Safer Technologies Program for Medical Devices

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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Preface

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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[1]

The FDA is introducing a new, voluntary program for certain medical devices and device-led combination products[2] that are reasonably expected to significantly improve the safety of currently available treatments or diagnostics that target an underlying disease or condition associated with morbidities and mortalities less serious than those eligible for the Breakthrough Devices Program; for example, this may include devices treating or diagnosing non-life-threatening or reasonably reversible conditions. Devices and device-led combination products are eligible for this program if they are subject to review under a premarket approval application (PMA), De Novo classification request ("De Novo request"), or premarket notification (510(k)). Consistent with the Agency's statutory mission[3] to protect and promote public health, FDA believes that this "Safer Technologies Program" or "STeP" will help patients have more timely access to these medical devices and device-led combination products by expediting their development, assessment, and review, while preserving the statutory standards for premarket approval, De Novo marketing authorization, and 510(k) clearance. FDA has modeled STeP on the principles and features of FDA's Breakthrough Devices Program as mandated in section 515B of the Federal Food, Drug and Cosmetic Act (FD&C Act) (21 U.S.C. 360e-3) and further

[1] The Office of Combination Products (OCP) and the Center for Drug Evaluation and Research (CDER) were consulted in the preparation of this guidance.

[2] A combination product is defined in 21 CFR 3.2(e). For purposes of this guidance, device-led combination products refer to combination products subject to review under a premarket approval application (PMA), premarket notification (510(k)), or De Novo classification request.

[3] See section 1003(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

described in the FDA guidance document entitled "Breakthrough Devices Program"[4] (hereinafter referred to as the "Breakthrough Devices Program guidance document"). As resources permit, FDA intends for STeP to incorporate similar features offered under the Breakthrough Devices Program, such as interactive and timely communications, early engagement on Data Development Plans (DDP), prioritized review, and senior management engagement.

For the current edition of the FDA-recognized standard(s) referenced in this document, see the FDA Recognized Consensus Standards Database.[5] For more information regarding use of standards in regulatory submissions, please refer to the FDA guidance titled "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices"[6] and "Standards Development and the Use of Standards in Regulatory Submissions Reviewed in CBER."[7]

FDA recognizes and anticipates that the Agency may need up to 60 days to perform activities to operationalize this Safer Technologies Program following issuance of the final guidance. FDA does not intend to accept requests for inclusion in STeP within this time period.

FDA's guidance documents, including this draft guidance, 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. Background

FDA is responsible for protecting and promoting public health by ensuring the safety, effectiveness, and security of medical products.[8] Additionally, FDA is responsible for advancing public health by helping to provide timely access to innovations that make medical products and their use safer and more effective.[9] In recent years, FDA has developed policies and implemented new programs designed to promote patient access to innovative and safe new therapies and diagnostics. An important example of this approach is the Breakthrough Devices Program, which superseded the Expedited Access Pathway and Priority Review Program. The Breakthrough Devices Program is intended to expedite the development and review of certain devices that meet the designation criteria for the program and treat life-threatening or irreversibly debilitating diseases or conditions.[10]

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[4] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/breakthrough-devices-program.
[5] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm.
[6] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices.
[7] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/standards-development-and-use-standards-regulatory-submissions-reviewed-center-biologics-evaluation.
[8] For more information about CDRH's vision for medical device safety, see "Medical Device Safety Action Plan: Protecting Patients, Promoting Public Health," available at https://www.fda.gov/about-fda/cdrh-reports/medical-device-safety-action-plan-protecting-patients-promoting-public-health.
[9] See FDA's "Mission," available at, https://www.fda.gov/about-fda/what-we-do.
[10] The designation criteria are defined in section 515B of the FD&C Act and described in the Breakthrough Devices Program guidance document.

FDA recognizes that, although medical products provide great benefits to patients, they also present risks. FDA strives to permit marketing only for products with a favorable benefit-risk profile. However, patients may experience a wide range of adverse events attributed to use of the medical product including those that are considered serious, resulting in death or serious injury.[11] These types of events may significantly impact patients and their quality of life. Safety and innovation are both important priorities for the Agency, and improvements in each of these areas are expected to result in increased quality of life and health benefits for patients, while providing a reasonable assurance of both safety and effectiveness.

As a complement to the Breakthrough Devices Program, FDA believes that advancements in medical devices that are ineligible for the Breakthrough Devices Program but offer a significant safety advantage in treating and/or diagnosing less serious diseases or conditions can also provide an important public health benefit. Therefore, FDA is developing STeP to help spur safety innovation for medical devices and to provide patients timely access to devices that are not eligible for the Breakthrough Devices Program and may offer significant improvements to the safety profile of available medical treatments.[12] FDA believes that efforts to improve safety are directly related to improving overall clinical benefits and may also help patients experience fewer serious adverse events.

III. Program Principles

Similar to the Breakthrough Devices Program, STeP is comprised of two phases. In the first phase, interested sponsors formally request inclusion in STeP through a Q-submission (Section IV and Appendix 1). The second phase encompasses actions to expedite the development of the device and the prioritized review of subsequent regulatory submissions (e.g., pre-submissions, marketing submissions) (Section V).

The principles below describe the philosophy of STeP and the approach FDA intends to take for review of devices accepted into the program. As resources permit, FDA intends to leverage many of the principles of the Breakthrough Devices Program for STeP in order to expedite the development and review of devices that have the potential to significantly improve safety. As part of the program, FDA and the sponsor should work collaboratively to define an efficient device development path towards obtaining an FDA marketing authorization. To benefit from the policies outlined for STeP, the commitment on behalf of the sponsor to resolve all scientific and regulatory issues in a timely manner should match that of FDA. FDA believes that effective communication (e.g., interactive review), collaboration, and the sponsor's commitment to fulfilling all regulatory and scientific requirements are necessary to expedite the availability of safe and effective medical devices.

[11] The types of events that must be reported to FDA pursuant to 21 CFR part 803 are described in the FDA guidance document entitled "Medical Device Reporting for Manufacturers," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/medical-device-reporting-manufacturers.

[12] See "Medical Device Safety Action Plan: Protecting Patients, Promoting Public Health," available at https://www.fda.gov/about-fda/cdrh-reports/medical-device-safety-action-plan-protecting-patients-promoting-public-health.

FDA intends to evaluate resources throughout the device development, assessment, and review processes to make the best use of FDA's resources and maximize the impact of STeP. However, when necessary, FDA plans to prioritize resources for the Breakthrough Devices Program over STeP because the Breakthrough Devices Program is statutorily mandated.

A. Interactive and Timely Communication

For devices accepted into STeP, FDA intends to provide interactive and timely communication with the sponsor during device development and throughout the review process for Q-submissions, Investigational Device Exemption (IDE) applications, PMAs, certain PMA supplements (i.e., Panel Track Supplements, 180 Day PMA Supplements), 510(k)s, and/or De Novo requests. To promote collaborative dialogue and interaction between FDA and the sponsor, both parties should, as applicable:

- agree on the goals of the interaction and feasibility of response timeframes prior to submission of, or early in the review of, one of the relevant regulatory submissions listed above;
- utilize redlined versions of documents being reviewed and/or revised interactively for transparent communication concerning proposed changes; and
- utilize summary tables, documents, and/or FDA correspondence (e.g., written feedback, meeting minutes) to communicate points of agreement, disagreement, or unresolved issues at the conclusion of a review period.

Given that there may be novel scientific aspects of products in STeP, FDA may need to interact with external experts or an Advisory Committee to reach various regulatory decisions.[13] In the event that such consultation is undertaken, FDA intends to follow the approach outlined in Section II.A, of the Breakthrough Devices Program guidance document.

B. Review Team Support

Regulatory submissions (i.e., Q-submissions, IDEs, and marketing applications as listed above in Section III.A.) for devices accepted into STeP come with review team support and senior management (e.g., Office director or designee representing Office director) engagement, as resources permit. Specifically, senior management intend to be involved in regulatory submissions for devices accepted into STeP to ensure adherence to programmatic principles and to support efficient and timely dispute resolution when points of disagreement cannot be resolved quickly.

FDA intends for review teams of devices in STeP to be trained on programmatic principles and features so that they are prepared to apply novel approaches to regulatory and device development challenges.

[13] For more information, see FDA's guidance, "Procedures for Meetings of the Medical Devices Advisory Committee," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/procedures-meetings-medical-devices-advisory-committee.

C. Review of Regulatory Submissions

FDA intends that the reviews of regulatory submissions for devices in STeP are prioritized in the appropriate review queue as resources permit and receive additional review resources, as available. Although prioritizing the review of devices in STeP is intended to help expedite patient access, FDA's past experience with the Priority Review Program[14] indicates that review times of the marketing submission may take longer for devices accepted into STeP than for other devices because their anticipated technological or design innovations may raise novel scientific issues. Similar to the Breakthrough Devices Program, we believe that STeP may enable patients to have more timely access to these devices than they would have otherwise had because of the earlier interaction between FDA and sponsors during the device development process to address issues related to meeting the statutory standard for marketing authorization.

Given that the purpose of STeP is earlier access to devices that address important safety issues, sponsors of devices under this program are expected to work interactively with FDA and respond to FDA requests, collect premarket and postmarket data, and market their devices, if authorized, in a timely manner. Sponsors of these devices should commit to resolving all scientific and regulatory issues during the review process.

D. Benefit-Risk Assessments and Pre/Post-Market Balance of Data Collection

As with all devices subject to either a PMA or De Novo request, devices accepted into STeP must meet the statutory standard of reasonable assurance of safety and effectiveness at the time of PMA approval or granting of a De Novo request. When deciding whether to approve a PMA or grant a De Novo request, FDA conducts a benefit-risk determination as described in the FDA guidance document "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications."[15] As part of the benefit-risk determination, FDA considers the totality of evidence regarding the extent of probable benefits and extent of probable risks of a device, including the extent of uncertainty in the benefit-risk information. For devices in STeP, FDA intends to use timely postmarket data collection, when appropriate for certain submission types, to facilitate expedited and efficient development and review as described in the FDA guidance documents, "Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval"[16] and "Consideration of

[14] 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 21st Century Cures Act), which applied only to PMAs. 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 submissions for devices. FDA withdrew this guidance on August 3, 2017. See https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/withdrawn-guidance.

[15] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/factors-consider-when-making-benefit-risk-determinations-medical-device-premarket-approval-and-de.

[16] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/balancing-premarket-and-postmarket-data-collection-devices-subject-premarket-approval.

Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions."[17]

When making substantial equivalence determinations for devices in STeP subject to 510(k) premarket review, FDA intends to follow the principles described in the FDA guidance document, "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]"[18] and, when appropriate, to apply benefit-risk policies in accordance with those described in the FDA guidance document "Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics."[19] As with devices reviewed under the PMA and De Novo pathways, devices accepted into STeP must meet the applicable statutory standard at the time of 510(k) clearance.

E. Efficient and Flexible Clinical Study Design

Specific indications or labeling statements regarding clinical benefit for devices in STeP should be supported by valid scientific evidence, including clinical data, in a manner consistent with least burdensome approaches as described in the FDA guidance document "The Least Burdensome Provisions: Concept and Principles."[20] For devices in STeP, FDA intends to consider proposals for efficient and flexible clinical study designs, including those incorporating real world data sources, that may be used to support the proposed indication and/or labeling.[21]

F. Manufacturing Considerations for PMA Submissions

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 device accepted for inclusion into STeP should submit PMA information as described in the FDA guidance, "Quality System Information for Certain Premarket Application Reviews."[22]

For application types that typically require a preapproval inspection (i.e., PMA), FDA intends to expedite the review of manufacturing and quality systems compliance, as applicable and as resources permit, for devices in STeP using approaches consistent with those established in Section II.G of the Breakthrough Devices Program guidance document.

[17] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/consideration-uncertainty-making-benefit-risk-determinations-medical-device-premarket-approvals-de.

[18] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k.

[19] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/benefit-risk-factors-consider-when-determining-substantial-equivalence-premarket-notifications-510k.

[20] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.

[21] See, for example, the guidance document "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices.

[22] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/quality-system-information-certain-premarket-application-reviews.

IV. Factors for STeP Acceptance and Review Process

Inclusion in STeP is only at the request of the sponsor and with FDA's agreement. To request acceptance into STeP, interested sponsors should first evaluate whether they believe their device meets the general eligibility factor (Section IV.A) and the specific program factors (Section IV.B).

A. General Eligibility Factor

To be eligible for STeP, the device should be subject to marketing authorization via the PMA, De Novo request, or 510(k) pathways.

As specified in Section I, FDA intends to consider device-led combination products for inclusion in STeP. However, as part of the review processes for acceptance into STeP, FDA intends to evaluate which constituent part of the product (i.e., device or drug/biologic) is providing the proposed safety improvement, and only consider products in which safety improvements are made to the device constituent part.

FDA intends to accept devices into STeP if FDA determines that, as described by the sponsor, the device meets the general eligibility factor specified here and both of the specific eligibility factors identified below.

B. Specific Eligibility Factors for Inclusion in STeP

For inclusion in STeP, devices:

1. should not be eligible for the Breakthrough Devices Program due to the less serious nature of the disease or condition treated, diagnosed, or prevented by the device; and

2. should be reasonably expected to significantly improve the benefit-risk profile of a treatment or diagnostic through substantial safety innovations that provide for one or more of the following:
   a. a reduction in the occurrence of a known serious adverse event,
   b. a reduction in the occurrence of a known device failure mode,
   c. a reduction in the occurrence of a known use-related hazard or use error, or
   d. an improvement in the safety of another device or intervention.

C. Considerations for Evaluating Specific STeP Eligibility Factors

(1) First Factor

The first specific eligibility factor in Section IV.B describes the severity of the disease or condition that a device in STeP is intended to address. A central tenet of the Breakthrough Devices Program is that only devices that treat or diagnose life-threatening or irreversibly debilitating diseases or conditions may be considered for designation based on certain statutory

criteria.[23] FDA recognizes, however, that medical products are used to treat a wide variety of health conditions not all of which have such serious morbidities, but which may still impact patients' health and quality of life. Timely access to safer, medical devices for less serious conditions is expected to be important in improving health outcomes, and it is these devices that are the focus of STeP. Specifically, FDA intends to include in STeP devices that have the potential to significantly improve the safety of existing treatments or diagnostics intended for use in diseases or conditions that would be considered non-life-threatening or reasonably reversible. These diseases or conditions could affect patient quality of life or be debilitating for short timeframes, their health consequences might not significantly impact daily function, and/or they might not progress to a more serious disease or condition.

(2) Second Factor

While the first specific eligibility factor considers the severity of the disease or condition the device is intended to address, the second factor in Section IV.B considers how a device in STeP is expected to improve the benefit-risk profile of a treatment or diagnostic compared to alternatives for the identified disease or condition, as well as the significance of the expected improvement. This second eligibility factor encompasses several elements including the anticipated significant improvement to the benefit-risk profile, the type of the safety innovation proposed, and whether the device addresses one of four specific categories of safety improvement. Below is a discussion of how FDA intends to consider each of these elements for the purpose of evaluating the second eligibility factor.

First, FDA intends to consider whether the device is reasonably expected to have a significant improvement in the benefit-risk profile relative to other available treatment or diagnostic alternatives for the disease or condition where there are known serious adverse events and/or safety concerns (e.g., as identified in an FDA Safety Communication or medical device recall,[24] or otherwise identified as a significant safety issue of public health importance). FDA expects that safety improvements generally should not compromise the device's effectiveness. Additionally, as part of this evaluation, FDA will consider whether the safety profile of the new device introduces the potential for new serious adverse events or use-related hazards due to the proposed innovation. For example, a modification to a device made for the purpose of realizing a safety improvement should not also be reasonably expected to increase the rate of a different type of serious adverse event associated with the device or its use. FDA anticipates that requests for STeP inclusion will primarily focus on medical devices offering a potential significant safety improvement over other medical devices that are legally marketed in the United States. FDA also intends to consider devices for inclusion in STeP that have the potential for significant safety improvements over the current standard of care, which may include FDA-approved drugs or biologics, or other technologies.

Second, FDA intends to consider the significance of the anticipated safety benefit and if the anticipated improvement in the benefit-risk profile is through substantial safety innovations. For the purposes of this evaluation, a substantial safety innovation is one that incorporates an

[23] The designation criteria are defined in Section 515B of the Federal Food, Drug and Cosmetic Act (FD&C Act) and described in the Breakthrough Devices Program guidance document.

[24] A collection of medical device safety information can be found at the following link: https://www.fda.gov/medical-devices/medical-device-safety.

innovative technological feature or represents an innovative use of a technology to accomplish the safety improvement. Illustrative examples of innovative technological features may include changes to surface physicochemical properties, software, or material manufacturing method. As part of this evaluation, FDA intends to consider the principles of operation of the device and preliminary data from non-clinical or clinical sources and/or literature analyses. A complete dataset of clinical evidence is generally not expected in a request for inclusion in STeP. FDA intends to evaluate if there is a reasonable expectation for technical and clinical success of the device based on information submitted by the sponsor.

Finally, FDA intends to consider how the device is reasonably expected to achieve the significantly improved benefit-risk profile by considering whether the device meets one of the following four sub-parts.

a. A reduction in the occurrence of a known serious adverse event

For this sub-part, the device should be reasonably expected to result in a significant reduction in the occurrence of a known serious adverse event. FDA recognizes that, while some medical products do not directly treat or diagnose life-threatening diseases or conditions, their use may be associated with very serious adverse events including patient death or serious injury or illness. These would include serious injuries or illnesses that lead to development of life-threatening conditions, disability or permanent damage, or subsequent treatment or intervention to prevent permanent impairment or damage.[25] Modifications to an existing medical device that address these serious adverse events or a proposed new device that would reduce the occurrence of these serious adverse events, based on the principles of operation of the device, would likely be considered to meet this sub-part. For the purposes of STeP, FDA intends to consider serious adverse events that are attributable or reasonably attributed to use of the device that occur in acute timeframes following treatment or diagnosis (days to months) as well as those that are associated with long term adverse outcomes (occur months to years following treatment or diagnosis). Illustrative examples of devices that meet this sub-part may be expected to improve safety by:

- significantly reducing or eliminating infections associated with death, life-threatening conditions, or permanent disability, or
- significantly reducing or eliminating debilitating symptoms that manifest after device implantation.

b. A reduction in the occurrence of a known device failure mode

For this sub-part of Factor 2, FDA intends to consider whether the device reduces the occurrence of a known failure mode[26] that results in serious adverse health consequences,[27] including those that result in death, are life-threatening, or involve permanent or long-term injuries to patients. Devices may be considered to meet this sub-part if the failure is known to occur and not solely if

[25] See "serious injury" as defined in 21 CFR 803.3(w).

[26] For the purpose of this guidance, "failure mode" means "the manner in which failure occurs" and is intended to be used within the context of a risk management framework which may include formal failure mode and effects analysis (FMEA). See, for example, IEC 60812: *Analysis techniques for system reliability – Procedure for failure mode and effects analysis (FMEA)* and ISO 14971: *Medical devices – Applications of risk management to medical devices*, for additional information.

[27] See "serious, adverse health consequence" as defined in 21 CFR 810.2(j).

there is a risk for the failure. Additionally, the failure mode should be associated with serious adverse health consequences for the patient.

c. A reduction in the occurrence of a known use-related hazard or use error

Medical devices should be safe and effective for their intended use(s) and condition(s) of use including, for example, intended users and use environments, and manufacturers should design their devices such that they incorporate features that mitigate use-related hazards or use errors. Generally, use-related hazards and use errors result from user operation of, or interaction with, the device and do not represent hazards that are consequences of either device or component failure or are inherent to device design or material features. FDA's guidance document "Applying Human Factors and Usability Engineering to Medical Devices,"[28] defines both use-related hazards and use errors. Use-related hazards and use errors that result in serious safety issues can and do occur and may affect not only the patient but also the user of the device. In addition to the patient, the user of the device may include a clinician or other person directly involved in the administration and use of the device. For the purposes of inclusion in STeP, FDA intends to consider medical devices with substantial safety innovations that improve upon use-related hazards or use errors associated with the device design or operational features rather than those associated with inadequate or unclear labeling (e.g., instructions for use).

d. An improvement in the safety of another device or intervention

When evaluating this sub-part, FDA intends to consider if the medical device is reasonably expected to offer a specific type of improved safety benefit for another medical device or intervention. In some cases, this improved safety benefit might come from the device being evaluated for inclusion in STeP acting as an accessory[29] to other medical devices. This subpart may, however, also apply to finished devices that are not accessories.

D. Additional Considerations for STeP Acceptance Review

(1) Regulatory Path

As described in Section III.A, as part of the acceptance process for STeP, FDA considers whether the planned marketing pathway is a PMA, De Novo request, or 510(k). However, accepting or denying a proposed device in STeP does not constitute a formal decision regarding the applicable regulatory pathway or device classification. Instead, accepting a device into STeP indicates that, based on the information provided in the request and other information known at the time, the Agency expects that submission of a PMA (or PMA supplement), 510(k), or De Novo request will be necessary for marketing authorization. When communicating acceptance or denial of a device into STeP, FDA does not intend to specify which type of marketing submission the sponsor will need to submit for the device.

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[28] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/applying-human-factors-and-usability-engineering-medical-devices.

[29] Medical device accessories are defined in the FDA guidance document entitled "Medical Device Accessories – Describing Accessories and Classification Pathways" (available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/medical-device-accessories-describing-accessories-and-classification-pathways) as a finished device that is intended to support, supplement, and/or augment the performance of one or more parent devices.

Additionally, some, but not all, devices accepted into this program that are intended to improve the safe use of another device under specific eligibility Factor 2d may be accessories to other devices. Acceptance of a device into STeP does not constitute a decision on whether the device is an accessory or on its risk classification. Please refer to FDA's guidance document "Medical Device Accessories – Describing Accessories and Classification Pathways"[30] for a discussion of how FDA evaluates whether a medical device is an accessory as well as the classification processes for devices that are considered accessories.

STeP is predicated upon expediting the development and review of devices that are reasonably expected to address significant safety issues associated with available treatments. Therefore, the safety improvement planned for the STeP device is relative to available technologies for treating or diagnosing the same disease or condition. FDA recognizes that many of the devices ultimately accepted into STeP are expected to offer safety improvements as compared to the use of other medical devices. Changes to a medical device that are intended to affect its safety profile and/or mitigate known safety issues are likely to require approval of a new PMA or PMA supplement,[31] granting of a new De Novo request, or clearance of a new 510(k).[32] As described in the FDA guidance document "Deciding When to Submit a 510(k) for a Change to an Existing Device,"[33] FDA anticipates that changes made to 510(k) devices intended to significantly affect safety, as is the intent of STeP, will require a new premarket submission to the FDA. The substantial equivalence evaluation in a 510(k) will not be impacted by acceptance of the device into STeP. However, proposed modification(s) may raise different questions of safety or effectiveness as compared to the unmodified version or other predicates. If the device cannot be found substantially equivalent through the 510(k) process,[34] the sponsor may choose to pursue marketing through either a PMA or De Novo request.[35]

[30] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/medical-device-accessories-describing-accessories-and-classification-pathways.

[31] The criteria for determining what type of application mechanism is needed when making device design or manufacturing changes to lawfully marketed PMA devices are described in 21 CFR 814.39 and elaborated on in the FDA guidance document entitled "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process.

[32] See FDA's guidance "Deciding When to Submit a 510(k) for a Change to an Existing Device" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device.

[33] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device.

[34] The framework for FDA's evaluation of substantial equivalence in 510(k) submissions is described in detail in the guidance document entitled "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k.

[35] See also https://www.fda.gov/medical-devices/premarket-submissions/premarket-approval-pma and "De Novo Classification Process (Evaluation of Automatic Class III Designation)" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/de-novo-classification-process-evaluation-automatic-class-iii-designation.

Finally, acceptance of a modified device into this program will not impact the obligations or responsibilities of a manufacturer with respect to any recall or correction (e.g., reporting requirements under 21 CFR 806). Please refer to the FDA guidance document "Distinguishing Medical Device Recalls from Medical Device Enhancements," which provides additional considerations for these types of device changes.[36]

(2) Timeframe for STeP Acceptance

Ideally, sponsors should submit a request for inclusion in STeP prior to FDA receipt of the marketing submission for that device. Additionally, FDA may consider requests for inclusion in STeP in parallel with a marketing submission or after a marketing submission has been submitted. It should be noted, however, that devices included in STeP during review of the marketing submission may not benefit from programmatic features to the same extent as those devices for which requests for inclusion in the program occur earlier in their development process.

(3) Multiple Devices for the Same Expected Safety Benefit

FDA might accept multiple devices into STeP that are intending to address the same safety issue or improvement. As a consequence, multiple regulatory submissions for devices intending to address the same safety issue may be pending simultaneously.

FDA recommends that each request for inclusion in STeP be limited to one device intending to address a significant safety concern(s).

E. Submitting a Request for Inclusion in STeP and FDA Review

Requests for inclusion in STeP should be submitted using the Q-submission process as described in the FDA guidance document "Requests for Feedback on Medical Device Submissions: The Q-Submission Program" (hereinafter, "the Q-Submission Guidance").[37] Requests for program inclusion should be sent to the Document Control Center at CDRH or CBER as applicable for the regulation of the device.[38] A sponsor intending to request inclusion in STeP should submit a Q-submission package containing the recommended information as described in **Appendix 1: Illustrative Example of a Request for Inclusion in STeP**. The inclusion request should be the only request contained in the Q-Submission. Requests for feedback on the device outside of the request for acceptance into STeP should be submitted separately. Furthermore, if sponsors are requesting inclusion in STeP and at the same time have other requests for feedback pending, they may wish to consider submitting those additional questions after FDA accepts or denies a device in STeP as FDA's feedback may incorporate STeP's additional programmatic features. In addition, note that requests for inclusion in STeP should be submitted separately from the submission of a marketing submission or IDE application.

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[36] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/distinguishing-medical-device-recalls-medical-device-enhancements.

[37] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.

[38] See FDA's guidance document "eCopy Program for Medical Device Submissions," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ecopy-program-medical-device-submissions.

FDA intends to accept or deny each request for inclusion in STeP within 60 calendar days of receipt. In general, FDA intends to interact with a sponsor by Day 30 regarding any requests for additional information needed to evaluate the request. It is helpful when a sponsor is available and responsive to FDA requests throughout FDA's review. If FDA does not receive additional information needed to evaluate a STeP request in a timely manner, it may result in denial of the request for inclusion in STeP.

F. Withdrawal and Disqualification from STeP After Program Acceptance

A sponsor may request to withdraw from STeP at any time. Such a request should be submitted in writing to FDA as a withdrawal amendment to the Q-submission number under which inclusion into STeP was requested.

FDA does not intend to disqualify a device from further participation in STeP on the basis of another STeP device that was intended to address the same safety issue receiving PMA approval, having a De Novo request granted, or receiving clearance of a 510(k).[39] However, FDA may disqualify a device from further participation in STeP at any time upon written notice to the sponsor if FDA determines that:

- for other reasons, the device is no longer eligible for STeP based on available information; or
- the information submitted in support of a request for inclusion in STeP, including, without limitation, the Q-submission requesting inclusion in STeP or any related premarket submission, contained an untrue statement of material fact or omitted material information, including false statements relating to data collection.

V. Mechanisms for Feedback on Development of Devices in STeP

To facilitate an interactive and expedited approach to device development and similar to features outlined for devices granted Breakthrough designation, as resources permit, FDA intends to offer sponsors of devices accepted into STeP several voluntary options for early and regular interaction with FDA as device development progresses. A sponsor who wishes to request feedback on a device that has been accepted into STeP may select one or more of the options described below in Sections A-C; use of these options is not mandatory.

The options available for STeP include (1) a sprint discussion (See Section V.A), and (2) review of a Data Development Plan (DDP) (See Section V.B). We consider these options to be subsets of pre-submissions. When submitting a request for feedback on a device accepted into STeP, sponsors should specify if they are requesting one of these special program features available to facilitate the expedited review. Additionally, sponsors of devices accepted into STeP also have the option to request feedback from FDA through mechanisms that are available for devices,

[39] This policy is consistent with program requirements for the Breakthrough Devices Program as required by section 515B(d)(3) of the FD&C Act (21 U.S.C. 360e-3(d)(3)).

generally. For example, they may submit traditional pre-submissions whose scope is more consistent with typical requests for feedback received through the pre-submission program (Section V.C). FDA intends to follow the approaches and review procedures for these optional mechanisms for feedback as outlined in Section IV. of the Breakthrough Devices Program guidance document.

The regulatory mechanisms described in this section for obtaining FDA feedback on devices in STeP may also be used for device-led combination products accepted into the program. However, it is important to note these products may raise additional scientific challenges which could influence the feedback that FDA provides. Interactive review of complex scientific issues requiring expertise from a different Center may require additional time to resolve. When CDRH or CBER receives a Q-submission, IDE, or marketing submission for a device-led combination product that has been accepted into STeP, CDRH or CBER intends to notify the consulting Center(s) of its receipt. Furthermore, the appropriate review staff from the consulting Center(s) should be included in relevant meetings to ensure that the entire combination product review team is aware of the issues discussed and that they are engaged, as needed, in the review.[40]

Sponsors should recognize that, even though the FDA may have already reviewed the sponsor's protocols/plans in a sprint discussion, DDP, or pre-submission, this does not guarantee approval, clearance, or granting of future marketing submissions. Additional questions may be raised during the review of the future submission when all information is available and considered as a whole. Although sprint discussions, DDP reviews, and pre-submissions 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 by the sponsor and other information known at that point in time.

FDA intends that the feedback the Agency provides in response to DDP requests, as part of a sprint discussion, or through the pre-submission process will not change, provided that the information submitted in a future IDE or marketing submission is consistent with that provided in the feedback request 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 the feedback was provided. For example, FDA might 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 intends to acknowledge a change in the advice and clearly document the rationale for the change and the appropriate managerial concurrence.

[40] While the lead Center is the primary contact point for combination product sponsors, OCP is available to participate in meetings or otherwise engage on regulatory matters for these products upon request (see section 503(g)(8) of the FD&C Act, 21 U.S.C. 353(g)(8)). For further information on combination products and OCP, see the OCP webpage at https://www.fda.gov/CombinationProducts/default.htm.

A. Sprint Discussion

To support sponsors needing timely resolution of non-clinical or clinical evaluation 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) which FDA intends to expedite from the review timelines for traditional pre-submissions[41] as resources permit. The number, format, and duration of interactions within a sprint discussion may vary based on project needs and should be defined *a priori* by the sponsor and FDA. FDA recommends that sponsors limit the content of the sprint request to one general topic (e.g., animal study protocol) and specific goals thereof.

During an open sprint review period, FDA recommends that the sponsor email draft meeting minutes to FDA for comment and inclusion in the administrative record for the sprint submission. Following closure of a sprint discussion, sponsors may additionally submit a formal meeting minutes Q-submission amendment to FDA for review that documents all of the teleconferences and/or face-to-face meetings held throughout the sprint review. To submit the formal meeting minutes Q-submission amendment, sponsors should use the process described in the Q-submission Guidance. FDA intends to follow the timeline and procedures established for other meetings under the Q-Submission Program when reviewing formal meeting minutes Q-submission amendments.

Additional information regarding the general conduct of a sprint discussion and example formats are included in Section IV.A of the Breakthrough Devices Program guidance document.

B. Data Development Plan (DDP)

Sponsors of devices in STeP may request coordination with FDA regarding review of a DDP. The DDP is an optional, 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. The DDP may include either clinical evaluation strategies, non-clinical testing approaches, or both, as well as the anticipated timeframe for submitting results of these evaluations to FDA for review (e.g., in an IDE application for a pivotal study). While the optimal timeframe for submission of a DDP will vary depending on the device, it may be most beneficial to initiate DDP discussions with FDA soon after acceptance into STeP. For additional information on DDPs, please refer to Section IV.B of the Breakthrough Devices Program guidance document. FDA encourages sponsors to consider the non-clinical testing that will be needed to support the regulatory review of their device early in development and to discuss the planned approach with FDA. Additionally, sponsors of devices accepted into STeP may outline in their DDP any proposals to evaluate the clinical impact of safety improvements that balance the amount of data collected pre- and post-market for PMAs.

FDA review of a DDP may follow a similar model as the sprint discussion described above and is not subject to an acceptance review. In general and as resources permit, FDA anticipates that feedback on a DDP will be provided in less time than would be expected for a traditional pre-

[41] Review timelines for Pre-Submissions are described in the FDA guidance document entitled "Requests for Feedback on Medical Device Submissions: The Q-Submission Program" available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.

submission.

C. Other Pre-Submissions for STeP Devices

FDA recognizes that some sponsors of devices accepted for inclusion in STeP may wish to engage with FDA on a broader scope of topics in a single pre-submission than may be discussed in one of the options presented above in Sections V.A and B. For these requests, the sponsor may submit a pre-submission as described in the Q-submission Guidance and specify that it is for a device accepted into STeP. As resources permit, review teams will prioritize these submissions and develop an appropriate timeline for feedback with the sponsor that, when possible, does not exceed review timelines for traditional pre-submissions.[42]

D. Regular Status Updates

FDA and the sponsor of devices accepted into STeP may agree to have regular (e.g., bimonthly) status updates outside of a formal regulatory submission to the Agency. Through these interactions, FDA and the sponsor may discuss general progress of the project (e.g., timeframe for a planned marketing submission) and next steps or plans for future discussions. Importantly, FDA does not plan to provide feedback on device development progress or data during status updates. For more detail regarding status updates, please refer to Section IV.E of the Breakthrough Devices Program guidance document.

[42] Review timelines for Pre-Submissions are described in the FDA guidance document entitled "Requests for Feedback on Medical Device Submissions: The Q-Submission Program" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.

Appendix 1: Illustrative Example: Recommended Contents of a Q-Submission Request for Inclusion in STeP

This appendix outlines the recommended information that should be included in a Q-submission requesting inclusion in STeP.

Background Information

Device Description: This section should provide an overview of the device or device-led combination product (including device, drug, and/or biologic constituent parts), including principles of operation and properties relevant to clinical function, if known. Images or engineering schematics are also encouraged for inclusion, as appropriate.

Expected Safety Improvement: This section should provide a clear description of the safety issue that the device is intending to address and rationale for the seriousness of the adverse events associated with the safety issue. Additionally, the sponsor should describe any technological advances or features of the device intended to improve safety.

Indications for Use: This section should present the sponsor's proposed indications for use. If the sponsor plans on including specific claims related to safety improvement, those claims should be included as well.

Regulatory History: This section should detail the history of previous FDA interactions and submissions, including feedback received and resolution of that feedback, as applicable. All relevant IDE, 513(g)[43], and Q-submission numbers should be included.

Justification for Meeting General Eligibility Factor

What is the planned marketing submission?

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

This section should provide a discussion of which marketing submission the sponsor plans to submit for the device, including a rationale for such selection. Only one submission type should be selected.

Justification for Meeting STeP Eligibility Factors

Eligibility Factor 1: The device seeking inclusion in STeP is "not eligible for the Breakthrough

[43] See FDA's guidance "FDA and Industry Procedures for Section 513(g) Requests for Information under the Federal Food, Drug, and Cosmetic Act" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-and-industry-procedures-section-513g-requests-information-under-federal-food-drug-and-cosmetic.

Devices Program due to the less serious nature of the disease or condition treated or diagnosed."

This section should provide a discussion regarding how the first STeP eligibility factor is met by the proposed device and indications for use.

Eligibility Factor 2: The device seeking inclusion in STeP is reasonably expected to significantly improve the benefit-risk profile of a treatment or diagnostic through substantial safety innovations that provide for one or more of the following:

a. A reduction in the occurrence of a known serious adverse event,

b. A reduction in the occurrence of a known device failure mode,

c. A reduction in the occurrence of a known use-related hazard or use error, or

d. An improvement in the safety of another device or intervention.

This section should provide a discussion of which sub-part(s) of Eligibility Factor 2 is/are met by the proposed device and indications for use. Please note that multiple sub-parts of Factor 2 may apply; however, meeting only one of these sub-parts would still support inclusion in STeP if the other eligibility factor is otherwise met. For each sub-part of Eligibility Factor 2 identified as being met, a discussion regarding how that sub-part is met should be included in the request for inclusion in STeP.