See CDRH Patient Engagement Advisory Committee on Advancing Health Equity in Medical Devices (September 6, 2023).

describes considerations related to the intended use of a device that may be related to the device's safety, effectiveness, benefits, and risks. Finally, this discussion paper includes generalized examples to further stimulate public feedback regarding FDA's assessment of a device's benefits and risks in light of the factors and considerations described here.

In general, a sponsor's approach to collecting, analyzing, and reporting clinical data will be specific to the technological characteristics and the intended use of the device under consideration. The intent of this discussion paper is to provide FDA's preliminary thinking on these topics and receive feedback from the public to assist FDA's development of a regulatory policy that will eventually help sponsors identify a target study population to adequately reflect the intended use population for a particular medical device. This document does not explicitly address clinical study conduct or methods for generating or analyzing clinical data, both of which are addressed in other documents.[8] Interested parties may also search for applicable guidance documents on FDA's website.[9] Sponsors may also contact FDA via the Q-Submission Program for clinical study questions related to a specific device.[10] Further, this discussion paper is not intended to provide a comprehensive background on medical device clinical studies or how medical devices are reviewed and regulated within the United States. For a general background on how medical devices are regulated in the United States (US), please see the materials available on FDA's website Device Advice: Comprehensive Regulatory Assistance.

III. Approach for Discussion

a. ***Development of Clinical Study Plan***

As noted above, we have committed to developing policy on when a device should be evaluated in diverse populations to support marketing authorization, so that the clinical data intended to support a marketing submission are representative of, and generalizable to, the intended use population identified for the device. This section of the document describes three considerations that may help inform design of a clinical study that adequately reflects the intended use population for a particular medical device. These considerations could be incorporated into an evaluation of relevant information (including existing data, clinical experience, published literature, etc.) to help identify study objectives as part of early study design activities. They are briefly presented here and described in more detail in the remainder of this section of the document.

- **Disease burden or condition** - How does the burden of the disease or condition under study vary across the US intended use population?
- **Physiology, anatomy, and pathophysiology** - How does the etiology, progression, and prognosis of a disease or condition under study vary across the US intended use population based on physiology, anatomy, and pathophysiology?
- **Technology** - How might the device technology introduce, exacerbate, or mitigate the potential for different outcomes across the study population?

[8] See e.g., FDA guidances titled "Collection of Race and Ethnicity Data in Clinical Trials;" "Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies;" "Digital Health Technologies for Remote Data Acquisition in Clinical Investigations." For additional information and resources, see FDA website on Clinical Trials Guidance Documents.
[9] See FDA website on Search FDA Guidance Documents.
[10] For more information about the Q-Submission Program, see FDA guidance titled "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program."

While these considerations are discussed sequentially, we note that they will likely overlap, and information from one may impact how a sponsor considers another. For example, information from an assessment of a device's technology may inform evaluation related to anatomy or disease progression. Accordingly, FDA believes that utilizing a synthesis of information from these three considerations may provide sponsors with a comprehensive understanding of aspects of the study question that may affect clinical outcomes or device performance.

A sponsor that has completed an evaluation of relevant information, incorporating the three considerations above, may be better able to determine whether or not differences in outcomes are expected between patient populations. When this evaluation determines that differences in clinical outcomes are expected between patient populations, adequate information on benefits and risks of a device is more likely to come from a study designed to address specific safety or effectiveness questions related to the identified differences. For example, the study may be designed to enroll and retain participants (i.e., "enriched") from certain populations for which differences are expected. Alternatively, when this evaluation of relevant information does not identify any expected differences in outcomes between patient populations, adequate information on benefits and risks of a device is more likely to come from a study designed to collect data from a broad population (e.g., one that reflects general US census population).

FDA believes that, ultimately, an evaluation of the relevant information will help identify sources of potential variability in expected outcomes or device performance within the intended use population. As sponsors consider various mechanisms to generate relevant safety and effectiveness information, they may choose to use this information to inform the study design, not only assessing inclusion and exclusion criteria, formulating necessary study procedures, or identifying specific data to collect, but also considering approaches (e.g., in the study monitoring plan) that may help ensure recruitment, enrollment, and retention of important patient populations into a clinical study.

FDA seeks input on the concept of incorporating the following considerations into a sponsor's or investigator's assessment of relevant information as part of the early study design process.

i. ***Disease burden or condition*** *- How does the burden of the disease or condition under study vary across the US intended use population?*

The first consideration that FDA has identified as important to a sponsor's evaluation of relevant information when designing a clinical study relates to how the burden of the disease or condition under study varies across populations in the US. This evaluation may include an analysis of the prevalence, incidence, and severity of the disease or condition in patient groups within the intended use population in the US for the subject medical device. Evaluating the burden of the disease or condition under study may allow sponsors to better understand the extent to which certain factors (e.g., demographics, socioeconomic status, comorbidities, access to care) might influence the prevalence, incidence, and severity of a disease or condition. Further, this information may be useful in understanding potential gaps in the available information regarding clinical outcomes and device performance in clinically relevant populations. An assessment of this type may be based on public and (if appropriate) non-public information, including information from previous clinical studies.

ii. ***Physiology, anatomy, and pathophysiology*** *- How does the etiology, progression, and prognosis of a disease or condition under study vary across the US intended use population based on physiology, anatomy, and pathophysiology?*

The second consideration that FDA has identified is whether differences in clinical outcomes are expected between patient populations when considering potential mechanisms of disease that

might impact outcomes. FDA is considering how this evaluation could incorporate information on physiology, anatomy, and pathophysiology of the disease or condition under study within the context of disease or condition etiology, progression, and prognosis. Variation in these elements across the US intended use population may be important to understanding potential differences in device performance and may help identify mechanisms or potential causes for those differences. For example, it may be important to consider whether a clinical investigation of a device intended to treat diabetes needs to explore the impact of differences in metabolism, digestion, physical size, bone density, or body mass index (BMI). Evaluating these differences could help identify important considerations for selection of research sites, inclusion and exclusion criteria, and clinical outcomes of interest.

*iii. **Technology** - How might the device technology introduce, exacerbate, or mitigate the potential for different outcomes across the study population?*

The third consideration FDA has identified addresses whether differences in outcomes are expected between patient populations due to the device itself. Generally, FDA's evaluation of safety and effectiveness encompasses the extent, if any, to which the principles of operation underlying the technology of the device are expected to impact how the device performs across the intended use population. It is important for FDA to understand whether the technology may operate differently in different populations within the intended use. To understand the potential for performance differences in the intended use population, it may be necessary to consider the underlying design principles (e.g., physical, mechanical, or electrical) through which the device achieves its intended effect. This type of information may be useful as study procedures are developed to more fully interrogate or mitigate a potential performance difference.

Similarly, it may be important to understand whether all intended users are likely to be able to use the device as designed. For example, differences between user populations may arise from device use aspects such as whether the device is intended for use in a home or professional care setting, and whether the device will be used by healthcare professionals, patients, or care-providers. Further, differences between user populations may arise from device use aspects such as whether the device is intended to be used alone or to interact or interface with other technologies (e.g., the device may require constant access to broadband internet service or be interoperable with devices that are intended to deliver different aspects of care). Finally, variations in the environment of use may impact the device's performance across the intended use population (e.g., if the device is intended to be cleaned and reused, consider whether all users will have access to necessary supplies and infrastructure, and will be physically able to accomplish the cleaning process).

b. Development of Clinical Study Plan – Discussion Questions

FDA is seeking feedback on the following discussion questions regarding how a sponsor or investigator could incorporate the three considerations discussed above into their assessment of relevant information as part of the early study design process to help ensure that a clinical study is designed to be representative of, and generalizable to, the intended use population identified for the subject device.

1. Other than the three considerations discussed above (disease burden or condition; pathology, anatomy, and pathophysiology; and technology), are there other factors that should be part of this evaluation of relevant information as sponsors identify a target population to address a clinical research question? In particular, FDA is interested in understanding what the public thinks will be important to help a sponsor design a study that can provide information on the

benefits and risks of a medical device in the intended use population.

2. As noted above, the three considerations reflect areas of evaluation that may impact each other.
    a. Does this potential overlap impact (negatively or positively) the process of designing a study that will provide information on the benefits and risks of a medical device in the intended use population?
    b. Are there situations in clinical research where evaluation of each of these considerations, in isolation, may be advantageous?
    c. For questions 2.a and 2.b above, please provide any relevant examples.

3. The three considerations discussed above are all intended to help sponsors identify a target study population. Because this evaluation will likely encompass data from multiple sources, and relevant information may suggest that several different factors may impact device performance, FDA is interested in understanding how sponsors would prioritize and operationalize information when identifying patient factors along with which outcomes might vary.
    a. How have sponsors prioritized considerations such as disease burden, biomedical factors (anatomy, physiology, pathophysiology), and technology in developing research questions?
    b. Are there examples of the types of data sources that sponsors have considered for obtaining relevant information related to the considerations identified above? What criteria have sponsors utilized when evaluating the suitability of a data source?

4. Are there any challenges sponsors have faced in obtaining, analyzing, reviewing, and utilizing relevant information from the areas of consideration identified by FDA? How have sponsors approached situations in which information on expected differences in outcomes between populations is limited (e.g., for novel technology) or conflicting?

5. As described above, a study may need to be designed to use an enriched population when the evaluation of relevant information suggests that differences in clinical outcomes are expected between patient populations. Please describe any other circumstances, outside of the three considerations discussed above (disease burden or condition; anatomy, physiology, and pathophysiology; and technology), that may prompt a sponsor to design a clinical study which enrolls an enriched population.

c. ***Considerations for FDA's Evaluation of Safety and Effectiveness***

The preceding section of this document discussed considerations that could help sponsors and investigators design studies that reflect the intended use population of a subject device, and so are more likely to provide information on the benefits and risks of a medical device in that population. When reviewing requests for marketing authorization, FDA evaluates the probable benefits and risks to determine whether there is a reasonable assurance the device will be safe and effective in the populations for which it is intended. With that in mind, FDA is seeking input on two important areas of consideration for the Agency when evaluating whether clinical data provided by sponsors are generalizable to, and representative of, the intended use population

identified for a particular device:

- **Clinical study population** - Consideration of the population included in the clinical data provided to support a premarket decision and the rationale given by the sponsor for the population.
- **Differences between populations** - Consideration of whether the data suggest that there are differences in outcomes between populations.

i. Clinical study population - Consideration of the population included in the clinical data provided to support a premarket decision and the rationale given by the sponsor for the population.

The first consideration that FDA has identified as being important to its evaluation of clinical data provided in a marketing submission involves the populations captured by the data, as well as information regarding the sponsor's rationale for determination of the appropriate study population. FDA understands that there are many aspects of study design and implementation that can impact the makeup of participants in a study. Generally, study populations should be selected and enrolled based on the clinical study question and the intended use of the device,[11] but issues related to study site selection, enrollment difficulties, and other factors may impact recruitment and retention and, ultimately, the final composition of the study population. Nonetheless, FDA's evaluation of safety and effectiveness for a device requires consideration of the "persons for whose use the device is represented or intended" (21 CFR 860.7(b)). As such, FDA believes it is important that the clinical study population reflect the intended use population.

Because FDA's evaluation of device safety and effectiveness must incorporate the patient population in which the device is intended to be used,[12] FDA considers it important to understand a sponsor's rationale regarding the relevance of the provided clinical data to the intended use population. This rationale may, for example, include information related to the processes used for selection and enrollment of populations in a clinical study, or it may provide information to help FDA understand difficulties that a sponsor encountered related to obtaining data from certain populations, as well as how those difficulties were addressed. In cases where FDA identifies uncertainty in the data regarding a device's benefit-risk profile, a clear understanding of the rationale used by the sponsor to determine the appropriate study population may help facilitate discussion and inform options for resolving questions.

ii. Differences between study populations - Consideration of whether the data suggest that there are differences in outcomes between populations.

The second consideration that FDA has identified as being important to its evaluation of clinical data provided in a marketing submission is whether the data suggest that there are differences in outcomes between populations. Although FDA's existing framework for evaluating the benefits and risks of devices in marketing submissions takes into account that device performance may vary across patient populations, FDA's premarket decision-making considers whether the benefit-risk profile is acceptable for all patients in the intended use population.[13] To this end, an important consideration is that FDA has access to information that addresses the extent to which device performance or patient outcomes may differ between populations. A

[11] For more information on study population selection, see FDA guidance titled "Design Considerations for Pivotal Clinical Investigations for Medical Devices."
[12] See 21 CFR 860.7(b).
[13] See 21 CFR 860.7(d)(1); 21 CFR 860.7(e)(1).

further aspect of this consideration is that patients, health care partners, care-providers, and the broader US population have important information that is both accessible and functionally comprehensible. Such information may allow patients and other interested parties to make more informed decisions based on how a device's performance is impacted by certain factors that vary across populations. FDA is also considering how it can best work with impacted parties to ensure that the regulatory review process allows for discussion and understanding of the potential reasons underlying differences in outcomes, as this may help FDA determine whether clinical data are generalizable to, and representative of, the intended use population in a more complete evaluation of the safety and effectiveness of the device.

d. ***Considerations for FDA's Evaluation of Safety and Effectiveness – Discussion Questions***

FDA is seeking to better understand how the two considerations discussed in Section IV.c above may be incorporated into its evaluation of clinical data provided in marketing submissions. Specifically, we are seeking feedback on how these considerations may be integrated into FDA's existing regulatory framework. We are interested in understanding the public's perspectives regarding the extent to which FDA's evaluation of safety and effectiveness can interrogate the reasons for differences in outcomes between populations within a broader context of clinical, technical, demographic, and socio-economic considerations. Some relevant questions include:

1. Are there other areas that should be considered as part of FDA's evaluation of safety and effectiveness, and how could this information be leveraged when FDA makes regulatory decisions?

2. One way a sponsor could provide a rationale regarding the clinical study population could be to include a summary of the analysis conducted by a sponsor on relevant information, as discussed in Section IV.a above. This summary could synthesize the analysis and background information into a discussion that explains the sponsor's decisions with respect to goals for the study composition and that addresses how the results of the study will provide for a comprehensive assessment by FDA of the device's safety and effectiveness in the US intended use population.
    a. If there are differences between the study population and the intended use population, what information could be provided to explain the differences and justify that the study population is still adequate to support a determination regarding a device's safety and effectiveness in the intended use population?
    b. Would such a summary be an effective way for sponsors to convey this information and the rationale for the target study population to FDA?
    c. Are there alternative mechanisms to provide this information?

e. ***Example Scenarios***

FDA believes the considerations for study design and the considerations for FDA discussed above may facilitate the determination of whether there is adequate information to assess the safety and effectiveness of a device in the intended use population.

For example, a marketing submission that includes clinical data from studies that adequately represent the intended use population may allow FDA to better understand any differences in

study outcomes reported by the clinical study. Such may allow FDA to better understand the probable benefits and risks associated with the device and how labeling can discuss these benefits and risks. In contrast, a marketing submission where data is absent on populations with known differences or where a study population does not adequately represent the intended use population may result in lingering questions regarding whether there are differences in outcomes between populations. These types of questions may impact FDA's understanding and the level of uncertainty regarding a device's benefits and risks.

To further explore areas of consideration, FDA has created a table (see Table 1 below) that explores the potential relationship between information on whether or not a clinical study adequately reflects the intended use population and potential considerations for FDA. Further, to facilitate public input. FDA has developed several examples utilizing hypothetical data to further explore this relationship. The table and examples below are intended to help illustrate concepts discussed in this document and to solicit public input and feedback on these concepts. While the table utilizes simplified or even binary answers of "yes" or "no" for simplicity, FDA anticipates that the review and consideration of such information will be more complex. Similarly, the generalized examples that follow are not intended to account for every detail or consideration that may take place during FDA's evaluation of safety and effectiveness. FDA hopes that Table 1 along with illustrative examples will allow the public to better understand these areas of consideration and provide feedback on the concepts discussed in this document. **FDA requests public comment and feedback regarding the table and example scenarios that follow.**

Table 1: Potential relationship between clinical study data and considerations for FDA

Available information suggests differences in patient populations	Specific population(s) included within clinical study	Clinical study data outcomes suggest differences in patient populations	Potential Considerations for FDA
Yes	Study population enriched to reflect the intended use population of the device	Yes	Labeling may be used to ensure transparency regarding the study population and any differences in benefits/outcomes.
Yes	Study population enriched to reflect the intended use population of the device	No	Labeling may be used to ensure transparency regarding the study population and any differences in benefits/outcomes.
Yes	Study population not enriched to reflect the intended use population of the device; does not reflect the US population	No	Absent clinical data introduces significant uncertainty on applicability of data to intended use population.
Yes	Study population reflects the US population	No	Absent clinical data may introduce uncertainty on applicability of data to intended use population.

Available information suggests differences in patient populations	Specific population(s) included within clinical study	Clinical study data outcomes suggest differences in patient populations	Potential Considerations for FDA
No	Study population reflects the US population	Yes	Postmarket data may be utilized to better understand differences in benefits/outcomes between specific populations. Labeling may be used to ensure transparency regarding the study population and any differences in benefits/outcomes.
No	Study population not enriched to reflect the intended use population of the device; does not reflect the US population	No	Postmarket data may be utilized to better understand differences in benefits/outcomes between specific populations.
No	Study population reflects the US population	No	Labeling may be used to ensure transparency regarding the study population.

Example 1:

This is a light-based diagnostic device. Studies of devices based upon similar technology have demonstrated that melanin impacts light absorption and may affect the diagnostic accuracy of the device. The clinical data for this submission comes from a study population that was 45% White, 30% Black, and 25% Asian.

Available Data Suggest Differences*:* Yes. Data from devices with similar technology indicated that melanin content may change the intensity of detected light, as well as optical pathways from the emitted light to detector, ultimately affecting the accuracy of the device.

Population(s) included: The study population was enriched for race.

Clinical Study Data Suggest Differences: No race-based differences are suggested by the clinical data.

Possible Considerations for FDA: The data appear sufficient to evaluate the impact of melanin content on the device's outcome. Labeling used to ensure transparency regarding the study population.

Example 2:

This diagnostic device is used to detect a disease that predominantly affects individuals of a very specific subpopulation of one racial group. The disease is exceedingly rare in other racial groups. The sponsor has designated individuals of this subpopulation with signs and symptoms of the disease as the intended use population. This subpopulation accounted for 100% of the study population.

Available Data Suggest Differences: Yes, the disease affects a specific subpopulation of one race and is exceedingly rare in other subpopulations or races.

Population(s) included: Enriched to reflect the intended use/affected population.

Clinical Study Data Suggest Differences: No. The study data were limited to one race.

Possible Considerations for FDA: Because of the specific population affected by the disease, indicate the device only for the study population in which it was tested. Labeling used to ensure transparency regarding the study population.

Example 3:

This device diagnoses a disease that is twice as prevalent in the Black population in the US. Black people also experience greater impairment and symptom severity from that disease compared to their White counterparts. The submission includes clinical study data from a population that was 98% White; there were 5 Black individuals in a study cohort of 350 individuals. The clinical data did not suggest a difference in outcomes between White and Black participants.

Available Data Suggest Differences: Yes. There are known racial differences in disease prevalence and severity and Black race is associated with worse outcomes.

Population(s) included*:* Not enriched to reflect the disease burden of Black individuals and not representative of the US population.

Clinical Study Data Suggest Differences: No; however, there was very little data on how the device functions in Black individuals. The lack of data introduces marked uncertainty that limits the benefit-risk analysis in the intended use population.

Possible Considerations for FDA: Data not considered to reflect the intended use population, or a determination of whether the benefits outweighed the risks of device use in the population for which it was intended.

Example 4:

This implantable device treats a disease that affects both females and males; however, females are historically under-represented in studies of both the disease and its treatment. The clinical study consisted of a cohort that was 25% female and 75% male. Both safety and effectiveness of the device are known to be affected by the size of the target anatomy, which is typically smaller in females compared to males. Initial analysis of the study data suggested sex-based differences in safety and effectiveness. Further analysis suggest that sex was a proxy for anatomic size.

Available Data Suggest Differences: No known sex-based differences in disease prevalence or treatment outcomes due to historical under-representation of females in clinical studies.

Population(s) included: Not enriched and not representative of the US population.

Clinical Study Data Suggest Differences: No. The differences in safety and effectiveness were determined to be size-based rather than sex-based differences**.**

Possible Considerations for FDA: The data indicated that the benefits outweigh the risks of device use for both females and males. The IFU for the device could specify the anatomic size

supported by the data. Post-market data would address uncertainty related to under-enrollment of females in the original clinical study.

Example 5:

This device is used to treat an anatomic abnormality that occurs in females and males with equal prevalence. The clinical study of the device found that female participants are at a higher risk of peri-procedural complications, although death from these complications is rare and the overall benefit-risk analysis is favorable in females and males.

The clinical study cohort had roughly equal numbers of males and females.

Available Data Suggest Differences: There are no sex-based differences in the prevalence of the abnormality.

Population(s) included: US Population

Clinical Study Data Suggest Differences: Yes. Peri-procedural complications more common in females but benefits outweighed the risks for both female and male participants.

Possible Considerations for FDA: Postmarket data could be utilized to better understand differences in peri-procedural outcomes between females and males. Labeling could ensure transparency regarding differences in outcomes.

IV. Conclusion

FDA recognizes the urgent public health need for innovative technologies that help to reduce barriers to achieving health equity and that help to improve health outcomes across diverse populations. Crucial to this effort is ensuring the availability and access of medical devices to all populations. Given the diversity of the US population, medical device clinical studies should adequately represent the population that is intended to use the device so that the information generated from the study can provide an understanding of device performance across populations.

The considerations described throughout this document are intended to explore how clinical studies may be designed to identify study populations that adequately represent the intended use population by utilizing relevant data to understand differences in outcomes between patient populations. The document also discusses how this information may further FDA's understanding and consideration of information related to a device's safety, effectiveness, benefits, and risks. Table 1 and the generalized illustrative examples can help the public to better understand these areas of consideration and provide feedback on the concepts discussed in this document.

This document is intended to stimulate discussion to inform further policy development for a potential regulatory approach. FDA will use feedback submitted to the docket to help inform future policy development in accordance with good guidance practices. Please submit your comments regarding the concepts in this discussion paper to https://www.regulations.gov, Docket No. FDA-2024-N-3616 by October 4, 2024.