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Breakthrough Devices Program

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on October 25, 2017.

You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact the Office of Device Evaluation (ODE) at 301-796-5550 or BreakthroughDevicesProgram@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

When final, this guidance will supersede "Expedited Access for Premarket Approval and De Novo Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions," issued on April 13, 2015.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

Preface

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CDRH

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please use the document number 1833 to identify the guidance you are requesting.

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Breakthrough Devices Program

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. 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 or Office responsible for this guidance as listed on the title page.

I. Introduction

This guidance document describes policies that FDA intends to use to implement section 515B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360e-2), as created by section 3051 of the 21st Century Cures Act (Cures Act) (Public Law 114-255) and section 901 of the FDA Reauthorization Act of 2017 (Public Law 115-52) (the "Breakthrough Devices Program"). The Breakthrough Devices Program is a voluntary program for certain medical devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. This program is intended to help patients have more timely access to these medical devices by expediting their development, assessment, and review, while preserving the statutory standards for premarket approval, clearance of a premarket notification (510(k)), and marketing authorization via the De Novo classification process, consistent with the Agency's mission[1] to protect and promote public health.

The Breakthrough Devices Program supersedes the Expedited Access Pathway (EAP), which was launched in 2015. The Breakthrough Devices Program contains features of the EAP as well as the Innovation Pathway (first piloted in 2011), both of which were intended to facilitate the development and expedite the review of breakthrough technologies.

The Breakthrough Devices Program also supersedes the Priority Review Program, which implemented statutory criteria for granting priority review to premarket submissions for medical devices[2] and included standard procedures to achieve an efficient priority review process.

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[1] Statement of FDA Mission can be found at https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/budgetreports/ucm298331.pdf.

[2] FDA's guidance, "Priority Review of Premarket Submissions for Devices," issued on May 17, 2013, implemented former section 515(d)(5) of the FD&C Act (as in effect prior to the date of enactment of the Cures Act), which applied only to premarket approval applications. Because of the potential public health importance of devices warranting priority review status, FDA also applied the priority review criteria to other types of premarket

FDA provides information about the Breakthrough Devices Program under the "How to Study and Market Your Device" section on the Device Advice website (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/ucm441467.htm).

FDA's guidance documents, including this one, do not establish legally enforceable responsibilities. Instead, guidance documents describe 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 the word *should* in Agency guidance documents means that something is suggested or recommended, but not required.

II. Program Principles

The principles below describe the philosophy of the Breakthrough Devices Program and, in general, the approach FDA intends to take in an effort to help expedite the development and review of devices designated as Breakthrough Devices under section 515B(d)(1) of the FD&C Act (21 U.S.C. 360e-2(d)(1)). FDA intends to evaluate resource allocation in collaboration with the sponsor throughout the device development process to make the best use of FDA's resources and maximize the impact of the Breakthrough Devices Program.

A. Interactive and Timely Communication

For Breakthrough Devices, FDA intends to provide interactive and timely communication with the sponsor during device development and throughout the review process[3] for Q-Submissions,[4] Investigational Device Exemptions (IDEs), Premarket Approval Applications (PMAs), Premarket Notifications (510(k)s), and/or De Novo classification requests ("De Novo requests"). This applies to devices as well as to device-led combination products.

To best facilitate collaborative dialogue, the following, where applicable, are recommended for communications between FDA and the sponsor:

- discussion and agreement between FDA and the sponsor regarding goals of interactions and feasibility of response timelines;
- use of "track changes" and redlined versions of any document being revised interactively to efficiently and transparently communicate any updates; and
- use of summary tables to document points of agreement and previous interactions.

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submissions for devices. FDA withdrew this guidance on August 3, 2017. See https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm425025.htm.

[3] See section 515B(e)(1)(D) of the FD&C Act (21 U.S.C. 360e-2(e)(1)(D)).

[4] For information on Q-Submissions, please refer to the FDA guidance, "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff," at https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf.

FDA also intends to assign staff to be available within a reasonable time to address questions by institutional review committees concerning the conditions and clinical testing expectations applicable to the investigational use of any Breakthrough Device.[5]

Given that there may be novel scientific aspects of products in the Breakthrough Devices Program, FDA may need to interact with external experts or an advisory committee to reach various regulatory decisions.[6] In the event that such consultation is undertaken, FDA will disclose to the sponsor, no less than five business days in advance, the topics for discussion. FDA will also provide the sponsor the opportunity to recommend external experts.[7]

B. Pre/Postmarket Balance of Data Collection

As with all devices subject to a PMA, Breakthrough Devices subject to a PMA must still meet the statutory standard of reasonable assurance of safety and effectiveness at the time of approval. For PMA devices designated as Breakthrough Devices, FDA intends to use timely postmarket data collection, when scientifically appropriate, to facilitate expedited and efficient development and review of the device.[8] In accordance with the FDA guidance, "Factors to Consider Regarding Benefit-Risk When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications" (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm517504.pdf), as part of FDA's benefit-risk determination for Breakthrough Devices subject to a PMA, FDA may consider the amount of data that may be collected in the postmarket setting, rather than premarket, and the level of acceptable uncertainty in the benefit-risk profile at the time of approval. In all FDA premarket approval decisions, there is some degree of uncertainty about the benefits and risks of the device. We may not have definitive answers to all questions relating to the benefits and risks of the device at the time of approval because the time and cost of such data collection would adversely affect public health by significantly delaying the availability of medical devices that may improve the health of patients (e.g., to do so for a particular device may require clinical studies that enroll thousands of subjects to more fully assess all risks, such as rare adverse events). The degree of uncertainty that FDA accepts at the time of approval depends on, among other factors, the probable benefits of the device.

FDA will only approve a PMA if it determines that there is reasonable assurance of safety and effectiveness. As part of the benefit-risk determination for Breakthrough Devices subject to a PMA, FDA may accept a greater degree of uncertainty of the benefit-risk profile for these devices if the uncertainty is sufficiently balanced by other factors, including the probable benefits for patients to have earlier access to the device (e.g., a device that treats a life-threatening disease when no alternative treatments are available) and adequate postmarket controls to support premarket approval. Generally, weighing the benefits against the risks for Breakthrough Devices for which we would accept a greater degree of uncertainty adds another

[5] See section 515B(e)(1)(H) of the FD&C Act (21 U.S.C. 360e-2(e)(1)(H)).
[6] See section 515B(e)(1)(G) of the FD&C Act (21 U.S.C. 360e-2(e)(1)(G)).
[7] See section 515B(e)(1)(F) of the FD&C Act (21 U.S.C. 360e-2(e)(1)(F)).
[8] See section 515B(e)(2)(C) of the FD&C Act (21 U.S.C. 360e-2(e)(2)(C)).

dimension to the benefit-risk calculus. Specifically, as part of FDA's benefit-risk determination, FDA intends to weigh the device's impact on patient health, including the probable benefit of earlier access to the device, against the probable risk of harm to patients from the device should subsequent data collection demonstrate that the device is ineffective or unsafe. FDA's guidance, "Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval" (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm393994.pdf) provides more information regarding FDA's current policy on balancing premarket and postmarket data collection during FDA's review of PMAs.

C. Efficient and Flexible Clinical Study Design

FDA intends to "take steps to ensure that the design of clinical trials is as efficient and flexible as practicable, when scientifically appropriate."[9] This may include, for example, consideration of the following; note that the below is not intended to be an exhaustive list:

- prespecified endpoints regarding the minimum clinically meaningful effect;
- intermediate and surrogate endpoints where evidence is provided to support the endpoint as reasonably likely to predict the clinical benefit of a device;
- composite endpoints with an explicit rationale for the meaningful effect size; and
- phased study design.

D. Review Team Support

For each Breakthrough Device submission received, FDA will route the submission to the appropriate organizational unit. An FDA manager in that unit will assess the submission and assign the most appropriate individual to lead the review team based upon training, expertise, experience, and the ability to quickly and interactively resolve complex issues. The review team lead, in conjunction with management, will determine the need for and assign additional staff with subject matter expertise to complete the review team. Staff reviewing Breakthrough Devices will be experienced with innovative approaches to regulatory science and clearly communicating FDA's expectations during the device development process.

Breakthrough Device review teams will undergo regular training to ensure consistent and efficient application of the principles and features outlined in this guidance document as well as to communicate productive examples across projects. This training may include team meetings, sponsor engagement, patient interactions, and participation at scientific and regulatory meetings to help ensure teams are up to date in the technological advancements of their respective areas of scientific and device expertise and prepared to apply novel approaches to regulatory and device

[9] See section 515B(e)(2)(B) of the FD&C Act (21 U.S.C. 360e-2(e)(2)(B)).

development challenges.

E. Senior Management Engagement

Senior management (e.g., Office director or designee representing Office director) will work with Breakthrough Device review teams to efficiently facilitate the sponsor's development of the device and FDA's review of related submissions. To support efficient and timely dispute resolution, senior management will be engaged in projects when points of disagreement that cannot be quickly resolved are identified by the FDA review team or the sponsor during the device development or review process.

F. Priority Review

All submissions for devices designated as Breakthrough Devices will receive priority review status, meaning that the review of the submission is placed at the top of the appropriate review queue and receives additional review resources, as needed. If multiple submissions for Breakthrough Devices are under review simultaneously, they are reviewed with priority assigned on a first-in-first-reviewed (FIFR) basis for each review cycle.

Although priority review for devices is intended to help expedite patient access to certain devices important to public health, FDA's past experience with the Priority Review Program indicates that review times may take longer for Breakthrough Devices than for other devices because of the novel scientific issues these devices may raise. We believe that the Breakthrough Devices Program may enable patients to have more timely access to these devices than they would otherwise because of the earlier interaction between FDA and sponsors during the device development process.

In order to benefit from priority review status under the Breakthrough Devices Program, the commitment on behalf of the sponsor to resolve all scientific and regulatory issues should match that of FDA. It will only be through effective communication (e.g., interactive review), collaboration, and a total commitment to fulfilling all regulatory and scientific requirements that FDA and the sponsor can speed the availability of safe and effective products.

G. Manufacturing Considerations for PMA Submissions

For submission types that typically require a preapproval inspection, FDA intends to expedite the review of manufacturing and quality systems compliance for devices in the Breakthrough Devices Program.[10] This includes, on a case-by-case basis and at FDA's discretion, allowing a sponsor to provide less manufacturing information in a PMA, such as when the sponsor has a good track record for quality systems compliance and there are no new manufacturing issues that could adversely impact product quality or performance.

[10] See section 515B(e)(1)(E) of the FD&C Act (21 U.S.C. 360e-2(e)(1)(E)).

A device must be in conformance with the Quality System regulation (QS Reg; 21 CFR part 820), and the sponsor must submit adequate information in a PMA to meet the requirements under section 515(c)(1)(C) of the FD&C Act (21 U.S.C. 360e(c)(1)(C)) and 21 CFR 814.20(b)(4)(v). As with other PMAs, sponsors of a Breakthrough Device should submit PMA information as described in the FDA guidance, "Quality System Information for Certain Premarket Application Reviews" (https://www.fda.gov/RegulatoryInformation/Guidances/ucm070897.htm).

In appropriate cases, FDA may also, at its discretion, forgo inspection of certain manufacturing sites prior to approval of a Breakthrough Device. In general, FDA would review the sponsor's quality system and manufacturing information and make a decision about inspecting finished device manufacturing sites as follows:

- Finished device manufacturing sites with no prior inspectional history or no inspectional history within the five-year period prior to the filing date of the application would be inspected before approval of the Breakthrough Device.

- Finished device manufacturing sites that have been inspected within the two-year period prior to the filing date of the PMA, for which the inspectional outcome was No Action Indicated or Voluntary Action Indicated and for which the inspectional coverage is relevant to this PMA, may be inspected after approval of the Breakthrough Device.

- Finished device manufacturing sites that have been inspected within a period of two to five years prior to the filing date of the application, for which the inspectional outcome was No Action Indicated or Voluntary Action Indicated and for which the inspectional coverage is relevant to this PMA, may be inspected after the Breakthrough Device is approved if, in addition to submitting all other information required in a PMA under section 515(c)(1) of the FD&C Act (21 U.S.C. 360e(c)(1)) and 21 CFR 814.20, the sponsor submits the following:

    - a declaration stating that all activities at the site comply with the QS Reg (21 CFR part 820); and

    - information, initially developed as part of design validation (21 CFR 820.30(g)) and current as of the filing date of the application, demonstrating that the sponsor's risk analysis activities included evaluation of risk associated with the design, manufacturing, and use of the device, and that risk has been reduced to acceptable levels. The sponsor could do this, for example, using standards such as the current FDA-recognized version of *ISO 14971: Medical devices – Application of risk management to medical devices*.

Where an inspection is not conducted prior to approval of the PMA for a Breakthrough Device, FDA intends to conduct an inspection within 12 months after approval. In appropriate circumstances, FDA may consider such a postapproval inspection that is classified as Official Action Indicated and for which deviations are not brought into QS Reg conformance within a reasonable time after receipt of written notice to be grounds for PMA withdrawal under section

515(e)(1)(E) of the FD&C Act (21 U.S.C. 360e(e)(1)(E)).

For clarification, when a PMA sponsor's manufacturing sites are not ready for inspection, or have been inspected and classified as Official Action Indicated, the sponsor may receive an approvable PMA letter pending a QS Reg decision from FDA. It should be noted that this applies to PMA sponsors that are manufacturing their own device as well as to sponsors who intend to have another entity manufacture their device for commercial distribution in the U.S. We generally would then approve the device once we have adequate assurances of compliance regarding the applicable quality systems of the manufacturer(s).

III. Program Features

The novelty of a Breakthrough Device can present key challenges because both the sponsor and FDA may face more uncertainty about how best to evaluate the device's safety and effectiveness. To expedite the development of these devices, FDA intends to offer sponsors a menu of options that offer opportunities for early and regular interaction with FDA as device development unfolds. A sponsor whose device has been designated as a Breakthrough Device may select one or more of the options described below in **Sections A-C** at any time prior to submitting a marketing application for that device; the sponsor need not, however, pursue any of these options. To request one of the options, a sponsor should submit a Pre-Submission following the processes outlined in the FDA guidance, "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff" (hereinafter, "the Pre-Submission Guidance;" https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf).

A. Breakthrough Device Sprint Discussion

To support sponsors needing timely resolution of potentially novel issues, FDA offers "sprint" discussions with the goal of reaching mutual agreement on a specific topic within a set time period (e.g., 45 days). The number and format of interactions within a sprint discussion may vary based on project needs and should be defined *a priori* by the sponsor and FDA. During a sprint discussion, the sponsor may provide additional information or revisions to initial proposals. The schedule of such interactions as well as the information and proposals to be discussed during the sprint discussion may be modified during the sprint discussion as agreed upon with FDA. To facilitate this intensive level of interaction, a sprint discussion should follow the parameters below. Points of disagreement that cannot be resolved quickly should be expeditiously elevated to senior management. In some cases, the sponsor may wish to consider FDA feedback after conclusion of the sprint discussion prior to determining whether agreement or disagreement exists and whether additional discussion is needed.

(1) Single Topic with Specific Goals

To allow for a detailed discussion and timely resolution, a sprint should have only one general topic (e.g., animal study protocol design, strategy for focused nonclinical testing, clinical

protocol discussion, statistical analysis plan review) and specific goals (e.g., determine primary and secondary endpoints for pivotal study). In a sprint discussion request, a sponsor should propose a topic and goals(s); please note that FDA may work with the sponsor to refine the topic and goal(s) as needed. It is recommended that a sponsor have no more than one sprint discussion open at a time. This will allow both FDA and the sponsor to devote sufficient resources to support a highly interactive, collaborative, and dynamic sprint process.

(2) Defined Interaction Schedule, Including Planned Participants

A sponsor should propose an interaction schedule and a defined end date (e.g., 45 days). FDA will propose revisions to the timeline, if needed, with the goal of reaching agreement on the timeline early in the sprint review. Since progress may require the presence of key individuals at meetings during the sprint discussion, the sponsor should propose their planned attendees (e.g., regulatory manager, animal study consultant, clinical consultant) and, as relevant, request FDA attendees with specific expertise (e.g., animal study reviewer, clinician, statistician).

The sprint discussion is intended to be highly interactive, and FDA understands that, based on an early interaction, the sponsor may choose to provide additional information to FDA to support later interactions for the sprint. If the sponsor provides new information to FDA during the sprint, FDA will attempt to incorporate the information into its review and feedback while still adhering to the agreed-upon timeline. However, depending on the extent of the new information provided and the time remaining for the review, revisions to the timeline may be needed.

(3) Clear Documentation of Interactions and Conclusions

FDA will provide summary feedback to the sponsor after the close of a sprint discussion. This summary will include the points of agreement, points of disagreement, if any, and points necessitating further discussion. To facilitate any review of new or revised information provided during the sprint, it is recommended that the sponsor provide “track changes” versions of any revised documents and/or clearly indicate with a summary table or timeline what changes or new information is being or has been provided. At the conclusion of the sprint discussion, the sponsor should develop draft minutes and provide the draft minutes as an amendment to the relevant Pre-Submission. Timing for submission of draft meeting minutes should be addressed in the sprint discussion schedule.

FDA intends that feedback the Agency provides in response to a sprint discussion will not change, provided that the information submitted in a future IDE or marketing application is consistent with that provided in the sprint submission and that the data in the future submission do not raise any important new issues materially affecting safety or effectiveness. FDA intends that modifications to its feedback be limited to situations in which FDA concludes that the feedback given previously does not adequately address important new issues materially relevant to a determination of safety or effectiveness that have emerged since the time of the sprint discussion. For example, FDA may modify its previous feedback if new scientific findings

emerge that indicate there is a new risk or an increased frequency of a known risk that affects FDA's prior advice, or if there is a new public health concern that affects FDA's prior advice. In such cases, FDA will acknowledge a change in the advice and will document clearly the rationale for the change, and the changed advice will be supported by the appropriate managerial concurrence.

Sponsors should recognize that even though the Agency may have already reviewed the sponsor's protocols/plans in a sprint discussion, this does not guarantee approval, clearance, or granting of future submissions. Additional questions may be raised during the review of the future submission when all information is reviewed and considered as a whole. Although sprint discussions are not decisional or binding on the Agency or the sponsor, it is FDA's intent to provide the best advice possible based on the information provided in the Pre-Submission and other information known at that point in time.

(4) Supporting Materials

To enable quick, efficient discussion of the sprint topic, it is important that the sponsor provide FDA with, and clearly reference, all materials needed to support review and interaction (e.g., a submission might contain an appendix with a draft protocol). FDA recommends that sponsors provide a rationale justifying their proposed approach within their supporting materials to best facilitate review and interactions.

(5) Example Sprint Discussion

The example sprint discussion below incorporates the concepts discussed above:

- On Day 7, following receipt of the submission, FDA and the sponsor hold an informational teleconference to walk FDA through the sponsor's materials and questions. During this meeting, FDA and the sponsor discuss an interaction schedule to facilitate collaboration and overall topics and goals for sprint interactions.

- On Day 14, FDA emails the sponsor with initial feedback and questions for upcoming discussion.

- On Day 21, FDA and the sponsor meet (via teleconference or face to face) to discuss FDA's initial feedback and questions. FDA and the sponsor discuss initial approaches for addressing any outstanding issues.

- On Day 28, based on the feedback received and the prior discussion, the sponsor provides additional information or revised supporting materials to FDA via email in response to outstanding issues.

- On Day 35, FDA and the sponsor meet via teleconference to discuss the revised supporting materials provided by the sponsor. Based on this discussion, FDA and the sponsor identify substantive areas of agreement and points necessitating further discussion, if any. The sponsor may wish to consider FDA feedback prior to determining

whether agreement or disagreement exists and whether additional discussion is needed. However, if any substantive points of disagreement are identified by FDA or the sponsor at this point, FDA develops a plan for how senior management will be involved to support quick resolution of the identified issues (see **Section II.E** above).

- On Day 40, the sponsor provides via email draft minutes from previous discussions including substantive points of agreement, points necessitating further discussion or points of disagreement, if any.

- On Day 45, FDA provides any edits to meeting minutes, including substantive points of agreement and points necessitating further discussion, if any. If there are no points of disagreement, FDA will close out the sprint discussion. If points of disagreement exist, FDA will proceed with the plan for senior management involvement to quickly address the outstanding issues, which might include a teleconference involving senior management by Day 50.

B. Data Development Plan (DDP)

Sponsors of Breakthrough Devices may request coordination with FDA regarding early agreement on a Data Development Plan (DDP). The DDP is a high-level document intended to help ensure predictable, efficient, transparent, and timely device assessment and review by outlining data collection expectations for the entire product lifecycle. It should describe the balance of premarket and, as applicable, postmarket collection of clinical and nonclinical data. FDA intends to work with the sponsor so that the plan is developed in a manner that is least-burdensome and predictable, while allowing for some measure of flexibility and adjustments as appropriate.

An example approach to a DDP can be found in Appendix 1: DDP Example Approach.

Importantly, the DDP should include both clinical and nonclinical testing approaches. In FDA's experience, sponsors often focus on clinical study design but tend to overlook potential hurdles raised by nonclinical issues. FDA encourages sponsors to consider the nonclinical testing that will be needed to support the regulatory review of their device early on and to discuss the planned approach with FDA. The DDP should discuss the nonclinical testing that would be conducted and the timing of such testing relative to planned clinical studies and a subsequent marketing application. It may be appropriate to allow clinical testing to begin based upon preliminary nonclinical results or with some nonclinical testing deferred, depending on the mitigations in place to protect study subjects.

FDA review of a DDP follows the same model as the sprint discussion described above. Please note that FDA and the sponsor may wish to discuss a complete DDP with all planned clinical and nonclinical testing for pre- and postmarket data collection, or a component or subset of the DDP (e.g., premarket nonclinical testing assessment plan).

C. Clinical Protocol Agreement

As described in section 515B(e)(2)(D) of the FD&C Act (21 U.S.C. 360e-2(e)(2)(D)), the Breakthrough Devices Program offers a mechanism for obtaining agreement in writing for clinical protocols, which will be considered binding on both FDA and the sponsor, subject to the following:

- Any changes to the previously agreed-upon protocol are agreed upon in writing by both FDA and the sponsor; or

- The director of the Office responsible for reviewing the device submission determines that a substantial scientific issue essential to determining the safety or effectiveness of the device exists. In this case, the director's decision must be provided in writing and can be made only after FDA has provided an opportunity to the sponsor to meet and discuss the substantial scientific issue(s). Such a meeting would need to include the Office director and clearly document the substantial scientific issue(s) discussed.

FDA will work interactively with sponsors who choose to pursue a clinical protocol agreement. Upon reaching agreement, FDA will issue a letter documenting the agreement reached.

D. Regular Status Updates

FDA and the sponsor of a Breakthrough Device may agree to have regular (e.g., bimonthly) status updates. Through these interactions, FDA and the sponsor may discuss general progress of the project and next steps or plans for future discussions. These interactions may be by email, teleconference, or face-to-face meeting, as agreed upon by FDA and the sponsor. These interactions may be between the primary FDA and sponsor contacts or may include additional participants as needed. Regular status updates provide an opportunity for a high-level view of the project and identification of potential hurdles, while a sprint discussion provides the opportunity for detailed feedback to address specific sponsor goals. A Pre-Submission is not recommended for status updates.

IV. Designation Request

A designation request is the mechanism by which sponsors request entry into the Breakthrough Device Program and FDA renders and communicates a decision.

A. Designation Criteria

The designation criteria, as defined in section 515B(b) of the FD&C Act (21 U.S.C. 360e-2(b)), provide for a program for devices:

> "(1) that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions; and

(2)(A) that represent breakthrough technologies;

(B) for which no approved or cleared alternatives exist;

(C) that offer significant advantages over existing approved or cleared alternatives, including the potential, compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patient's ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies; or

(D) the availability of which is in the best interest of patients."

In addition, section 515B(c) of the FD&C Act (21 U.S.C. 360e-2(c)) states:

"Any such request for designation may be made at any time prior to the submission of an application under section 515(c) [21 U.S.C 360e(c)], a notification under section 510(k) [21 U.S.C. 360(k)], or a petition for classification under section 513(f)(2) [21 U.S.C. 360c(f)(2)]."

B. Designation Considerations

(1) Device Provides for More Effective Treatment

In determining whether a device meets the criterion of providing "for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or condition,"[11] FDA considers the following three factors:

a. Whether a Device Provides for "More Effective" Treatment or Diagnosis

Because decisions on requests for designation will be made prior to premarket review of a device, for the purposes of designation, FDA believes it is appropriate to consider whether there is a reasonable expectation that a device *could* provide for more effective treatment or diagnosis relative to the current standard of care (SOC) in the U.S. A complete set of clinical data is not required for designation. Instead, a sponsor should demonstrate a reasonable expectation that the device could provide for more effective treatment or diagnosis of the disease or condition identified in the proposed indications for use. This includes a reasonable expectation that the device could function as intended (technical success) and that a functioning device could more effectively treat or diagnose the identified disease or condition (clinical success). Mechanisms for demonstrating a reasonable expectation of technical and clinical success could include literature or preliminary data (bench, animal, or clinical). For example, a sponsor might provide preliminary bench data to support the potential for technical success and literature to support that a given principle of operation could more effectively treat or diagnose the identified disease or

[11] See section 515B(b)(1) of the FD&C Act (21 U.S.C. 360e-2(b)(1)).

condition.

b. Whether a Disease or Condition is "Life-Threatening"

FDA considers a disease or condition life-threatening for purposes of the Breakthrough Devices Program if it is a disease or condition for which the likelihood of death is high unless the course of the disease is interrupted in a population or subpopulation. Examples of life-threatening diseases or conditions include, but are not limited to, acute stroke, myocardial infarction, cancer, and trauma.

c. Whether a Disease or Condition is "Irreversibly Debilitating"

For purposes of the Breakthrough Devices Program, FDA considers a disease or condition associated with morbidity that has substantial impact on day-to-day functioning to be irreversibly debilitating for a population or subpopulation. Short-lived and self-limiting morbidity will usually not be sufficient. Irreversible disease or conditions may, in certain cases, include diseases or conditions that are persistent or recurrent. Whether a disease or condition is "irreversibly debilitating" is based on its impact on such factors as survival, day-to-day functioning, and the likelihood that the disease or condition, if left untreated, will progress to a more serious disease or condition. Examples include cancer, amyotrophic lateral sclerosis (ALS), stroke, and large ST segment elevation myocardial infarction (STEMI; while patients with STEMI and stroke can improve with medication and rehabilitation, the effects are not reversible and can be debilitating).

(2) Device Represents Breakthrough Technology

When determining whether a device represents a "breakthrough technolog[y],"[12] FDA considers the potential for a device to lead to a clinical improvement in the diagnosis, treatment (including monitoring of treatment), cure, mitigation, or prevention of the life-threatening or irreversibly debilitating condition. Examples of breakthrough technologies include:

- A transcatheter heart valve that is delivered transcutaneously and does not require open heart surgery, thereby decreasing the risks of the procedure. This breakthrough technology has the potential to provide a clinically meaningful advantage in a patient population with few options.

- An internal hemostatic device for the temporary control of bleeding from junctional wounds and non-compressible wounds, which are not amenable to tourniquet application in the battlefield. This device offers immediate care for severe bleeding wounds in a battlefield setting until surgical care is available, offering patients a potentially life-saving treatment when other methods of stopping severe bleeds are not an option.

- A gene signature test that provides prognostic information for a cancer patient such that

[12] See section 515B(b)(2)(A) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(A)).

the information helps clinicians personalize the benefit-risk profile of a variety of therapeutic options and treatment strategies.

- A genetic test capable of identifying DNA mutations using blood from cancer patients may offer patients a more convenient, non-invasive sampling method compared to surgery, which has the potential for serious risks.

(3) No Approved or Cleared Alternatives Exist

When determining whether the device meets the criterion that "no approved or cleared alternatives exist"[13] FDA considers whether there is a drug, biological product, or device that has received FDA marketing authorization after premarket review for the same indications being considered (i.e., whether there is an alternative product that FDA has approved, cleared, or licensed, or for which FDA has granted a De Novo request).

In addition, to be considered an "approved or cleared" alternative, a product should be consistent with the U.S. SOC. There may be a substantial number of currently approved or cleared medical products with varying relevance in the diagnosis and treatment of a life-threatening or irreversibly debilitating disease in the U.S., including devices that are no longer used or are used only rarely. FDA's determination as to whether there is an approved or cleared alternative generally focuses only on options that reflect the current SOC for the specific indication (including the disease stage) for which the product is being developed.

In evaluating the current SOC, FDA considers recommendations by authoritative scientific bodies based on clinical evidence and other reliable information, including such information submitted by the sponsor, that reflects current clinical practice. In the absence of a well-established and documented SOC, FDA may consult with special government employees (SGEs) or other experts for advice in assessing whether an approved or cleared medical product is relevant to the current SOC. When a proposed indication for the new device targets a subset of a broader disease population, the SOC for the broader population, if there is one, generally is considered available therapy for the subset. Over the course of new device development, it is foreseeable that the SOC for a given condition may evolve (e.g., because of the approval of a new device or new information about alternative treatments).

Examples of devices for which no approved or cleared alternative exists at the time designation is requested include:

- An ablation catheter that offers the potential ability to treat atrial fibrillation. Catheters were approved for treatment of atrial flutter, and there was no legally marketed ablation catheter indicated for the treatment of atrial fibrillation. Therefore, at the time of review, the ablation catheter met the criteria for "no approved or cleared alternative."

- A first-of-a-kind testing device to aid in the diagnosis of Parkinson's Disease. While

[13] See section 515B(b)(2)(B) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(B)).

devices exist to monitor tremors that may be associated with Parkinson's Disease, no device intended to aid in the diagnosis of Parkinson's Disease has received FDA marketing authorization. A device that could differentiate between Parkinsonian and non-Parkinsonian Disease tremor would be considered first-of-a-kind and meet the criterion for having "no approved or cleared alternatives."

(4) Device Offers Significant Advantages over Existing Approved or Cleared Alternatives

In determining whether a device meets the criterion of offering "significant advantages over existing approved or cleared alternatives,"[14] FDA considers the potential, compared to existing approved or cleared alternatives, "to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies."[15]

Examples of devices that have the potential to offer significant advantages of existing approved or cleared alternatives include:

- a diagnostic product intended to improve diagnosis or detection of a life-threatening or irreversibly debilitating disease or condition in a way that would lead to improved outcomes (e.g., an in vitro diagnostic product (IVD) for earlier diagnosis of preeclampsia);

- a product intended to improve or prevent a serious treatment-related side effect associated with an available product for treating a life-threatening or irreversibly debilitating disease or condition; and

- a product intended to treat a life-threatening or irreversibly debilitating disease or condition that does not have a serious adverse effect associated with an available product for treating this disease/condition.

(5) Device Availability is in the Best Interest of Patients

In determining whether the device meets the criterion "availability [of the device] is in the best interest of patients,"[16] FDA considers whether the proposed device and indications for use provide another type of specific public health benefit.

An example of a device, the availability of which is in the best interest of patients, could be a

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[14] See section 515B(b)(2)(C) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(C)). As noted above in **Section IV.B(4)** of this draft guidance, for purposes of the Breakthrough Devices Program, we consider an "approved or cleared alternative" to be a product that FDA has approved, cleared, or licensed, or for which FDA has granted a De Novo request.

[15] See section 515B(b)(2)(C) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(C)).

[16] See section 515B(b)(2)(D) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(D)).

group of molecular tests to identify a large number of potential pathogens simultaneously, including common, rare, and/or emerging pathogens. More rapid access to more detailed diagnostic information can better guide optimal patient care and may yield better patient outcomes. However, these devices also suffer major challenges not only in comparing against reference methods but also in obtaining the appropriate sample base to reliably verify the more rare pathogens in the panel. This can result in the target panel of these tests being reduced in order to generate data to support FDA marketing authorization. The Breakthrough Devices Program may facilitate device developers' ability to test new wide-scope IVDs for both common and rare pathogens, resulting in devices with a broader diagnostic scope being brought to market. Also, this could allow for more rapid approval or clearance of modifications to these tests as new and emerging pathogens are discovered or proposed for addition to the panels.

In addition, the criterion of being in the best interest of patients may apply when the device has a benefit for patients who are unable to tolerate available therapy, whose disease has failed to respond to available therapy, or for whom the treatment can be used effectively with other critical agents that cannot be combined with available therapy. This criterion may also apply if the device:

- avoids serious harm that can occur with available therapy;
- avoids serious harm that causes discontinuation of treatment of a life-threatening or irreversibly debilitating disease or condition; or
- reduces the potential for harmful interactions with other therapies.

In addition, this criterion may apply to a device that was designed or modified to address an unanticipated serious failure occurring in a critical component of an approved device for which there are no alternatives or for which alternative treatment would entail substantial risk of morbidity for the patient. A device may also satisfy this criterion if it provides an additional benefit, such as improved patient compliance that is expected to lead to a reduction in serious adverse outcomes. Furthermore, this criterion may apply if the device addresses an emerging or anticipated public health need, such as a device shortage or public health emergency.

A product developed by a sponsor who is working with a federal agency on the development of medical devices to address a national security issue may be considered to meet this criterion. To support a request for designation under this criterion, it may be helpful to include a letter in the designation request from the federal agency (e.g., Department of Defense, Department of Homeland Security) identifying the specific device or device type and indicating that its commercial availability is of particular importance to our national security.

Examples of devices for which availability is in the best interest of patients are as follows:

- an insulin pump that features a new mechanism to detect low blood glucose and automatically stop insulin delivery; and
- an IVD assay that detects a genomic variant for the purposes of identifying patients with

certain cancers who are eligible for treatment with a specific drug. In some situations, for those patients who do not possess the variant, a therapeutic product may have severe toxicities and be detrimental without providing benefit to the patient. For this reason, use of the assay is necessary for safe and effective use of the drug and is therefore in the best interest of patients. For more information on in vitro companion diagnostic devices, please refer to the FDA guidance, "In Vitro Companion Diagnostic Devices" (https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM262327.pdf).

(6) Additional Considerations

a. Regulatory Path

In determining whether designation has been requested "any time prior to the submission of an application under section 515(c) [21 U.S.C 360e(c)], a notification under section 510(k) [21 U.S.C. 360(k)], or a petition for classification under section 513(f)(2) [21 U.S.C. 360c(f)(2)],"[17] FDA considers:

- whether the expected marketing application for the device is a PMA, 510(k), or De Novo request; and
- whether or not the marketing application has been received.

Sponsors should indicate which marketing application type (PMA, 510(k), or De Novo request) they intend to submit and include a rationale for this approach in support of their Breakthrough Device designation request. FDA's designation decision does not constitute a formal decision regarding the applicable regulatory pathway or device classification but does indicate that, based on the information provided in the designation request and other information known at the time, the Agency expects that submission of a PMA, 510(k), or De Novo request will be required. FDA does not intend to specify in its decision on the designation request which marketing application the sponsor will need to submit for the subject device. A sponsor must submit a request for designation prior to submission of the marketing application. FDA will not consider requests for designation contained within a marketing application or after a marketing application has been submitted.

b. Multiple Devices with Same Intended Use

Breakthrough Device designation may be granted for multiple devices with the same proposed intended use. However, when a Breakthrough Device has been approved or cleared or has had a De Novo request granted, no other devices with the same intended use will be designated as a Breakthrough Device, unless the criteria for designation described above are met in light of the first Breakthrough Device's market availability.

[17] See section 515B(c) of the FD&C Act (21 U.S.C. 360e-2(c)).

For example, Device X was accepted into the Breakthrough Devices Program after FDA determined (1) that there was a reasonable expectation it could provide for more effective treatment of a life-threatening disease and (2) that it represented a breakthrough technology and offered significant advantages over existing approved or cleared alternatives. A De Novo request was later granted for Device X, allowing for marketing. Device Y has the same intended use as Device X and is now requesting designation into the Breakthrough Devices Program on the basis of providing a significant advantage over Device X. Even though Device Y has the same intended use as Device X, Device Y is eligible for Breakthrough Device designation because it offers significant advantages over an approved or cleared alternative, Device X.

c. Combination Products

Device-led combination products are eligible for Breakthrough Device designation. However, it is important to note that these products may raise unique scientific and regulatory challenges. Further, it may not be possible to apply all of the policies described in this guidance to combination products that receive Breakthrough Device designation due to such challenges as well as challenges associated with coordinating review with a different Center.

C. Designation Review Process

A request for Breakthrough Device designation should be submitted as a Q-Submission following the process outlined in the Pre-Submission Guidance. An example approach[18] for a request for Breakthrough Device designation is provided in **Appendix 2: Illustrative Example: Breakthrough Device Designation Request**. The Breakthrough Device designation request should be the only request contained in the Q-Submission. Other Q-Submission topics should be submitted separately. Furthermore, if sponsors are pursuing Breakthrough Device status and at the same time have Q-Submission questions, sponsors may wish to consider submitting the questions after FDA renders a designation decision. This is because the Breakthrough Device status may impact the feedback FDA provides.

Please note that FDA may identify devices that may be good candidates for the Breakthrough Devices Program and recommend that sponsors of such devices consider applying to the program.

In addition, note that designation should be requested *separately* from the submission of a marketing or IDE application, not within such application. As noted above in **Section IV.B(6)** of this guidance, the designation request must also be submitted before the submission of a marketing application for the device.

FDA will issue a grant or denial decision for each Breakthrough Device designation request

[18] Section 515B(f)(1)(B) of the FD&C Act (21 U.S.C. 360e-2(f)(1)(B)) indicates that this guidance shall "provide a template for requests under subsection (c)." The illustrative appendix provides an example approach.

within 60 calendar days of receiving such a request.[19] In general, FDA intends to interact with a sponsor by Day 30 regarding any requests for additional information needed to inform the designation decision. It is helpful when a sponsor is available and responsive to FDA requests throughout the review timeline. If FDA does not receive additional information needed to make a decision on a designation request in a timely manner, it may result in denial of the Breakthrough Device designation request.

D. Designation Withdrawal

A sponsor may request to withdraw from the Breakthrough Devices Program at any time. Such a request should be submitted in writing to FDA as a withdrawal amendment to the Q-Submission under which designation was granted.

FDA will not withdraw designation on the basis of another Breakthrough Device or a device given priority review under former section 515(d)(5) of the FD&C Act (as in effect prior to the date of enactment of the Cures Act) with the same intended use receiving PMA approval, having a De Novo request granted, or receiving clearance of a 510(k).[20] However, FDA may withdraw designation at any time upon written notice to the sponsor if FDA determines that:

- for other reasons, the device is no longer eligible for a Breakthrough Device designation according to the criteria outlined in section 515B(b) of the FD&C Act (21 U.S.C. 360e-2(b)), based on available information; or

- the information submitted in support of a request for Breakthrough Device designation, including, without limitation, the designation request package or any related premarket submission, contained an untrue statement of material fact or omitted material information, including false statements relating to data collection.

[19] FDA's decision on a request for designation as Breakthrough Device constitutes a "significant decision" under section 517A of the FD&C Act (21 U.S.C. 360g-1), as amended by section 3051 of the Cures Act. Additional information regarding CDRH's interpretation of section 517A and the procedures applicable to a request for review of a significant decision by CDRH under section 517A is available in the respective FDA guidances, "Center for Devices and Radiological Health Appeals Processes: Questions and Answers about 517A" (https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM352254.pdf) and "Center for Devices and Radiological Health Appeals Processes" (https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM284670.pdf).

[20] See section 515B(d)(3) of the FD&C Act (21 U.S.C. 360e-2(d)(3)).

Appendix 1: DDP Example Approach

This appendix provides an example of information found to be helpful in a Data Development Plan (DDP).

Background Information

Device Name: Name of the device.

Device Description: Overview of the product, including principles of operations (including device components) and properties relevant to clinical function, if known. Images or engineering schematics are also encouraged for inclusion, as appropriate.

Indications for Use: Indications for use for which designation was granted (see **Appendix 2: Illustrative Example: Breakthrough Device Designation Request**).

Data Collection Plan

The table(s) below present example approaches to consider for identifying the planned nonclinical testing and clinical studies.

Nonclinical Test	**Reference standard, method, acceptance criteria, objective, etc.**	**Timeline**
Test name/type. *Examples: Electromagnetic compatibility, biocompatibility, sterilization, mechanical fatigue testing, animal study, address disapproval concerns #1-10 in FDA's G160001 letter dated 1/31/2016.*	Relevant standard, description of method, acceptance criteria, objective, etc. to describe testing expectations. *Examples: IEC 60601-1-2; cytotoxicity, sensitization, and irritation testing per ISO 10993; assess operability of device; see disapproval concern language.*	When test results should be provided to FDA. *Examples: In feasibility study IDE, in pivotal study IDE, in marketing application, in postapproval study.*

Clinical Study
Type of clinical study. Note that this table should be repeated for each clinical study. *Examples: early feasibility, feasibility, stage I pivotal, stage II pivotal, pivotal, postapproval.*

Purpose	Purpose of study. *Examples: To demonstrate basic safety and proof of principle for XXXXX device; to demonstrate superiority to control with respect to surrogate endpoints; to confirm adequacy of surrogate endpoints in prediction of mortality and morbidity benefit.*
Study Design	Study design information. *Examples: Single-center, nonrandomized; multi-center randomized, double-blinded.*
Study Population	Study population, which should align with indications for use requested. *Example: Patients with upper extremity and lower extremity spasticity secondary to stroke, who meet all other study inclusion criteria and none of the study exclusion criteria.*
Inclusion Criteria	Inclusion criteria. *Examples: Patients over 18 years of age, on optimal medical therapy, and who have had symptoms for >3 months; to be determined pending feasibility study result but will align with requested indications for use.*
Exclusion Criteria	Exclusion criteria. *Examples: Patients eligible for physical therapy or surgery, unable to provide informed consent, enrolled in clinical study for same condition; to be determined pending feasibility study results but will align with requested indications for use.*
Safety Endpoints	Safety endpoints. *Example: No statistically-based safety endpoint, but the below adverse events will be captured; treatment-related adverse events as defined below <30%>.*
Effectiveness Endpoints	Effectiveness endpoints. *Examples: No statistically-based effectiveness endpoint, but the following parameters will be captured; patient success defined as improvement of ≥2 points on Quality of Life (QOL) scale and study success defined as >75% patients meeting success criteria; to be determined based on effect size estimates from feasibility study.*

Follow-Up Schedule	Follow-up schedule. *Example: Subject participation will last approximately 4 weeks as indicated below, adverse events will be captured throughout study, Week 1: enrollment, informed consent, baseline assessment, Week 2: procedure, Week 3: electrical parameter collection and QOL assessment, Week 4: electrical parameter collection and QOL assessment, study exit; to be determined based on feasibility study results.*

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Appendix 2: Illustrative Example: Breakthrough Device Designation Request

This appendix provides an example of information that may be helpful to include in a request for designation into the Breakthrough Devices Program.

Background Information

Device Description: This section provides an overview of the product, including principles of operation (including device components) and properties relevant to clinical function, if known. Images or engineering schematics are also encouraged for inclusion, as appropriate.

Indications for Use: This section presents indications for use for which you are requesting designation. The indications for use should clearly outline a patient population that meets the designation criteria.[21]

Regulatory History: This section details the history of previous FDA interactions and submissions, including feedback received and resolution of that feedback, as applicable. All relevant IDE, 513(g), and Q-Submission numbers should be included.

Designation Criteria

Criterion 1: Device "provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions."[22]

This section provides a discussion regarding how the first designation criterion is met by the proposed device and indications for use.

Criterion 2: Device meets one of the criterion's components below:

(A) Device "represent[s] breakthrough technolog[y];"[23]

(B) "[N]o approved or cleared alternatives exist;"[24]

(C) Device "offer[s] significant advantages over existing approved or cleared alternatives, including the potential, compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care (such as through self-directed personal assistance), or establish long

[21] See section 515B(b) of the FD&C Act (21 U.S.C. 360e-2(b)).
[22] See section 515B(b)(1) of the FD&C Act (21 U.S.C. 360e-2(b)(1)).
[23] See section 515B(b)(2)(A) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(A)).
[24] See section 515B(b)(2)(B) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(B)).

term clinical efficiencies;"[25] *or*

(D) Device availability "is in the best interest of patients."[26]

This section provides a discussion of which component(s) of Criterion 2 is/are met by the proposed device and indications for use. Please note that multiple components may apply; however, only one of these components must be met. For each component of Criterion 2 identified as being met, a discussion regarding how that component is met should be included.

Relevant patient preference information[27] may be included to support that a device and indications for use meet Criteria 1 and 2 above. Relevant patient perspectives could be based on attributes of the device type and/or patient population, or the specific device under review. Examples include, but are not limited to:

- information that captures relative desirability or acceptability of outcomes or other attributes that differ among alternative health interventions to patients, or the value patients place on the treatment or diagnosis;
- patient tolerance of risk to achieve benefit (e.g., given disease severity, chronicity);
- how well patients are able to understand the benefits and risks; or
- any other relevant patient-centric assessments.

Designation must be requested "any time prior to the submission of an application under section 515(c) [21 U.S.C 360e(c)], a notification under section 510(k) [21 U.S.C. 360(k)], or a petition for classification under section 513(f)(2) [21 U.S.C. 360c(f)(2)]."[28]

What is the planned marketing application?

- *PMA;*
- *De Novo request; or*
- *510(k).*

This section provides a discussion of which marketing application you plan to submit for your

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[25] See section 515B(b)(2)(C) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(C)).
[26] See section 515B(b)(2)(D) of the FD&C Act (21 U.S.C. 360e-2(b)(2)(D)).
[27] For additional information, please see the FDA guidance, "Patient Preference Information – Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and *De Novo* Requests, and Inclusion in Decision Summaries and Device Labeling" (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm446680.pdf) .
[28] See section 515B(c) of the FD&C Act (21 U.S.C. 360e-2(c)).

device, including a rationale for your selection. Only one application type should be selected. This discussion should state whether any marketing application for the device has already been submitted to the FDA for review, providing the submission number as applicable.