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Qualification of Medical Device Development Tools

Guidance for Industry, Tool Developers, and Food and Drug Administration Staff

Document issued on July 17, 2023.

Document originally issued on August 10, 2017.

This document supersedes Qualification of Medical Device Development Tools: Guidance for Industry, Tool Developers, and Food and Drug Administration Staff issued August 10, 2017.

For questions about this document, contact the Medical Device Development Tools program by e-mail at MDDT@fda.hhs.gov.



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

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Preface

Public Comment

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Qualification of Medical Device Development Tools

Guidance for Industry, Tool Developers, and Food and Drug Administration Staff

This guidance represents 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 document provides guidance on a voluntary program for qualification of medical device development tools (MDDTs) for use in evaluating devices subject to regulation by Center for Devices and Radiological Health (CDRH). CDRH believes that this policy will facilitate the development and timely evaluation of medical devices, by providing a more efficient and predictable means for collecting the necessary information to support regulatory submissions and associated decision-making.

The purpose of this guidance is to describe the framework for voluntary proposal and qualification of an MDDT, including definitions of applicable terms, criteria for evaluating an MDDT for a specific context of use, considerations for qualification, and the contents of a qualification package. For purposes of this guidance, a submitter is a person, group, consortium, or organization (including the federal government) that takes responsibility for and initiates the MDDT qualification process using the procedures described in this guidance.

This guidance does not discuss the review of MDDTs (also referred to as "tools" in this guidance) that are submitted in individual premarket regulatory submissions for use with a particular medical device, nor does it address the specific evidentiary or performance expectations for the qualification of an individual MDDT submission.

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances 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 guidances means that something is suggested or recommended, but not required.

II. Definition of Key Concepts

For the purposes of this guidance, the following definitions apply and are consistent with the recent Biomarkers, Endpoints, and other Tools (BEST) resource.[1] This section includes brief definitions followed by examples and other explanatory information about the terms.

- **Medical Device Development Tool (MDDT)** is a method, material, or measurement used to assess the safety, effectiveness, or performance of a medical device. An MDDT is scientifically substantiated and can be qualified for use in device evaluation and to support regulatory decision-making within a specified context of use.

- **Context of Use (COU)** is a statement that fully and clearly describes the way the MDDT is to be used and the medical device development-related purpose of the use.

- **Performance Criteria** are objective performance measures of the MDDT outlined in the qualification plan that describe how the tool can be considered as suitable within the proposed context of use. Performance criteria may include, for example, measures of the proposed tool's consistency (across different sites and operators), accuracy and sensitivity. The performance criteria should be accompanied by acceptance criteria that outline when the performance criteria are satisfied and when the tool can be relied upon for regulatory decision making.

- **Proposal Package** is the initial MDDT submission or MDDT Proposal where the MDDT submitter provides the tool description, regulatory utility (how the tool supports safety, effectiveness, or performance of a medical device in a regulatory submission), qualification plan, and performance criteria to describe the expected performance of the tool.

- **Qualification Package** is the documented evidence, following the proposed qualification plan, comparing the actual performance of the proposed MDDT to the performance criteria detailed in the Proposal.

- **Qualification** is a conclusion based upon FDA review of the MDDT Qualification Package. A qualification decision signifies that the MDDT can be relied upon to facilitate regulatory decision making when it is used according to the qualified COU.

[1] The qualification definition in this guidance is consistent with the BEST definition. *See* BEST (Biomarkers, EndpointS, and other Tools) Resource; Glossary, https://www.ncbi.nlm.nih.gov/books/NBK338448/.

In general, MDDTs can be categorized into three types, distinguished primarily by how the tool measures relevant parameters: Non-clinical Assessment Models (NAMs), Biomarker Tests (BTs),[2] and Clinical Outcome Assessments (COAs).[3]

1. A **Non-clinical Assessment Model (NAM)** is a non-clinical test model or method that measures or predicts parameters of interest in regard to device safety, effectiveness, or device performance.

   Examples of NAMs include:
   - human or animal-based models to replace clinical testing;
   - *in vitro* models to replace animal testing;
   - tissue and other material phantoms to evaluate imaging or other devices; and
   - physics-, chemical- or biological- based computational models.

   Qualified NAMs may be used to evaluate a new material property, modifications to an existing design, or a device feature historically evaluated through other bench, animal, or human testing.

2. A **Biomarker Test (BT)** is a test or instrument used to detect or measure a biomarker.

   Reliable biomarkers can help reduce uncertainty during device development and evaluation by providing predictions about device performance. BTs used to measure biomarkers in patients before treatment can be used to select patients for inclusion in a clinical trial. BTs used to detect changes in biomarkers following treatment may predict or identify safety problems related to a therapeutic device or reveal the response to an intervention expected to predict clinical benefit from treatment.

   It is important to note that a BT being considered for qualification is conceptually independent of the biomarker (e.g., sphygmomanometer vs. blood pressure). A biomarker, however, cannot be qualified without a reliable means to measure it. In assessing BTs for qualification, CDRH will evaluate both the strength of evidence supporting the biomarker for the specified COU, as well as the performance characteristics of the test(s) used to provide the biomarker data. Test validity (e.g., precision and accuracy) should be demonstrated for the proposed COU.[4]

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[2] https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/glossary.biomarker/

[3] https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/glossary.clinical-outcome-assessment/

[4] The amount and type of new evidence needed to support qualification of a BT may also depend in part on whether there is any test or instrument for measurement of the biomarker that is already FDA cleared or approved for clinical use through premarket review, and if so, whether the proposed COU for the BT is consistent with the indication for use of the cleared or approved device. To qualify a BT to measure a biomarker for which there is no corresponding FDA cleared or approved device, test performance characteristics (e.g., precision and accuracy) should be demonstrated for the proposed COU. In contrast, MDDT qualification proposals involving an FDA cleared or approved test, or involving biomarkers for which FDA has established the analytical performance criteria necessary for measurement for the specified COU, can make use of existing data that support the analytical validity of the test, so long as the MDDT submitter is legally authorized to do so. In either case, qualification depends on meeting performance criteria for the test as an MDDT for the proposed COU.

3. A **Clinical Outcome Assessment (COA)** describes or reflects how a person feels, functions, or survives and can be reported by a health care provider, a patient, a non-clinical observer (such as a parent), or through performance of an activity or task. COAs could be collected in the clinic or remotely (e.g., collected with the use of digital health technologies).

   A COA includes not only the measure that produces a score, but also the clearly defined methods and instructions for administering the tool, a standard format for data collection, and well-documented methods for scoring, analysis, and interpretation of results in the targeted patient population. COAs can measure treatment benefit directly or indirectly (e.g., a diary of rescue pain therapy used for pain intensity).

   The four common types of COAs are patient-reported outcome (PRO) measures,[5] clinician-reported outcome (ClinRO) measures,[6] observer-reported outcome (ObsRO) measures,[7] and performance outcome (PerfO) measures.[8] Other COAs used as a measure of patient benefit, safety, may be qualified as MDDTs.

III. Overview

A. What is an MDDT & MDDT qualification?

An MDDT is a method, material, or measurement used to assess the safety, effectiveness, or performance of a medical device. An MDDT is scientifically substantiated and can be qualified for use in device evaluation to support regulatory decision-making. Examples of MDDTs are non-clinical assessment models (NAMs), biomarker tests (BTs), and clinical outcome assessments (COAs). The use of a qualified MDDT by a medical device manufacturer is voluntary.

Qualification is a conclusion based upon FDA review of the MDDT Qualification Package. Qualification reflects CDRH's expectation that, within a specified context of use (statement that describes the conditions and boundaries within which the MDDT has been qualified for use), the results of an assessment that uses an MDDT can be relied upon in device evaluation and to support regulatory decision-making. In brief, qualification is a voluntary process to establish the scientific rigor associated with an MDDT for a specific use in supporting regulatory decision-making.

The intent of this voluntary CDRH MDDT program is to promote the development and use of MDDTs to streamline device development and regulatory evaluation. Once an MDDT is qualified for a specific COU, CDRH encourages MDDT developers to make their qualified MDDT(s) publicly available, which can include under a licensing arrangement, so that the MDDT(s) can be used by any medical device manufacturer for the qualified COU. CDRH reviewers should accept the MDDT for the qualified COU without the need to reconfirm the

[5] https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/glossary.patientreported-outcome/
[6] https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/glossary.clinicianreported-outcome/
[7] https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/glossary.observerreported-outcome/
[8] https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/glossary.performance-outcome/

suitability and utility of the MDDT when used in a CDRH regulatory submission. CDRH review divisions maintain the responsibility for evaluating regulatory submissions using the totality of evidence in addition to the information obtained from a qualified MDDT.

The existence of a qualified MDDT does not convey a requirement that the tool must be used during the device development or regulatory evaluation processes. Other scientifically valid tools or approaches may also be used. Moreover, the qualification of a tool does not prohibit the qualification of a similar tool with the same COU.

The availability of qualified MDDTs that can be utilized by many medical device manufacturers is expected to aid in streamlining device development and regulatory evaluation. To advance these goals, FDA only intends to qualify tools where FDA can make public certain high-level information about the existence of qualified tools and their utility. FDA will not make public any proprietary information without permission from the MDDT developer. FDA communication related to qualified MDDTs is discussed in more detail in Section V below.

B. Why is MDDT qualification beneficial?

Qualification, as described in this guidance, is intended to increase predictability in device evaluation and improve efficiency in regulatory decision-making by making it clear to medical device manufacturers that FDA accepts assessments from a qualified MDDT in support of demonstrating safety, effectiveness, or performance of a medical device, without need to reconfirm suitability and utility of the MDDT, when used within the qualified COU.

Furthermore, the MDDT program provides a mechanism for leveraging advances in regulatory science. Advancements in regulatory science help bridge the gap between research and development of medical devices and the delivery of high quality, safe, and effective devices to patients. CDRH is committed to advancing regulatory science, which provides the tools, standards, and approaches needed to evaluate the safety, effectiveness, and performance of the devices we regulate. Through continued advances, such as with the MDDT program, CDRH is modernizing the regulatory evaluation process and reducing the time and resources needed to develop and assess new medical devices.

Qualification also facilitates tool development and adoption, including through collaboration in a non-competitive setting, where multiple interested parties (individuals/stakeholders, companies/consortia, or organizations) may work together and pool resources to expedite development, validation, and use of an MDDT. CDRH encourages the formation of consortia or other collaborations to foster MDDT development programs to increase the efficiency of tool development through joint efforts and to reduce the resource expenditure of any individual person or company. As further detailed in this guidance, stakeholders who wish to discuss developing an MDDT for potential qualification should contact FDA.

Qualification also presents advantages for CDRH pertaining to review resources. Historically, if there was interest in using a particular tool to generate evidence in support of regulatory decisions, such as a PRO measure, each FDA device review team evaluated the data justifying the tool use for each regulatory submission on a case-by-case basis. With this program, the

review of the tool and its relevant data takes place outside the review of the individual regulatory submission and instead, is reviewed during the MDDT qualification process. Once qualified, the tool can then be relied upon by FDA staff within the qualified COU, without further detailed review of the suitability of the MDDT. Stakeholders can find instructions for using a particular qualified MDDT in the publicly available qualification summary documentation (i.e., the "MDDT Summary of Evidence and Basis of Qualification (SEBQ)") available at: https://www.fda.gov/medical-devices/medical-device-development-tools-mddt#mddts.

C. How could MDDTs be used in device evaluation and regulatory decision-making?

MDDTs can be used in demonstrating safety, effectiveness, or device performance and to support regulatory decision-making by facilitating the efficient provision of supporting evidence in non-clinical or clinical settings. MDDTs may be used in a variety of ways to collect, evaluate, and/or predict bench or *in vivo* performance. In addition, MDDTs may have a variety of roles in a device clinical study such as patient selection, study population enrichment, monitoring treatment response, predicting or identifying safety problems related to treatment with a medical device or identifying patients who are or are not candidates for certain forms of therapy. Appropriate use of qualified MDDTs may increase the efficiency of the device development and evaluation process by providing reliable predictions about device performance or by identifying patients more likely to respond to treatment or experience disease progression in the near future. Some examples of the specific roles for MDDTs in device evaluation include:

- to reduce test duration or minimize sample size, or replace a standardized non-clinical bench performance test, e.g., using as a computational model;
- to replace an evaluation typically conducted in human studies with an evaluation done in animal or engineering models;
- to reduce or minimize the use of animals, e.g., using a simulation, tissue scaffolds;
- for selection of clinical study subjects;
- to stratify patient population by predicted risk and/or effectiveness outcomes;
- for study population enrichment;
- for an intermediate endpoint measurement to support predictions for successful study outcomes;[9, 11]
- to determine technical parameters to inform labeling to ensure patient safety (e.g., MRI Safety Information, toxicology);

[9] An **intermediate endpoint** is itself a clinical endpoint concerning a symptom or measure of function that is not the ultimate outcome of the disease. Improvement according to an intermediate endpoint is of value to patients even if this does not lead to reduced morbidity or mortality. An intermediate endpoint may also be a clinical endpoint measured at an earlier timepoint than has historically been accepted. A treatment effect shown by an intermediate endpoint may also be taken as reason to expect a favorable ultimate outcome; in this sense the intermediate endpoint plays the role of a surrogate. For example, exercise tolerance is sometimes used as an intermediate endpoint in trials of treatments for heart failure.

- to develop a surrogate endpoint;[10, 11]
- for remote monitoring and endpoint collection;
- to provide standardized verification or validation tools for device algorithms or models; and
- for developing post-market surveillance methodologies such as methods or models capturing real world outcomes.

IV. CDRH Qualification Decision Framework

The voluntary qualification process consists of two phases, the Proposal Phase and Qualification Phase, which are described below.

We recommend eCopy submission packages be submitted electronically via the CDRH Customer Collaboration Portal ("CDRH Portal") as discussed in the following website: https://www.fda.gov/medical-devices/industry-medical-devices/send-and-track-medical-device-premarket-submissions-online-cdrh-portal. Once submitted via the CDRH Portal, the submission will be received by the CDRH Document Control Center (DCC). Alternatively, submission packages may be mailed to the CDRH DCC. The current mailing address for CDRH's DCC is provided on the eCopy Program for Medical Device Submissions webpage at https://www.fda.gov/medical-devices/how-study-and-market-your-device/ecopy-program-medical-device-submissions.

Use of the CDRH Premarket Review Submission Cover Sheet[12] for submissions made to CDRH is highly recommended to facilitate correct login and prompt routing to the appropriate review group. Submissions for these requests should be identified as an "MDDT" in the cover letter. Note that MDDT proposals and qualification packages, previously tracked as Informational Meeting Q-Submissions, are now tracked with a universal tracking number (UTN).

A. Proposal Phase

The goal of the proposal phase is an initial assessment to determine if the MDDT is suitable for qualification through the MDDT program. When determining whether to qualify a proposed MDDT, CDRH will first review the MDDT Proposal Package. The ability to review a proposal will depend on available FDA resources. Note that even if the tool is not yet fully developed,

[10] A **surrogate endpoint** is a measurement used in trials as a substitute for a clinical endpoint, and is expected to reflect clinical outcomes based on epidemiologic, therapeutic, pathophysiologic, or other scientific evidence. For example, blood pressure measurements are sometimes used as endpoints in trials of antihypertensive therapeutics, as a surrogate for clinical endpoints of stroke, myocardial infarction, or mortality.

[11] Use of **intermediate or surrogate endpoints** may allow for smaller trials or shorter follow-up, or be easier to measure than traditional clinical outcomes of a disease or condition. Optimal conditions for using intermediate or surrogate endpoints include when the traditional endpoint is a rarely occurring event or delayed in its presentation (as in certain chronic diseases); when measurement of the endpoint is invasive, uncomfortable, costly, or easily confounded; or when the treatment effect is small, and therefore would require trials of impractical size in order to meet statistical significance.

[12] See Form 3514, https://www.fda.gov/media/72421/download

CDRH intends to review proposals for these tools. If the proposal is accepted, CDRH will review the Qualification Package with the qualification data.

Those interested in seeking qualification should begin by submitting a proposal. A complete Proposal Package should include the following:

- **MDDT Description**
  - A description of the MDDT with sufficient detail for CDRH to understand the tool and how the tool is intended to support an assessment of safety, effectiveness, or performance to facilitate regulatory decision making.
  - The category of the MDDT (NAM, BT, COA) with appropriate explanation as described in Section IV.
  - A statement declaring if the proposed MDDT is a cleared or approved medical device.
  - A statement if the MDDT has been previously submitted to the MDDT Program or through the Drug Development Tool Program.[13]
  - A description of how the MDDT achieves the specified output. This could include schematics, photos, figures, engineering drawings, as well as labeling and instructions for use.

- **Context of Use (COU)**

  The COU is a key aspect of qualification. The amount and strength of evidence needed to support qualification depends largely on the defined COU.

  Once an MDDT is qualified, the COU defines the boundaries within which the available data adequately support use of the MDDT.

  The COU should describe the specific role of the MDDT in device development. A complete COU should include the following:

  - What the MDDT is intended to measure or assess (i.e., input and output of the tool).
  - How the tool is intended to be used, by whom, and the role of the MDDT in regulatory evaluation (e.g., for use in clinical studies, this includes the study population or disease characteristics, as well as specific use – diagnosis, patient selection, study endpoints).
  - The phase(s) of medical device development in which tool measurements can be used (e.g., design evaluation, animal testing, early clinical study, pivotal clinical studies to support market application, post-market study, or changes).
  - The limitations and constraints to the applicability of the tool (e.g., intended population, input parameters, environment of use).

[13] https://www.fda.gov/drugs/development-approval-process-drugs/drug-development-tool-ddt-qualification-programs

Since the COU is central to the appropriate use of the MDDT, we recommend that the COU be conveyed prominently when a tool developer offers its MDDT to medical device manufacturers.

- **Performance criteria**
  - The performance criteria for the MDDT should be objectively defined (where possible). The performance criteria should be accompanied by acceptance criteria that outline when the performance criteria are satisfied and when the tool can be relied upon for regulatory decision making.

- **Qualification Plan**
  - The MDDT submitter should provide a complete plan for collecting evidence to demonstrate that the tool reliably and accurately meets its intended purpose.
  - The qualification plan should include information and protocols describing how each performance criterion will be addressed.

- **Assessment of advantages and limitations** (see Section IV.B for additional details)
  - For the proposed COU and plan for evidence generation, the advantages and limitations around tool use should be identified.
  - The advantages should highlight the impact of tool use in support of regulatory decision making.
  - The limitations should accurately detail the conditions under which the tool should not be used or may not provide a meaningful assessment of safety, effectiveness, or performance of a medical device.

  The advantages and limitations may be further refined in the Qualification Phase, after a review of the evidence.

CDRH plans to review proposals with strong potential to meet a public health need and facilitate regulatory decision making. Each of the following include factors that would weigh in favor of the regulatory utility of the tool:

- MDDT provides a safety, effectiveness, or performance assessment of medical devices intended for life-threatening and/or serious diseases or conditions, underserved populations such as pediatric patients, or to promote and advance health equity.

- MDDT provides a safety, effectiveness, or performance assessment for novel or innovative technology with no established paradigm for regulatory assessment.

- MDDT provides an assessment where there are no/poor alternatives or an unmet scientific need (e.g., no consensus standards or established methods).

- Use of the MDDT allows for safer or less invasive, easier, more convenient, or less variable measurements than the alternative.

- Use of the MDDT has the potential to impact multiple device development programs.

For proposals that potentially meet one or more of the above factors, CDRH intends to notify MDDT submitters of its decision regarding proposal acceptance in writing approximately 90 days from receipt of the proposal. For proposals that are accepted, CDRH intends to recommend suitable next steps for the submission (e.g., request for revision, advance to qualification). For those proposals not accepted, CDRH plans to also provide the factor(s) contributing to this decision.

B. Qualification Phase

The goal of the qualification phase is to determine whether, for a specific COU, the tool is qualified based on the evidence provided. CDRH intends to review the evidence submitted in the Qualification Package in support of the proposed COU, and determine whether that evidence meets the performance criteria and supports the agreed upon Qualification Plan that was defined in the accepted MDDT Proposal. If the performance of the tool does not meet the performance criteria, then CDRH may make a determination to not qualify the tool, or may recommend a change to the COU within which the tool can be used to support regulatory decision-making. A complete Qualification Package should include:

- **MDDT Description** (as described above in Section IV.A).

- **COU** (as described above in Section IV.A).
    - The COU may be further refined during the Qualification Phase, based upon the review of the evidence submitted in support of the MDDT.

- **Qualification Plan** with all descriptive elements and protocols (as described above in Section IV.A).

- **Tool Evidence:**
  The amount and strength of evidence needed to support qualification of an MDDT will vary depending on the COU and the tool type. For example, an MDDT proposed for use for a specific medical device may need less data than a tool for use across different device types. The latter use may need more evidence of its validity due to the broader applicability or due to potential limitations of accepting an inaccurate MDDT. Submitters should explain how the strength of evidence for use of the MDDT is adequate to support the proposed COU. Evidence may include performance characteristics of the tool that would affect the usefulness of an MDDT, such as:

    - **Tool Performance Characteristics**: This evidence should demonstrate that the tool provides accurate and precise measurements. Sufficient data should be provided to adequately describe performance characteristics of the tool. Depending on the tool type, this evidence may include analytical, clinical, construct validity, external validity, reduction of bias, verification of the constitutive model, uncertainty quantification, and/or numerical convergence.

The type of evidence needed will vary depending on the tool type and COU and may include (but is not limited to):

- design verification;
- simulation results from computational models;
- bench performance data (including full test reports and protocols);
- animal performance data (including full test reports and protocols);
- clinical data (including full test reports, protocols, and all appropriate (pre-specified) statistical analyses to demonstrate the relationship between the tool and the COU);
- human factors testing; and/or
- literature articles (the full text article, a summary and a description of how the article supports qualification).

- **Reliability and Reproducibility**: This evidence should describe the degree to which the tool measurement is related to the outcome of interest. This should include evidence on the strength of that relationship and that the outcome of interest is repeatedly demonstrated in multiple studies or as a class effect.

- **Assessment of Advantages and Limitations of Qualification**

When assessing advantages and limitations, CDRH intends to consider the following factors:

- **Assessments of Advantages of Using the MDDT:**

  - **Type of advantage(s).** Advantages may include: significantly accelerating the time to develop and evaluate devices; allowing for shorter or smaller clinical or non-clinical studies; allowing for safer or less invasive, easier, more convenient, or less variable measurements than the alternative; and expediting the development of a novel technology of public health importance.

  - **Magnitude of advantage(s).** This may include: whether there is a potential to impact multiple device development programs; whether the COU addresses safety, effectiveness, or performance assessment of devices intended for life-threatening and/or serious chronic diseases or conditions, diseases/conditions where there are no or poor alternatives, underserved populations such as pediatric patients, or addresses health and healthcare disparities; or whether the MDDT is to be used for novel technology where there is no established paradigm for regulatory assessment.

- **Assessments of Limitations of Using the MDDT:**

- **Type of limitation(s)**. This includes an assessment of the conditions under which the performance of the tool is outside the performance criteria and the tool should not be applied or relied on for regulatory decision making.

- **Magnitude of limitation(s).** The scope of impact of making a decision based on inaccurate conclusions from a MDDT is based on the severity of risk, a comparison of the MDDT to its alternatives, and considering the COU.

- **Likelihood of limitation(s).** CDRH will consider how likely a particular risk is to occur. This could be based on the evidence in support of tool validity. For example, for a BT, this could be the likelihood of the MDDT reporting a false positive, false negative or false estimate of predictive value.

- **Mitigation of limitation(s).** The use of mitigations may minimize the risks of relying on the MDDT. For example, alternative complementary sources of information or confirmatory data from later time points may mitigate risks of decision-making based on information from an MDDT.

- **Summary of Evidence and Basis of Qualification** (see Section V)

CDRH plans to review the qualification package based on the decision framework described in Section IV. CDRH intends to qualify the MDDT if the tool is adequately described, the proposed COU is appropriately defined, the strength of evidence supports use of the MDDT within the proposed COU, and the probable advantages of using a tool outweigh the limitations for the proposed COU. Once CDRH has determined whether or not to qualify a tool, CDRH intends to notify the MDDT submitter in writing of the decision.

CDRH also intends to make public certain high-level information about MDDTs that are qualified, as described in Section V.

C. Potential Changes to Qualification Status

After an MDDT is qualified, its developer may wish to modify or expand its COU in response to new data or changing science. Modification or incremental expansion of the qualified COU over time may be undertaken through the MDDT program. There may also be situations where the basis upon which an MDDT was qualified has changed, and CDRH may re-evaluate the qualification decision.

D. Regulatory Considerations and Related Recommendations

Some MDDTs may meet the definition of a device in section 201(h) of the FD&C Act. Whether an MDDT is a medical device under section 201(h) of the FD&C Act will often depend on how

it is intended to be used. For example, if the MDDT is only for use in device development/ evaluation and is not for use in diagnosing or treating patients or study subjects, it is unlikely that it would be a device. On the other hand, if the MDDT is intended for use in diagnosing or treating, or aiding in the diagnosis or treatment of subjects in a clinical study or in clinical settings (outside of a clinical study), it would likely be a device and would not be an MDDT. Some MDDTs may have both device and non-device uses.

MDDT use in Clinical Studies

Devices intended for use in clinical investigations are exempt from most requirements applicable to devices, including premarket clearance or approval, as long as the investigation complies with applicable requirements, such as those under 21 CFR Part 812, or is exempt from such requirements.[14] As MDDTs would typically be used in the research or investigation of a medical device, MDDTs that are devices would typically be exempt from clearance, approval, and other device requirements, as long as the clinical investigation is compliant.

The use of an MDDT in a medical device clinical study does not change the Investigational Device Exemption (IDE) requirements for a given investigation (see 21 CFR Part 812). MDDT qualification does not obviate the need for a device developer to meet existing regulatory requirements or alter the benefit-risk threshold for regulatory decision-making related to a medical device; rather, it can facilitate the development and regulatory evaluation of a medical device by providing a more efficient and predictable means for collecting the necessary information to make regulatory assessments.

Qualification of an MDDT versus Clearance or Approval of a Medical Device

FDA qualification of an MDDT is different from FDA clearance or approval of a medical device. The type of evidence needed to support MDDT qualification is not the type of evidence that is needed to support marketing authorization for a medical device. As described in Section IV.B, FDA intends to evaluate tool performance characteristics, reliability and reproducibility when making qualification determinations. For clearance or approval, FDA evaluates whether the device is substantially equivalent or has a reasonable assurance of safety and effectiveness. As a result, using a qualified MDDT for clinical treatment or diagnosis of a patient when it is not cleared or approved could cause unexpected harm to patients.

Use of such tests for clinical diagnostic purposes may mislead healthcare providers and cause serious adverse health consequences to patients, who are not aware they are being diagnosed or treated based on results of tests with research or investigational products. To avoid confusing or misleading healthcare providers or patients, we recommend that tool developers make clear to users that qualification does not constitute FDA clearance or approval of the product as a medical device. For example, prominent statements that a tool developer makes in MDDT labeling and promotional materials regarding the qualification of its product by FDA as an

[14] If the device that is the subject of the investigation is significant risk, as defined at 21 CFR 812.3(m), the investigation, including use of the MDDT, is subject to all requirements in 21 CFR Part 812. If the device that is the subject of the investigation is not a significant risk device, the abbreviated requirements listed under 21 CFR 812.2(b) apply to the investigation, including the use of the MDDT. Investigations, including the use of an MDDT, that meet the criteria for one of the exemptions described at 21 CFR 812.2(c), including 812.2(c)(3), are not required to comply with 21 CFR Part 812 with the exception of section 812.119.

MDDT could be accompanied by language clarifying that the qualification of an MDDT does not constitute FDA clearance or approval. As another example, a tool developer could prominently convey that the qualified COU only applies to the use of the product in device development or evaluation, and that the tool has not been cleared or approved by FDA. In addition, to avoid labeling that is misleading, manufacturers of MDDTs that are also legally marketed medical devices should separate FDA-regulated labeling from materials used for the product as an MDDT. Tool developers may see different ways to address these labeling concerns and are encouraged to discuss other approaches with the FDA review team when proposing its MDDT.

MDDT qualification as compared to consensus standards and device-specific FDA guidance

The MDDT program[15] is not meant to replace the consensus standard development and recognition processor FDA's issuance of device-specific guidance documents. FDA views the MDDT program as a complementary program for evaluating and recognizing tools that are useful for medical device evaluation and to support regulatory decision-making.

Consensus standards are typically technical methods. For methods and approaches that are mature and that the community recognizes as a consensus standard, obtaining FDA recognition of the voluntary consensus standard may be a more appropriate pathway than MDDT qualification.

V. Communication to Public of FDA Qualification Decisions

Once an MDDT is qualified for a specific COU, FDA intends to accept its use by any medical device manufacturer for that COU. The intent of the voluntary FDA MDDT program is to promote the development and widespread use of tools to streamline device development and regulatory evaluation. FDA only intends to qualify tools where high-level information about such tools can be made publicly available. Specifically, FDA intends to publicly disclose a summary of evidence and basis of qualification (SEBQ) for qualified tools. An SEBQ includes:

- A brief description of the tool and the principle of operation.
- The qualified COU (as described in Section IV).
- A general summary of the evidence reviewed in support of tool qualification and a discussion of the strength of that evidence.
- An assessment of the advantages and limitations of using the MDDT for its qualified COU (as described in Section IV).
- Contact information for how a medical device manufacturer can contact the tool developer for access to the tool.

Any MDDT submitter with questions about the content and detail FDA intends to provide in an SEBQ should raise those with FDA during the proposal phase. FDA will obtain written permission from the tool developer before publishing the SEBQ to ensure that no proprietary information is shared.

[15] MDDT Program is available at https://www.fda.gov/medical-devices/medical-device-development-tools-mddt

Nothing about the MDDT program is intended to place limitations or requirements on MDDT licensing or fees, or the degree of access to intellectual property associated with an MDDT that a tool developer may give to a medical device manufacturer.