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DELIVERABLE 12: MDUFA IV INDEPENDENT ASSESSMENT – FINAL REPORT

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1. EXECUTIVE SUMMARY

Pursuant to the Medical Device User Fee Amendments of 2017 (MDUFA IV) Commitment Letter, the Food and Drug Administration (FDA) and device industry agreed to a comprehensive, independent assessment of FDA's process for conducting premarket review of medical devices.

Medical device user fees were first established under the Medical Device User Fee and Modernization Act of 2002 (MDUFMA), which required medical device manufacturers to pay a fee to FDA when submitting certain types of submissions for review. In turn, FDA agreed to achieve and report on certain performance goals and invest in additional activities to improve the medical device review process. These user fee agreements, which now include registration of establishments and listing of their devices, have been renegotiated with industry and signed into law every five years to renew the fee structure, performance goals, and other commitments to improve the medical device review program. In 2017, Congress enacted MDUFA IV as part of the FDA Reauthorization Act (FDARA), which governs device user fees and associated commitments from Fiscal Year (FY) 2018 through FY 2022.

Among the commitments in the MDUFA IV Commitment Letter was for FDA and industry to participate in a comprehensive assessment of FDA's premarket review program, conducted by an independent consulting firm. For this independent assessment, Booz Allen evaluated 11 assessment areas relevant to FDA's premarket medical device submission review processes to determine the impact of these areas on review performance and efficiency and determine whether FDA adhered to the commitments outlined in the MDUFA IV Commitment Letter. Booz Allen developed recommendations based on its findings across the assessment areas along with additional considerations for maturing the premarket review program. Table 1-1 details the specific objectives of the independent assessment within each of the 11 assessment areas.

Table 1-1. Objectives of Booz Allen's Independent Assessment for Each Assessment Area

Assessment Area	Objective of Assessment
Premarket Review Efficiencies	Evaluate FDA's premarket review program to identify efficiencies that have been realized as a result of process improvements and investments under MDUFA III and IV
Infrastructure and Full-Time Equivalent (FTE) Allocations	Evaluate premarket review program infrastructure and allocation of FTEs; specifically assess the hiring of FTEs as agreed to in MDUFA III and IV commitments
Training and Alignment	Assess the alignment of resource needs with the training and expertise of hires
Quality Management Program	Assess the effectiveness of the Quality Management program
Deficiencies	Assess the proportion of deficiencies in which FDA references the basis for the deficiency determination
Pre-Submission Program	Assess CDRH's Pre-Submission program
Third Party Review Program	Assess the efficiency of the Third Party Review program and suggest process improvements
Digital Health Program	Assess the effectiveness of the Digital Health program
Patient Science and Engagement (PSE) Program	Assess the effectiveness of the Patient Science and Engagement program
Real-World Evidence (RWE)	Assess the effectiveness of the Real-World Evidence program
Special 510(k) Conversions	Analyze conversions of Special 510(k)s to Traditional 510(k)s

Overall, the assessment found that FDA met the relevant commitments for the program areas specified for the independent assessment as agreed upon in the MDUFA IV Commitment Letter, with the exception of one guidance document that is pending final publication. This outcome is particularly notable given the disruptions caused by the ongoing Coronavirus Disease 2019 (COVID-19) public health emergency (PHE) and associated shifts in priorities and resources needed for the Center for Devices and Radiological Health's (CDRH) response. The full report details the findings and conclusions for each of the 11 assessment areas.

2. BACKGROUND

Device user fees enable the Agency to improve the consistency and efficiency of premarket review through investments in programs and processes. Under the provisions of MDUFA IV, Booz Allen performed an independent assessment of FDA's adherence to the MDUFA IV Commitment Letter and the effectiveness of certain programs targeted for improvement across 11 assessment areas.

CDRH is responsible for protecting and promoting public health by ensuring patients and providers have access to safe and effective medical devices and radiological products. To support these efforts, Congress gave FDA the authority to collect device user fees from medical device companies under MDUFMA. Congress intended for these user fees to complement appropriations and provide CDRH with the resources to review medical devices more efficiently and effectively. As part of MDUFMA, FDA published a Commitment Letter that outlined a series of performance goals and initiatives to promote the efficiency, consistency, and transparency of the premarket review process. FDA continues to update user fees in coordination with Congress and industry through a new series of commitments in 2007 (MDUFA II), 2012 (MDUFA III), and 2017 (MDUFA IV).

The MDUFA III and MDUFA IV Commitment Letters required independent assessments of FDA's medical device premarket review program. Under MDUFA III, the independent assessment took place in two phases. Phase 1 resulted in 11 recommendations for FDA to improve the premarket review process, information technology (IT) infrastructure, training and retention policies and practices, and quality management (QM) systems. CDRH responded with a Plan of Action to implement near-term activities for addressing the Phase 1 recommendations and long-term plans for further improving the efficiency of the cited processes and programs. Phase 2 of the assessment determined that FDA had completed the implementation projects to meet each of the 11 Phase 1 recommendations, but that there was insufficient time to assess the outcome and impact on the review program. Similarly, the MDUFA IV independent assessment took place over two phases, with the first phase serving as the culmination of the MDUFA III program evaluation. During this phase, it was found that FDA's efforts had resulted in positive impacts and outcomes of the medical device premarket review program. In addition, the final report identified additional opportunities to build on the success of these efforts, such as by enhancing review performance metrics and analytics, bettering search capabilities within CDRH IT systems, and developing resources to facilitate structured electronic submissions.

In this, the MDUFA IV Phase II assessment, Booz Allen evaluated whether FDA met the goals set forth in the Commitment Letter. For purposes of this report, various submission types (e.g., Premarket Approval Applications [PMAs], premarket notifications [510(k)s], Humanitarian Device Exemptions (HDEs), and De Novo requests) are collectively called marketing applications and the FDA decisions made on these applications collectively called marketing authorizations or marketing authorization decisions. The report examines 11 assessment areas relevant to the premarket review process: 1) Deficiencies; 2) Digital Health program; 3) Infrastructure and FTE Allocations; 4) Patient Science and Engagement program; 5) Pre-Submission program; 6) Premarket Review Efficiencies; 7) Quality Management program; 8) Real-World Evidence; 9) Special 510(k) Conversions; 10) Third Party Review program; and 11) Training and Alignment. While assessing these areas, Booz Allen identified additional considerations for continuous improvement in the premarket review program.

3. METHODOLOGY

Booz Allen developed a structured approach to assess FDA's adherence to its MDUFA IV commitments across the specified assessment areas.

To accomplish the objectives of this assessment, Booz Allen developed a methodology to evaluate progress in each assessment area, determine whether FDA met its MDUFA IV commitments, and identify opportunities to further improve the premarket review process. Booz Allen conducted the evaluation in three phases: 1) Plan Assessments; 2) Conduct Assessments; and 3) Report Findings, as depicted in Figure 3-1.

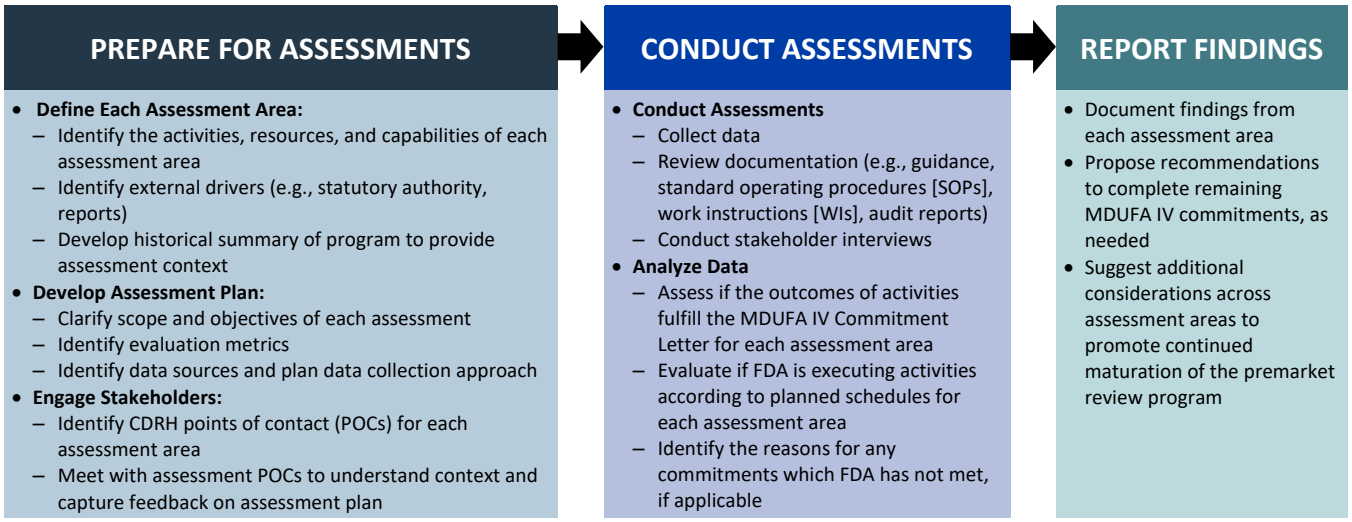


Figure 3-1. Booz Allen's Evaluation Methodology

The initial phase required developing a plan and documenting an approach for each assessment area. This involved defining the scope of each assessment area, identifying the necessary data and sources, and meeting with designated points of contact from each assessment area to validate our approach. In the next phase, Booz Allen gathered quantitative and qualitative data from various sources, including CDRH subject matter experts (SMEs), and internal and public-facing documentation. Booz Allen analyzed these data to determine whether the relevant MDUFA IV commitments were met and assess the effectiveness of targeted programs. In the final phase, Booz Allen documented the findings, recommendations, and potential additional areas for consideration in this report. FDA stakeholders and device industry organization representatives (i.e., Advanced Medical Technology Association [AdvaMed], Medical Device Manufacturers Association [MDMA], Medical Imaging and Technology Alliance [MITA]) were engaged throughout the process. Table 3-1 outlines the data sources used during this assessment.

Table 3-1. Summary of Data Sources Reviewed During the Independent Assessment

Category	Sources	Purpose
Documents and Training	Public documents (e.g., guidance, strategic plans, MDUFA III and IV annual and quarterly reports)	• Understand FDA plans and activities for meeting the MDUFA IV commitments • Determine whether FDA published guidance specified by the MDUFA IV commitments • Evaluate trends in FDA performance metrics
	Internal FDA procedural documents (e.g., SOPs, WIs)	• Understand FDA's infrastructure, processes, and procedures • Determine how FDA updated its internal processes and resources
Data	Communications data (e.g., internal emails, FDA webpage, news/press releases)	• Document FDA activities towards meeting the MDUFA IV commitments (e.g., meetings, staff outreach) • Gain insight into how FDA communicates program updates
	FDA audit data (e.g., audits conducted by Quality Management and Organizational Excellence program)	• Evaluate efforts toward meeting commitments for the Quality Management, Deficiencies, and Third Party Review assessment areas • Better understand audit program outputs
	Internal FDA submission and review data[1] (e.g., Pre-Submissions, Special 510(k) Conversions, Deficiencies)	• Evaluate FDA's progress toward meeting its commitments • Understand trends in program metrics
	FDA survey and evaluation data (e.g., Pre-Submission program survey of industry and FDA respondents, training evaluation data)	• Understand FDA employee and industry perspectives on the Pre-Submission program • Gain insight into Kirkpatrick[2] evaluation of training program
Stakeholder Engagement	Meetings with FDA assessment area points of contact	• Gain overview of assessment area and program activities • Discuss assessment progress and findings
	Meetings with industry organization stakeholders	• Understand industry's perspective on assessment areas • Discuss FDA's progress and initiatives

Based on the information gathered from these data sources, Booz Allen assessed whether FDA fulfilled the MDUFA IV Commitment Letter requirements and evaluated the effectiveness of select programs. In cases where FDA did not meet a requirement, Booz Allen assessed FDA's progress towards meeting the commitment and noted the remaining activities needed to meet the requirement. Booz Allen compiled and documented the results of all assessment areas in this evaluation report along with any recommendations and additional considerations for further improving the premarket review process or best practices to apply across other assessment areas.

[1] More details about analysis of these data can be found in their respective report sections.
[2] FDA worked with Kirkpatrick Partners to develop evaluations of its training programs.

4. ASSESSMENT FINDINGS

The findings in this section are organized and presented by the assessment areas defined for the independent assessment in the MDUFA IV Commitment Letter. Appendix A outlines the MDUFA IV Commitment Letter assessment areas that align to the findings in each section.

4.1 Premarket Review Efficiencies

To achieve its mission of protecting and promoting public health, FDA's premarket review program provides the Center with a pathway for staff to perform comprehensive reviews of medical device submissions to ensure they are safe and effective before approving them for marketing in the United States. The MDUFA IV commitments related to premarket review are multifaceted, with some focused on total submission review times shared between FDA and industry, while others are performance metrics for different stages in CDRH's review process. In addition, the Agency committed to exploring several other improvements related to updated infrastructure and promoting increased communication with applicants.

To meet these commitments, Booz Allen found that FDA developed and updated premarket and interactive review tools and processes, as well as implemented new opportunities for FDA and applicants to interact during premarket review of submissions. In addition, FDA met its commitments by having an independent consulting firm assess and describe the improvements that FDA made to the premarket review process, as well as how these initiatives have promoted consistency and efficiency in device review.

The assessment findings are presented in four sections:

- 4.1.1 Impact of Review Tools and Process Improvements on Consistency;
- 4.1.2 Effect of Review Process Changes on Efficiency and Communication;
- 4.1.3 Implementation of a Total Product Life Cycle (TPLC) Approach for Holistic Premarket Review; and
- 4.1.4 Total Time to Decision Outcomes and Feasibility of Establishing TTD Baselines.

4.1.1 IMPACT OF REVIEW TOOLS AND PROCESS IMPROVEMENTS ON CONSISTENCY

FDA has initiated or expanded several major activities focused on continuous improvement of review consistency in recent years. These include developing various tools for both review staff and industry, as well as establishing programs designed to streamline internal processes and facilitate consistency and quality in device reviews. This section describes how FDA met each of the commitments shown in Table 4-1. The findings are described in the following sections, organized by the tool or process improvement:

- 4.1.1.1 Submission Memo and Review Templates (SMART);
- 4.1.1.2 Electronic Submission Template and Resource (eSTAR);
- 4.1.1.3 Focal Point Programs;
- 4.1.1.4 Process Improvement Program.

Table 4-1. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Evaluate FDA's premarket review program to identify efficiencies that should be realized as a result of the process improvements and investments under MDUFA III and IV. • Develop electronic submission templates that will serve as guided submission preparation tools for industry to improve submission consistency and enhance efficiency in the review process. • By FY 2020, the Agency will issue a draft guidance document on the use of the electronic submission templates. FDA will provide an opportunity for public comment on the guidance. No later than 12 months after the close of the public comment period, the Agency will issue a final guidance. FDA will implement the guidance once final. In addition, the Agency will update the Guidance "eCopy Program for Medical Device Submissions" to reflect the respective changes to the technical standards and specifications.

4.1.1.1 SUBMISSION MEMO AND REVIEW TEMPLATES (SMART)

SMART templates are designed to promote a more consistent premarket review process by organizing the memo into sections by topic area (TA) (e.g., labeling, biocompatibility) and integrating current policies, regulations, and procedures based on the type of submission into a single document. SMART templates can push and pull information to and from CDRH's IT systems, and include several features to facilitate consistent decision-making and documentation, including: sub-templates and help-text to guide reviewers through specific aspects of the review; example language for potential deficiencies; automatic inclusion of certain sections (e.g., electromagnetic compatibility in electronic devices) based on the device under review; and integration into CDRH's Correspondence Generator (CorGen) tool to assist reviewers in drafting communications to applicants.

Use of SMART for all 510(k)s began in 2015, with development of templates for De Novos and Q-Submissions in 2017, 513(g)s in 2018, and Investigational Device Exemptions (IDEs) in 2020. FDA is also developing a combined template for PMAs and HDEs, with full implementation planned for October 2021. Under MDUFA IV, FDA has continued to update SMART templates as needed to align with new review policies and processes as well as new or updated Guidance. FDA has established procedures for revising and deploying templates and communicating those updates to staff. FDA has hosted multiple training courses, as well as developed a series of training videos, to improve awareness and implementation of the templates for staff.

4.1.1.2 ELECTRONIC SUBMISSION TEMPLATE AND RESOURCE (ESTAR)

CDRH began the transition to electronic submissions in 2014 and, after incorporating lessons learned from its eSubmitter platform, launched the eSTAR in 2020. eSTAR is a dynamic PDF template designed to assist applicants in compiling a submission, organizing by section, and adding attachments, which is then sent to FDA. eSTAR capabilities and features include automation and guided development for each section of the submission, integration of resources (e.g., guidance documents and the product code database), and automatic submission verification, which allows some submissions to bypass the Refuse to Accept (RTA) (also referred to as Acceptance Review) phase of premarket review.

The eSTAR layout mirrors FDA's SMART templates, making it easier for reviewers to cross-reference sections between the submission and review memo. To standardize the process for reviewing eSTAR submissions, CDRH also developed resources to explain the differences in the review processes for eSTAR submissions and non-eSTAR submissions, including how to navigate the electronic format, thereby promoting a smoother expansion of eSTAR to other submission types. In addition, the eSTAR layout is consistent with the International Medical Device Regulators Forum (IMDRF) model, which aims to reduce the burden on sponsors applying for device approval in multiple countries.

In February 2020, FDA began a voluntary eSTAR pilot program to evaluate the performance of eSTAR, with the participation of 32 medical device companies. As of August 23, 2021, FDA received 100 eSTAR submissions, of which 38 have a final decision (i.e., 33 cleared, three withdrawn, two deemed not substantially equivalent [NSE]), while the other 62 are open in various stages of review. Limited data from the preliminary rollout of eSTAR indicated that eSTAR submissions had higher rates of deficiency letters (first cycle) in both FY 2020 and FY 2021 when compared to the non-eSTAR cohort, as well as longer total time to decision (TTD) of eSTAR submissions in FY 2020, although this latter trend reversed in FY 2021. These early results from the pilot point to some potential challenges, though these indicators may not be accurate predictors of future performance given the size of the sample submission and maturity of the effort (i.e., unfamiliarity with the eSTAR format and process). In addition, FDA indicated the COVID-19 response and ongoing impacts to workload have impacted eSTAR performance. FDA has received positive feedback from several companies on their experiences with eSTAR, noting the potential for streamlining submission preparation, prompts for required documentation, and the template's user-friendly layout.

FDA also met its commitment by publishing Guidance on the use of electronic submission templates by FY 2020.[3] This overarching Guidance outlines how FDA plans to implement electronic submission requirements for various premarket submission types, along with a description of submission types which must be submitted electronically and those which are exempt. As noted in this 2020 Guidance, FDA plans to develop individual guidance documents to specify the formats and other requirements for the various premarket submission types. The first such guidance, regarding electronic submission of 510(k)s, is prioritized for publication in 2021.

4.1.1.3 FOCAL POINT PROGRAMS (FPP)

CDRH designed FPPs to promote quality and consistency in device review by identifying baseline knowledge for all review staff within a TA, as well as advanced training for specialized review staff. In addition, for files that require specialized expertise, the reviewer can request a consult from a Focal Point, a specialized staff member with advanced training in and knowledge of the TA who is capable of consulting on complex scientific and regulatory issues. Each Office of Health Technology (OHT) has a Focal Point and a back-up Focal Point who serve as points-of-contact with Lead Reviewers (LR), responding to inquiries and helping to triage review issues by determining if the review requires baseline or advanced knowledge. The Focal Point can then either provide the LR with resources, conduct the consult review him or herself, or connect the LR to a TA Reviewer or Subspecialist if the review requires highly specific expertise, as outlined in Figure 4-1. Each FPP has a roster of all Focal Points with their contact information that the Center updates as needed. The SMART templates also include links to the FPP rosters within each relevant section to expedite the consult review process.

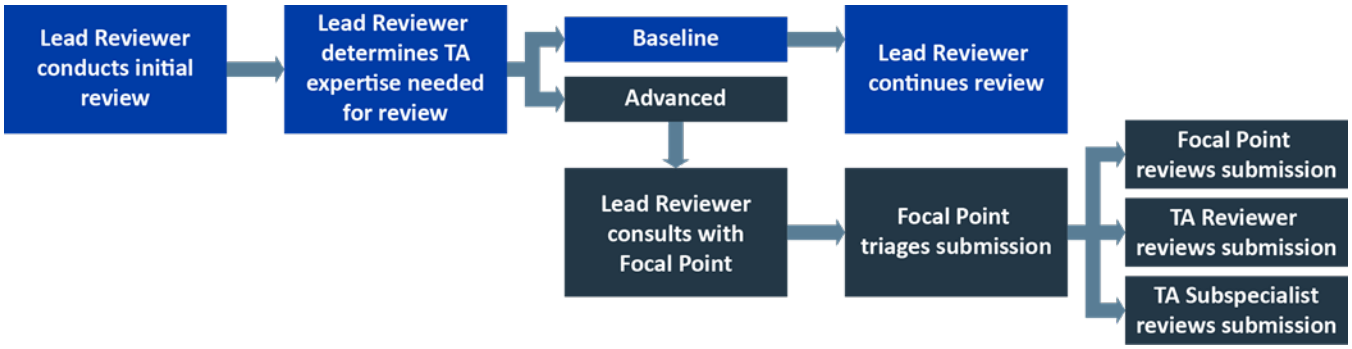


Figure 4-1. Procedure for Requesting Focal Point Program Consults

CDRH originally piloted the first FPP TA in November 2016 for Biocompatibility. The Center's Quality Management and Organizational Excellence (QMOE) program conducted an audit of that FPP in 2019, which revealed that reviewers executed 86% (55/64) of FP consult requests in accordance with its internal established processes and that 97% (62/64) of consult requests required specific information from Focal Points that reviewers could not have sourced locally (i.e., from within the reviewer's OHT), demonstrating the value of the program.

Building on the Biocompatibility FPP, the Center significantly expanded the program and established FPPs for Electromagnetic Compatibility and Magnetic Resonance Safety in 2018 and three new FPPs for Cybersecurity, Digital Health, and Human Factors in March 2021. CDRH tailored each FPP to meet the specific needs within the TA. For example, the Biocompatibility Focal Points meet bi-weekly to discuss submissions under review in real-time, given the volume of Biocompatibility consults needed, while the Cybersecurity FPP focuses on training focal points to ensure they have the necessary expertise to serve as effective resources within their OHTs. CDRH established an FPP Committee to provide strategic and operational oversight. The Committee periodically requests staff proposals for new TAs and prioritizes them based on available resources and potential regulatory impact throughout the Center (i.e., cross-cutting over multiple OHTs).

[3] "Providing Regulatory Submissions for Medical Devices in Electronic Format, Submissions Under Section 745A(b) of the Federal Food, Drug, and Cosmetic Act: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/131064/download – accessed 9/8/2021

4.1.1.4 PROCESS IMPROVEMENT PROGRAM (PIP)

FDA established its PIP in 2018 (formerly known as the Business Process Improvement initiative) to increase the efficiency, repeatability, and effectiveness of the Center's operations while employing Lean Six Sigma methodologies to improve performance, reduce variation, and remove unnecessary process steps. FDA identified its core business practices across several areas (e.g., operations/support, premarket, communications/outreach), and, as of June 2021, the Agency completed 48 individual improvement projects to streamline 44 core processes. Project topics range from premarket submission types (e.g., harmonizing review process variations into a single review process for De Novo submissions) to cross-cutting areas like consults and staff training. Two examples—the Premarket Harmonization and Team Review PIP projects—illustrate efforts to optimize premarket review through a collaborative approach to review and decision-making, which are described further below.

The Team Review project, completed in March 2020, reconceptualized how review teams could more effectively evaluate, incorporate, and communicate information during premarket reviews, which could form the basis for future improvements to potentially decrease staff burden. As part of this project, FDA staff developed a Collaborative Team memo structure with common elements applicable across all premarket submission types, proposed a possible integration of the memo structure into an existing SMART template, and drafted a Team Review process and procedures that defines critical collaboration points. The intent of these efforts is to increase collaboration among review teams and streamline management review and documentation, representing potential improvements over the current device review processes (e.g., by setting up collaborative workspaces and using a shared memo to conduct and document reviews as a team). Proposed next steps include piloting the draft memo structure and process, which the staff could expand and implement across other SMART templates if successful.

In January 2020, FDA launched the Premarket Harmonization project aimed to design a single, overarching premarket review process to harmonize terminology and simplify the common steps used across different premarket submission types. Through this project, FDA began to develop a single, "lean" premarket review process to support early identification and escalation of issues that arise during review. Though that work was paused in April 2020, a new initiative is underway focused on submission design thinking. As part of premarket harmonization efforts, FDA also standardized the terminology between different submission types, including: the entity who provides the information (e.g., Requestor, as opposed to applicant/submitter/sponsor); several process steps (e.g., Hold Notice, as opposed to Additional Information Letter/Major Deficiency Letter), and actions (e.g., Final Decision, as opposed to Cleared/Approved/Granted). FDA also created a complementary document which details a team-based collaborative concurrence process to reduce the number of handoffs. Overall, these updates are intended to accelerate leadership concurrence on resolutions and communication to review staff, as well as make it easier to train new reviewers.

4.1.2 EFFECT OF REVIEW PROCESS CHANGES ON EFFICIENCY AND COMMUNICATION

This section describes how FDA met each of the commitments shown in Table 4-2. The findings are described in the following sections:

- 4.1.2.1 Formal Interactions; and
- 4.1.2.1 Informal Interactions.

FDA implemented several process changes in recent years to increase communication between review staff and applicants during premarket review. CDRH developed, piloted, and implemented these communication channels, which occur at various points throughout the review process, during the MDUFA IV timeframe.

Table 4-2. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Evaluate FDA's premarket review program to identify efficiencies that should be realized as a result of the process improvements and investments under MDUFA III and IV. • Continue to incorporate an interactive review process to provide for, and encourage, informal communication between FDA and applicants to facilitate timely completion of the review process based on accurate and complete information.

Figure 4-2 shows an overview of the review process and several opportunities for increased interaction. These include both formal interactions, which are structured for specific circumstances, and informal interactions, which are typically phone calls and emails to exchange scientific and regulatory information outside of these structured processes and can occur throughout device review.

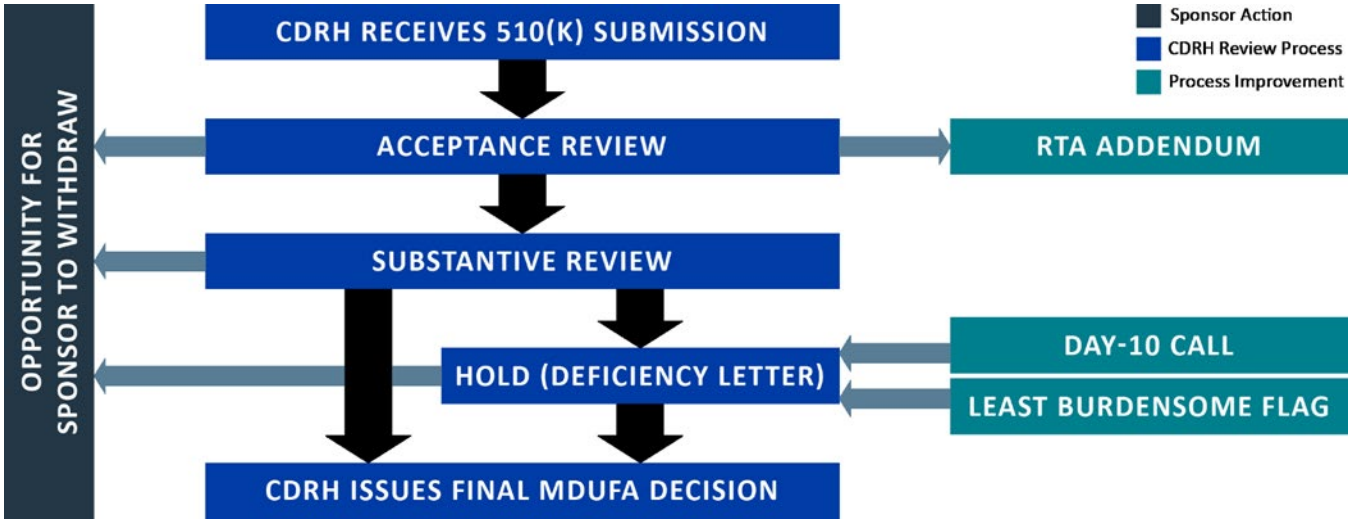


Figure 4-2. 510(k) Review Process and Formal Interactions

4.1.2.1 FORMAL INTERACTIONS

RTA Addendum

Acceptance Review is the first stage of review to ensure a file is administratively complete. In 2019, FDA introduced the RTA Addendum as an option for reviewers of both 510(k) and De Novo submissions to promote early communication with applicants. Reviewers can use the RTA Addendum when there are administrative issues that do not affect the RTA decision but nonetheless sponsors should resolve prior to the final decision (e.g., a missing test report that is necessary but not listed in the RTA Checklist). Although FDA can use the RTA Addendum for files regardless of the acceptance decision, in practice, the addendum is usually issued following a "not accepted" decision. This provides sponsors with an opportunity to preemptively resolve both the RTA and substantive issues while the file is on RTA hold, creating a potential efficiency in the review process. Booz Allen was unable to determine how frequently an RTA Addendum was issued because usage is not independently tracked by CDRH's IT system.

Day-10 Call

Following Acceptance Review, FDA conducts a Substantive Review of the applicant's submission. If a submission lacks necessary information that reviewers cannot request interactively, FDA will place the submission on hold and send the applicant a deficiency letter outlining the identified issues and requested information. FDA introduced the Day-10 Call (i.e., a 30-minute teleconference) in 2018 as a mechanism for 510(k) applicants who have had submissions placed on hold to ask clarifying questions about the deficiencies cited to identify the information needed by FDA to complete the review. Greater understanding of the deficiencies can ensure the applicants' responses are complete, which can improve the efficiency of review and prevent further deficiencies or holds on the submission. As noted at the bottom of each 510(k) deficiency letter, applicants may request a Day-10 Call, during which FDA will address the applicant's questions, confirm understanding of the deficiencies outlined, and discuss whether a separate Q-Submission meeting is necessary to review new data or proposed testing plans in response. Reviewers document phone calls in the administrative record, but CDRH's IT system does not capture the phone calls, making it challenging to identify the submissions where a Day-10 Call occurred and track the number and trends.

Least Burdensome (LB) Flag

FDA launched the LB Flag Pilot program for 510(k)s in February 2018 as a mechanism for an evaluation of any request for additional information that a sponsor believes is inconsistent with LB principles.[4] In February 2019, the LB Flag transitioned from a pilot to an established process for 510(k) submissions, and in January 2021, CDRH expanded the LB Flag to PMA, HDE, and De Novo submissions.

To use the LB Flag process, the policy states that sponsors should first attempt to resolve their concerns through discussion with CDRH staff (e.g., an email or Day-10 Call). A sponsor may elect to "throw the flag" by submitting a summary of the flagged deficiencies, along with their communications with FDA, and the rationale for their request. CDRH senior management then conducts an internal review and aims to issue a response to the applicant within three weeks.

Between February 2019 and April 2021, sponsors used the LB flag for only 19 of 4,700 (0.4%) 510(k) submissions that received a deficiency letter. Most LB flags were related to requests for additional required testing. Table 4-3 shows a breakdown of the resolutions. In the nine cases where a flag was "denied," OHT management determined that the deficiency was in alignment with LB principles and noted the device modifications did warrant additional testing or explained why a proposed testing plan did not adequately address the original deficiencies identified. For the three "partially granted" LB Flags, CDRH upheld its deficiency letter but granted the sponsor flexibility in resolving the request. CDRH deemed flags thrown after the 60 days or with more than two TAs "ineligible." In these instances, FDA afforded the applicants the opportunity to discuss their concerns with CDRH through other mechanisms, such as Submission Issue Request (SIR) (i.e., a type of Q-Submission). For the four cases that received "other" decisions, CDRH addressed the applicant's concerns via an SIR.

Table 4-3. Resolution of LB Flags for 510(k)s

Resolution	Number Receiving Decision
Granted	0
Partially Granted	3
Denied	9
Ineligible	3
Other	4

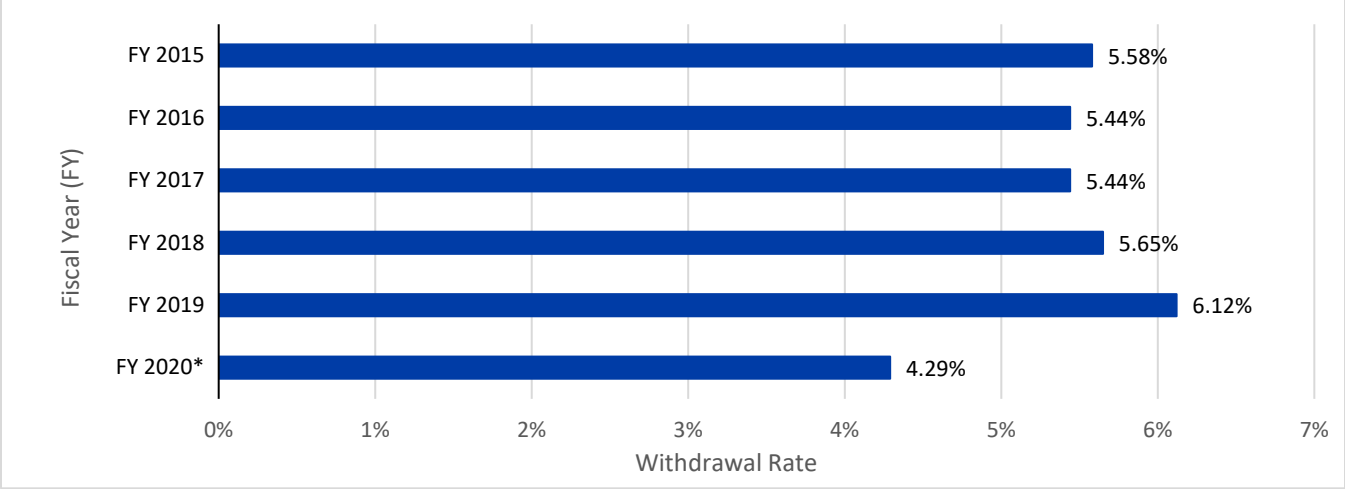
Note: Data from February 1, 2019 to April 1, 2021.

Updates to Communications on Withdrawals

A withdrawal occurs when an applicant voluntarily requests to discontinue FDA review of a marketing application, which may be prompted by several factors including business or regulatory considerations. Applicants and FDA have a shared interest in minimizing withdrawals, given the resources invested in both developing and reviewing a submission. Although they can occur at any point prior to the final decision, more than half occur due to unresolved deficiencies after sponsors responded to an additional information request.[5] The rate of withdrawals has remained steady in recent years, ranging from 4-6%, shown in Figure 4-3. These data represent withdrawals only and do not include "deletions," which occur when sponsors do not respond to requests for additional information within the allotted timeframe. Deletions occurred 1.5-5% of the time (between FY 2018 and FY 2020), which represents an additional inefficiency for FDA and industry.

[4] LB principles, defined as requesting the minimum amount of information necessary through the most efficient manner possible to address a regulatory question or issue, play a critical role in how FDA staff conduct device reviews and request additional information from sponsors.

[5] "MDUFA IV Independent Assessment of FDA's Device Review Process Management, Phase 1," FDA https://www.fda.gov/media/119435/download – accessed 6/7/2021



*Since the FY 2020 cohort is incomplete, this value may change once all MDUFA Decisions are issued.

Note: FY 2015 – FY 2017 data from December 14, 2018 MDUFA III Performance Report, FY 2018 – FY 2020 data from August 3, 2021 MDUFA IV Performance Report.

Figure 4-3. 510(k) Withdrawal Rates from FY 2015 – FY 2020

While steady, low withdrawal rates reflect a consistent process, FDA has taken additional actions to better understand the reasons for withdrawals and enhance efficient use of reviewer resources. To enhance communication and potentially reduce the number of withdrawals, FDA has initiated process changes and updates including use of the SMART template, updated internal resources, updated acknowledgement letter, and training for managers. In 2020, FDA began using SMART templates to document the reason for a withdrawal request for cases in which sponsors provide a reason for withdrawal. This documentation could facilitate future analysis of the circumstances surrounding withdrawals and help target process and communication improvements to minimize the withdrawal outcome. FDA also updated its internal resources to provide reviewers with information on use of withdrawals, the steps involved, and best practices for withdrawal conversations with sponsors (e.g., never recommending that an applicant withdraw its submission). FDA made an additional update to the language in the acknowledgement letter, which FDA automatically sends to the submitter to reaffirm that the withdrawal is a voluntary action by the sponsor that will result in termination of FDA's review of the submission.

4.1.2.2 INFORMAL INTERACTIONS

Customer Collaboration Portal (CCP)

As part of its Center-wide Digital Transformation initiative, CDRH is developing a web-based platform to facilitate communication and information exchange between Center staff and industry applicants, known as the CCP. Based on feedback gathered from both FDA staff and industry, CDRH determined that the top priorities for the portal include ease of use and timeliness in response to user needs. To meet these priorities, CDRH designed the CCP as an agile system capable of responding quickly to requests and is providing training to educate users on the portal's capabilities.

The first iteration of the CCP consists of a secure, web-based progress tracker that displays the review status of premarket submissions, meeting CDRH's MDUFA IV commitment to implement a new information management system that provides an industry dashboard that displays near real-time submission status. In March 2021, CDRH began a soft launch of the tracker for Traditional 510(k) submissions, enrolling a total of 100 industry volunteer participants. CDRH invited participants to provide feedback on the tracker's usability, the utility of the information provided, and the tracker's functions and features. FDA successfully completed the soft launch and used the feedback in the August 30, 2021 full launch of the tracking feature for Traditional 510(k)s. The tracking tool is now available to anyone who is the official correspondent of an active Traditional 510(k) under review. CDRH will incorporate additional submission types and features as the Center continues to build out the tracking functionality in an iterative approach. By increasing the visibility and accessibility of the review progress and status,

CDRH aims to improve the transparency of the premarket review process and reduce the number of status-related inquiries to review staff.

Updates to Interactive Review

As part of the MDUFA IV Commitment Letter, FDA committed to continuing interactive review practices to encourage informal interactions between CDRH staff and applicants. Interactive review may occur through phone calls, emails, and/or faxes, and it allows reviewers to facilitate a collaborative exchange of information with sponsors to resolve issues and promote efficient review of the data necessary to make a final decision. In July 2019, CDRH updated an existing internal resource to clarify the purpose of interactive review and provide recommendations for interacting with sponsors at various points throughout the premarket review process, summarized in Table 4-4. While CDRH has encouraged reviewers to interact with sponsors more frequently, reviewers ultimately decide whether to use interactive review based on factors such as overall workload, expected sponsor response time, and complexity of the issue.

Table 4-4. Examples of Interactive Review Throughout the Review Process

Review Phase	Examples of Interaction(s)	Potential Benefit of Interaction
During RTA Review	Request RTA checklist items interactively	Helps avoid delays in file acceptance and increase likelihood file acceptance
During Substantive Review	Request information or images; Communicate significant concerns where earlier notification may facilitate a timelier sponsor response	Facilitates a collaborative approach to resolving issues and provides reviewer with necessary information to conduct a complete and efficient review
While the File is on Hold	Quick, limited pre-review of applicants' proposed responses to deficiencies, though a reviewer may recommend an SIR when multiple issues are involved	Preemptive check to communicate that sponsors' responses are adequate
During Final Review and Recommendation	Finalize changes to 510(k) Summary and administrative documents; Final labeling modifications	Resolves remaining issues as early as possible in the review cycle

4.1.3 IMPLEMENTATION OF A TOTAL PRODUCT LIFE CYCLE (TPLC) APPROACH FOR HOLISTIC PREMARKET REVIEW

This section describes how FDA met each of the commitments shown in Table 4-5.

Table 4-5. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• CDRH will explore transitioning to a similar TPLC model building in the other device areas based on the lessons learned from its experience with OIR and taking into account the Center's mission, vision, strategic priorities, and development of a patient-centric benefit-risk framework for regulatory and non-regulatory decision-making across the TPLC.

In 2019, CDRH underwent a reorganization to support a TPLC approach, designed to be capable of adapting to future organizational, regulatory, and scientific needs. A key change was the formation of the Office of Product Evaluation and Quality (OPEQ), a super office that is responsible for the end-to-end evaluation and oversight of device products throughout a product's lifecycle. OPEQ is organized by product-specific OHTs with premarket, postmarket, and compliance functions all residing within a given OHT. By housing these functions within one unit, the Center intends to promote information sharing and cross-skills development, minimize organizational levels of review, and optimize decision-making by allowing employees to leverage their knowledge of premarket and postmarket device information. Figure 4-4 outlines the functions of the 10 OPEQ Offices.

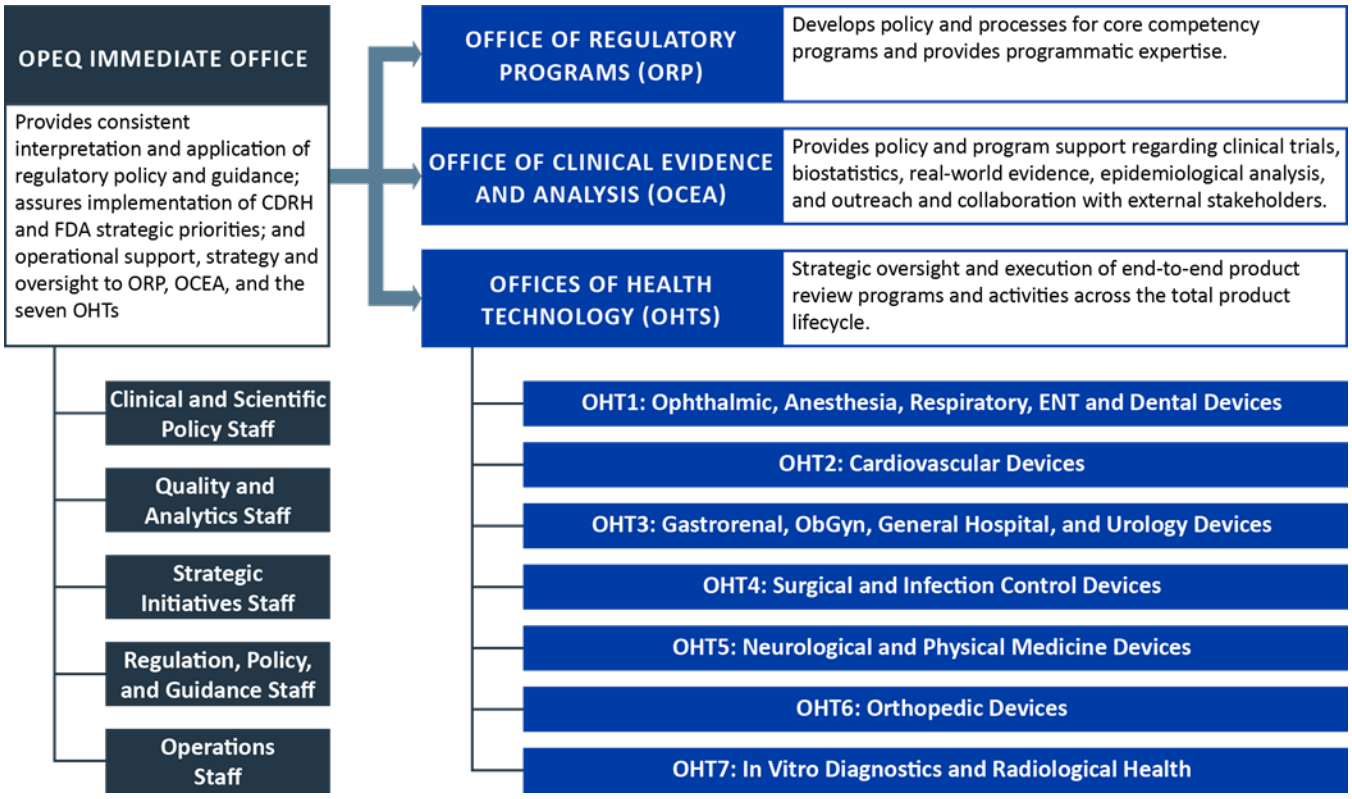


Figure 4-4. Organization and Functions of the Offices within OPEQ

To foster a more integrated approach to premarket review, CDRH developed its Minors program as part of its TPLC reorganization, which provides employees with the opportunity to broaden and deepen their knowledge without the need to transfer into another position or go on detail. Employees may spend up to 20% of their time working in areas outside of, but related to, their primary area responsibility (i.e., their major). Through this professional development program, CDRH seeks to strengthen its bench of employees with cross-cutting expertise needed to support device review across the TPLC and manage workload across the organization. The Minors program includes four possible types to gain proficiency in new areas, including: technical/scientific, regulatory process, regulatory policy, or a combination of the above.

4.1.4 TOTAL TIME TO DECISION OUTCOMES AND FEASIBILITY OF ESTABLISHING TTD BASELINES

As part of the MDUFA IV commitments, FDA and industry agreed to the shared outcome goal of TTD. Some stakeholders have expressed interest in development of a TTD baseline to inform TTD goals. Development of a baseline depends on several dynamic variables such as product complexity, risk, and other characteristics, which may be challenging to standardize. Table 4-6 describes some of these variables for 510(k)s. In addition to these product and submission characteristics, changes in FDA policies and processes can also impact TTD and establishment of a baseline. For example, FDA intends to exempt several low-risk medical devices from premarket notification requirements, as described in a 2019 Guidance.[6] Although this could increase review efficiency by allowing reviewers to focus on more complex submissions, a potential tradeoff is that the exemption of devices with lower-than-average review times could increase overall average TTD for 510(k)s. Although many of the characteristics associated with increased complexity are on the rise, CDRH has met the TTD goal in FY 2018 for both 510(k)s (goal= 124 days; performance= 123 days) and PMAs (goal= 320 days; performance= 262 days).[7] As

[6] "Intent to Exempt Certain Unclassified Medical Devices from Premarket Notification Requirements: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/89238/download – accessed 8/31/2021
[7] "December 15, 2020 MDUFA IV Performance Report," FDA https://www.fda.gov/media/144600/download – accessed 9/23/2021

of September 30, 2020, neither of these two cohorts had met the decision threshold to calculate the average TTD for FY 2019 nor FY 2020. FDA will report the average TTD for these FYs in future reports once the cohorts have met the decision threshold.

Table 4-6. Variability in Characteristics of 510(k)s

Description and Degree of Difference	Impact of Difference
Submission Length: Increase from average of 266 pages (CY 2003) to 1,185 pages (CY 2017)	Longer submissions take more time to review on average
Requires Consult: Increase from 24% (FY 2013) to 39% (FY 2018) of 510(k) reviews involving at least one consult review from a SME	Files requiring consult review from SME generally have higher TTD than those without
Device Classification: Decreasing share of 510(k)s for Class I devices 10% (FY 2003) to 4% (FY 2018)	Class I devices are generally lowest risk and have historically below average review times
Type of 510(k): Increasing share of 510(k)s are Traditional or Abbreviated (71% in FY 2008 to 84% in FY 2018) rather than Special or Third Party (29% in FY 2008 to 16% in FY 2018)	Traditional and Abbreviated 510(k) generally take longer to review than Special or Third Party 510(k)s
Submission Origin: Increasing share of 510(k)s come from applicants outside the U.S. (31% in FY 2007 compared to 44% in FY 2019)	Files from non-U.S. applicants tend to have more initial quality issues than those from U.S. applicants and thus take longer to review

4.1.5 CONCLUSION

FDA met the MDUFA IV commitments to develop an electronic submission template and publish Guidance on the use of these templates. In addition, the Agency encouraged interactive review and informal communication, and implemented a series of process improvements designed to improve efficiency and consistency in premarket review. Some of these efforts are more established and used throughout the Agency, whereas FDA has implemented others more recently, such as better documentation of the reason for submission withdrawal, which could allow for a better understanding of the circumstances associated with them. FDA also met the commitment to explore the transition to a TPLC approach by implementing a TPLC reorganization and establishing a new super office (i.e., OPEQ) focused on the end-to-end review of medical devices. The super office integrates premarket and postmarket review staff into product-specific OHTs for a more holistic approach to device review.

4.2 Infrastructure and FTE Allocations

To improve the capacity and consistency of premarket review, FDA must use all available resources, including human capital, in an efficient manner. Premarket reviewers and supervisors require a highly specific set of skills and expertise. The MDUFA IV commitments for Infrastructure and FTE Allocations are largely focused on enhancing the premarket scientific review capacity through reviewer and supervisor recruitment, hiring, and retention, and by leveraging external expertise.

Booz Allen found that FDA met its MDUFA IV commitments enhancing and supplementing scientific review capacity, augmenting existing human resources (HR) services, implementing the TPLC reorganization to enable a reduction in its supervisor to employee ratio, and using authorities and new programs to retain high-performing supervisors.

The assessment findings are presented in the following two sections:

- 4.2.1 MDUFA III and IV Hiring Targets and Strategies to Enhance Review Capacity; and
- 4.2.2 Reduce Supervisory Ratio and Retain High-Performing Supervisors.

4.2.1 MDUFA III AND IV HIRING TARGETS AND STRATEGIES TO ENHANCE REVIEW CAPACITY

This section describes how FDA met each of the commitments shown in Table 4-7. The findings are described in the following five sections:

- 4.2.1.1 Hiring under MDUFA III;
- 4.2.1.2 Positions Filled Under MDUFA IV;
- 4.2.1.3 Leverage External Experts;
- 4.2.1.4 Obtain Supplemental Recruitment and Staffing Support; and
- 4.2.1.5 Establish Tiger Team to Improve Hiring.

Table 4-7. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• The Agency will also apply user fee revenues to enhance and supplement scientific review capacity by hiring device application reviewers as well as leveraging external experts needed to assist with the review of device applications. To ensure such additional positions are filled by qualified experts, the Agency will apply user fee revenues to recruitment and hiring. • CDRH intends to enter into an Inter-Agency Agreement (IAA) with the Office of Personnel Management (OPM) to provide supplemental recruitment and staffing support throughout MDUFA IV to augment existing FDA Human Resources services.

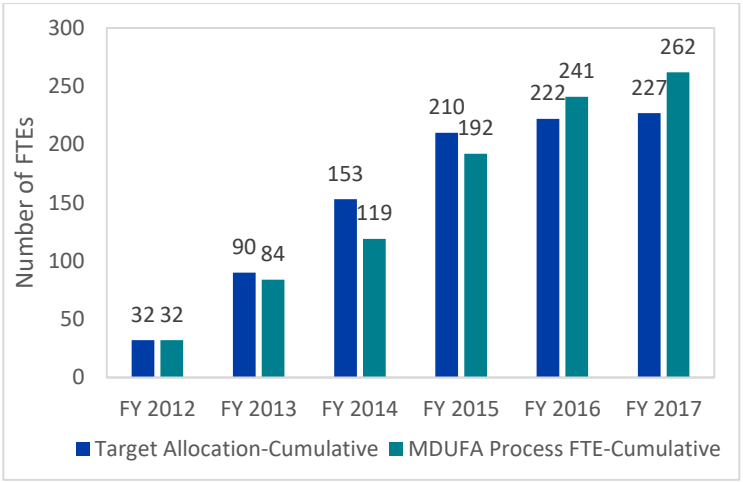
4.2.1.1 HIRING UNDER MDUFA III

Hiring targets were set for each year of MDUFA III (FY 2013 – FY 2017) to support MDUFA-related activities. FDA reported on progress using "MDUFA Process FTEs" because there was no system in place to track MDUFA positions directly during MDUFA III. MDUFA Process FTEs reflect a paid staff year of MDUFA program work.[8] It is calculated by dividing the estimated total number of regular straight-time hours worked by employees in support of MDUFA-related activities by the number of compensable hours applicable to each FY. Time reporting estimates were based on time reporting surveys conducted for a two-week period during each quarter of the FY. FDA updated and refined its time reporting codes in 2013 to more closely align with the activities outlined by MDUFA III.

The MDUFA III FTE target allocation was 227 FTEs, representing 32 FTE "pre-hires" in FY 2012 along with 195 FTEs between FY 2013 and FY 2017. Figure 4-5 shows the cumulative allocation targets compared to the estimated MDUFA Process FTEs. FDA added an estimated 262 MDUFA Process FTEs between 2012 and 2017, exceeding the goal of 227 FTEs.

4.2.1.2 POSITIONS FILLED UNDER MDUFA IV

During MDUFA IV (FY 2018 – FY 2022), FDA committed to hiring additional reviewers. FDA has a hiring target of 217 employees by the end of FY 2021, with allocations to specific commitment areas each year. To support hiring activities, FDA invested in a new mechanism, the Position-Based Management (PBM) Tracker, to individually track the status of positions supporting MDUFA IV commitment areas using a MDUFA IV tag. Table 4-8 shows the MDUFA IV targets by commitment area and year, along with the actual number of positions filled. FDA has achieved 92% of its aggregate, cumulative target for FY 2018 – FY 2020, hiring for 174 of the 189 positions allocated, as of the end of FY 2020. FDA met or exceeded its hiring targets for Patient Input (120%, 6/5) and Time Reporting (200%, 2/1) and has nearly met its targets for Premarket Review (92%, 135/146), Quality Management (93%, 14/15), Digital Health (80%, 8/10), Real-World



*32 MDUFA III pre-hires were allocated for FY 2012 (i.e., one year before MDUFA III).

Figure 4-5. MDUFA III Target FTE versus MDUFA Process FTE: Cumulative Comparison by FY

[8] "FY 2019 MDUFA Financial Report Required by the Medical Device User Fee Amendments," FDA https://www.fda.gov/media/136034/download – accessed 5/3/2021

Evidence (71%, 5/7) and Standards (80%, 4/5) as of the end of FY 2020. Note that these data reflect the number of positions filled; data were not available to distinguish between internal candidates and new hires.

Table 4-8. MDUFA IV Cumulative Hiring Targets and Positions Filled

Commitment Area	FY 2018		FY 2019		FY 2020		FY 2021	
	Target	Filled	Target	Filled	Target	Filled	Target	Filled
Premarket Review*	91	79	116	101	146	135	161	N/A
Digital Health	7	7	7	7	10	8	13	N/A
Real-World Evidence	5	5	6	5	7	5	10	N/A
Science of Patient Input	3	4	4	5	5	6	6	N/A
Quality Management	10	2	12	5	15	14	20	N/A
Standards	3	2	4	4	5	4	5	N/A
Time Reporting	0	0	0	0	1	2	2	N/A
Total	119	99	149	127	189	174	217	N/A

*Includes four positions within the Center for Biologics Evaluation and Research (CBER).
Note: N/A = Not Applicable, as FY 2021 had not closed at the time of this report.

4.2.1.3 LEVERAGE EXTERNAL EXPERTS

FDA leverages external experts to enhance scientific review capacity through Special Government Employees (SGE) and the Network of Experts (NoE) program. SGEs are external experts appointed to perform temporary duties on an intermittent basis. SGEs support special assignments (i.e., Agency Directed Assignments [ADA]). SGEs may participate in review, guidance development, and scientific peer review of Agency materials (e.g., literature reviews, discussion papers). FDA increased its use of external experts, issuing five ADAs to SGEs in FY 2018 to 12 ADAs in FY 2020, shown in Figure 4-6. These ADAs were deployed Center-wide and not necessarily specific to OPEQ.

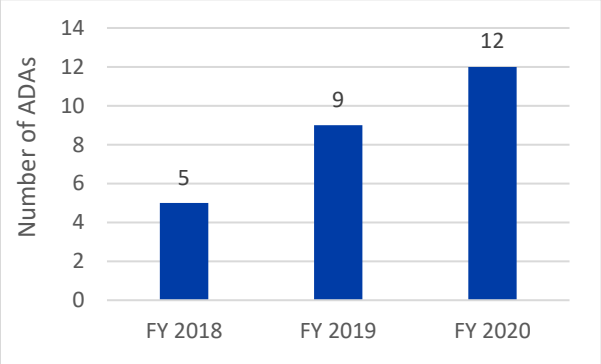


Figure 4-6. Number of ADAs Issued by CDRH

The aim of the NoE program is to facilitate rapid exchange of scientific, engineering, and medical expertise from a network of external experts affiliated with academic institutions as well as scientific and professional organizations. FDA uses the program to address general scientific questions as well as questions about a product line, medical indication, or specific product, including pending submissions. While it may take several months for the SGE screening and clearance process, the NoE program allows FDA to more quickly (i.e., within 2-3 weeks) access external expertise for assignments that do not require screening. There was an average of 14 NoE requests per year between FYs 2018 and 2020, with more than half of requests focused on the premarket space.

4.2.1.4 OBTAIN SUPPLEMENTAL RECRUITMENT AND STAFFING SUPPORT

To enhance recruitment and hiring capabilities under MDUFA IV, FDA entered into an IAA with OPM to augment its human capital resources. OPM provided support to update position descriptions (PD) throughout CDRH, as well as allow offices across OPEQ to use the same PDs to hire staff in identical roles, further streamlining the hiring process. As part of the IAA, CDRH developed 700 interdisciplinary PDs applicable across OPEQ offices. The interdisciplinary PDs reflect standard position roles and responsibilities (e.g., reviewer, assistant director) and requirements tailored to a specific scientific background (e.g., chemistry). The IAA with OPM also provided FDA with additional resources needed to draft Cures recruitment packages, which strengthened FDA's ability to make use of the 21st Century Cures Act (Cures Act) hiring authority.

4.2.1.5 ESTABLISH TIGER TEAM TO IMPROVE HIRING

CDRH established a Hiring Tiger Team in October 2019 to help increase hiring, accelerate the hiring process throughout the Center, and address the ongoing effects of prior hiring challenges (e.g., government-wide hiring freeze in 2017; government shutdowns in 2018 and 2019; Public Health Service Commissioned Corps new hire restrictions; complications with position classification; changes in the use of Direct Hire Authority (DHA) which

extended time to hire). FDA tasked the Hiring Tiger Team with addressing two main hiring impediments within the Center: time to hire and the time to classify positions. The Hiring Tiger Team was comprised of representatives from the CDRH Division of Workforce Management (DWM), the Office of Talent Solutions (OTS) (within the Office of the Commissioner), and each CDRH Office. The Hiring Tiger Team worked collaboratively with DWM and OTS to develop and implement several strategies to expedite and improve the hiring process, shown in Table 4-9.

The Hiring Tiger Team also collaborated on recruitment strategies with DWM and hiring managers across CDRH to shape strategies for recruiting candidates with highly specialized skills in new and emerging areas. The team holds hiring conversations on a regular basis to discuss the staffing model, vacancies, hiring goals, and to determine the most appropriate hiring authorities for recruitment. FDA recently launched a marketing program in CDRH to target recruitment efforts by collecting and reviewing resumes from candidates for hard-to-fill roles.

Table 4-9. Tiger Team Hiring Strategies

Tiger Team Strategy	Implementation
Recruitment Dashboard	Implemented recruiting dashboards to provide real-time recruitment updates.
Schedule for Posting DHA and Recent Graduate Student Positions	Coordinated with OTS to develop a schedule to post both DHA and recent graduate hiring announcements to help hiring managers improve the prioritization of candidate reviews.
Resume Repositories	Created resume repositories to help match job seekers to vacancies throughout the Center. Lists of job seekers expressing interest in CDRH vacancies through different mediums (e.g., email, social media) are compiled and shared with hiring managers.
Access to "Certificates"	Created a process for HR office representatives across Centers to share lists of qualified applicants who have previously applied, referred to as "certificates." This coordination allows for identification of viable candidates for open positions, prior to posting announcements.
Expedite the Offer Process	Established a process to expedite the job offer process in coordination with the OTS by committing to extend a tentative/final offer within three days of making a selection.
Streamline the DHA Process	Implemented an approach to streamline the DHA hiring process by limiting the number of applications received to the first 100 received or closing the announcement after five days.
Increased Use of Available Hiring Authorities	Collaborated with DWM and OTS to strategize the most effective hiring strategy needed to fill CDRH vacancies on an individual basis. Hiring Authorities include the Cures Act, DHA, Pathways (i.e., a mechanism to recruit and hire well-qualified students and recent graduates), and Title 42(g) Staff Fellows (i.e., a non-competitive hiring authority used to fill interdisciplinary scientific and engineering positions).

The Hiring Tiger Team has been superseded by collaborative efforts between the Office of Management (OM)/DWM and Office program management who develop and implement solutions to address recruitment and hiring operations throughout the Center. DWM human capital advisors collaborate with hiring managers across CDRH to shape recruitment strategies based on specific hiring needs.

Tiger Team Strategy: Cures Act Hiring Authority

The Cures Act provided FDA with a new authority to support the recruitment and retention of outstanding and highly qualified professionals who support the development, review, and regulation of medical products. Previously, the Agency did not have specific federal hiring and pay authorities tailored to its needs. Specifically, the Cures Act allows FDA to expedite the hiring process and create an Alternative Pay Structure (APS), which can be used to increase annual compensation for new hires as well as existing personnel in key scientific, technical, and professional occupations.

Implementation of the Cures Act pay authority has largely focused on executive and supervisory positions. CDRH made 108 appointments across the Center under the Cures Act authority through the end of FY 2020. There were 91 supervisory appointments, shown in Figure 4-7, of which 74 were within OPEQ. The following section presents additional information on use of the Cures Act pay authority.

Tiger Team Strategy: Streamline Direct Hiring Authority

DHA is a long-standing source of hiring authorization, intended to address a severe shortage of candidates or critical hiring need. DHA permits the appointment of individuals without regard to competitive rating, ranking, or

veterans' preference for certain mission-critical occupations. Recent Agency-wide process changes have impacted timeliness and effectiveness of DHA hiring, including: the requirement to apply through USAJOBS, reclassification of existing position descriptions, and the mechanism for communicating the status of actions. Due to the normally high volume of submissions and the extended time it took to qualify applicants, the Hiring Tiger Team implemented a strategy to limit the number of applicants to the first 100 or the announcement would close after five days. This process allowed CDRH and hiring managers to receive the certificate of eligible applicants much faster than before. In addition, the Hiring Tiger Team collaborated with the Center's HR and hiring managers to create a consistent schedule for posting DHA announcements to ensure a steady stream of qualified candidates and to allow managers to anticipate and appropriately plan for filling vacant positions.

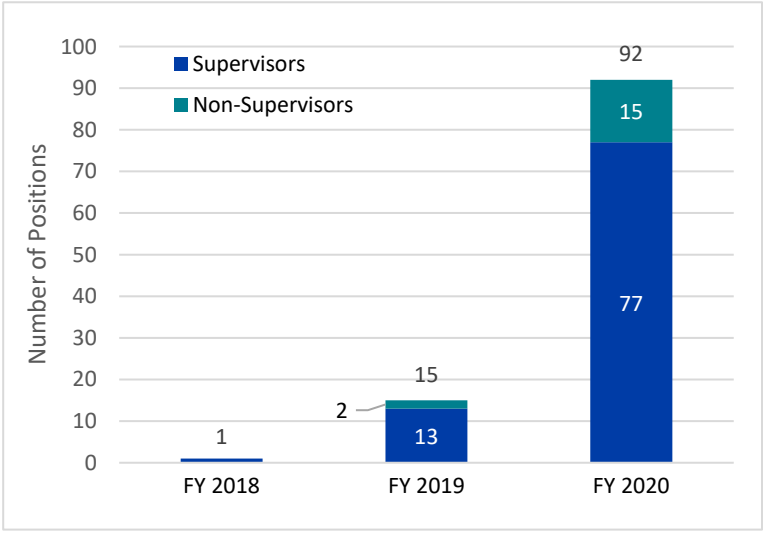


Figure 4-7. Number of Positions Aligned to Cures Act Pay Structure

4.2.2 REDUCE SUPERVISORY RATIO AND RETAIN HIGH-PERFORMING SUPERVISORS

This section describes how FDA met each of the commitments shown in Table 4-10. The findings are described in the following two sections:

- 4.2.2.1 Reduce the Supervisory Ratio; and
- 4.2.2.2 Retain High-Performing Supervisors.

Table 4-10. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• The Agency will apply user fee revenues to reduce the ratio of review staff to front line supervisors in the premarket review program to improve consistency. • The Agency will apply user fee revenues to retain high-performing supervisors in the premarket review program.

4.2.2.1 REDUCE THE SUPERVISORY RATIO

The TPLC reorganization for OPEQ led to the addition of five offices, five divisions, and 13 teams, shown in Table 4-11. The new structure supported the creation of additional frontline supervisory positions (e.g., assistant directors), leading to a reduction in supervisor ratio. The formalization of the team lead role was another important factor in balancing the workload of frontline supervisors. Team leads provide technical support to reviewers and support frontline supervisors in managing communications, assignments, deadlines, and review of work products across the team. Information on the number of CDRH team lead positions was not available at the time this report was published.

Table 4-11. Impact of TPLC OPEQ Reorganization on Organizational Structure

Organizational Structure	Prior to Reorganization December 2016	Post OPEQ Reorganization June 2020
Offices	4	9
Divisions	23	28
Branches/Teams	86	99

FDA agreed to reduce the ratio of premarket review staff to front line supervisors under MDUFA IV. The average ratio has decreased from 12:1 and 11:1 for Office of Device Evaluation (ODE) and Office of In Vitro Diagnostics and Radiological Health (OIR), respectively, to an average ratio of 10:1 for OHTs 1-7, shown in Table 4-12.

Table 4-12. Supervisory Ratio Before and After TPLC Reorganization

	Prior to Reorganization December 2016		Post Reorganization September 2020
	ODE	OIR	OHTs 1-7
Range	10:1 to 13:1	10:1 to 14:1	9:1 to 13:1
Average	12:1	11:1	10:1

4.2.2.2 RETAIN HIGH-PERFORMING SUPERVISORS

The Cures Act provides FDA with new hiring and pay authority to support both the recruitment and retention of outstanding and highly qualified professionals, as discussed above. Existing employees and new hires in certain scientific, technical, and professional occupations are eligible to receive higher salaries under the APS. Employees that achieve a certain performance rating are eligible for the higher salaries. Implementation of the Cures Act pay authority has been used for 91 supervisors from FY 2018 to 2020.

Another tool available to help retain supervisors is the individual retention incentive. FDA may use this incentive after determining it is essential to retain the employee if they have unusually high or unique qualifications, or if there is a special need of the organization for the employee's services, among other considerations laid out in the internal Individual Retention Incentives guidance document. FDA must renew individual retention incentives annually. These incentives do not permanently increase base compensation, but FDA can renew them for up to five years. Two supervisors received an individual retention incentive in FY 2018 and again in FY 2019. In FY 2020, two different supervisors received individual retention incentives.

4.2.3 CONCLUSION

FDA met the MDUFA IV Commitment Letter requirements to enhance scientific review capacity, including meeting MDUFA III hiring targets and being on track to meet MDUFA IV hiring targets. To improve the tracking of MDUFA positions under MDUFA IV, FDA created the PBM Tracker to monitor the status of MDUFA IV positions by commitment area. To address hiring challenges (e.g., government shutdowns), FDA implemented a Hiring Tiger Team, obtained OPM's support to enhance its recruitment and hiring capabilities, and leveraged external experts. In addition, FDA reduced the supervisory ratio and used Cures Act pay authority and Individual Retention Incentives to help retain staff.

4.3 Training and Alignment

The professional development of new and existing employees is vital to FDA's mission. Multiple departments within CDRH collaborate across several training programs to respond to the individual learning needs of the Center's staff by developing training that is both targeted and personalized. The Reviewer Training Curriculum serves as the foundational learning opportunity for reviewers, while the Scientific and Regulatory Training Curriculum and On-the-Job Training programs provide additional supports to improve medical device reviewer's capacity for conducting quality reviews. CDRH has in place and continues to develop a comprehensive evaluation plan to promote additional changes to these programs and further quantify the impact of its training on premarket review timelines.

The MDUFA IV commitments for training are focused on improving training for new and existing reviewers and coordinating with the CDRH Quality Management Program to provide more targeted and personalized training to staff. In addition, FDA committed to achieving Kirkpatrick Level 3 for curriculum-based premarket training (i.e., assessment of work performance behavior change), as well as Kirkpatrick Level 4 for curriculum-based premarket training (i.e., evaluating the effectiveness of the training activities on relevant premarket program metrics and goals) by the end of FY 2020.

Booz Allen found that FDA met its MDUFA IV commitments by improving training for new and existing reviewers, providing more targeted and personalized training to staff, and implemented curriculum-based training based on the Kirkpatrick framework.

The assessment findings are presented in two sections, which align to the MDUFA IV commitments:

- 4.3.1 Improve Training for New and Existing Premarket Reviewers; and
- 4.3.2 Assess Impact of Curriculum-based Premarket Training Using the Kirkpatrick Framework.

4.3.1 IMPROVE TRAINING FOR NEW AND EXISTING PREMARKET REVIEWERS

This section describes how FDA met each of the commitments shown in Table 4-13. The findings are described in the following three sections:

- 4.3.1.1 Improved Reviewer Certification Program (RCP);
- 4.3.1.2 Improved Experiential Learning Program (ELP); and
- 4.3.1.3 Cross-Center Coordination to Improve Training.

Table 4-13. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• FDA will continue to improve training for new and existing reviewers under this agreement. • FDA training efforts will be closely coordinated with the Quality Management Program to provide more targeted and personalized training to staff.

4.3.1.1 IMPROVED REVIEWER CERTIFICATION PROGRAM (RCP)

The RCP is a critical component of CDRH's reviewer training program, serving as the foundational learning opportunity for new reviewers. The Division of Employee Training and Development (DETD) initiated improvements to RCP, prior to MDUFA IV, through the "RCP Refresh" in 2015 and 2016. The RCP Refresh involved development of online courses, streamlining the curriculum from 10 months to two months, and dividing courses into Core and Advanced RCP. The Core curriculum provides essential content through self-paced, online, and instructor-led courses to prepare reviewers to meet CDRH review standards. The Core RCP culminates in a training capstone, which integrates online and classroom experience to provide an interactive, hands-on activity for new reviewers to demonstrate their learning (e.g., review a sample 510(k) submission, write a deficiency letter). The Advanced RCP courses supplement the core curriculum and further support the premarket review process.

Further program improvements were implemented under the "RCP Revamp," which focused on addressing the procedural changes resulting from the TPLC reorganization. DETD gathered input through a 2017 TPLC Gallery Walk Survey and a premarket needs assessment. DETD administered the needs assessment to personnel involved in premarket review (e.g., reviewers, consultants, inspectors), supervisors of personnel involved in premarket review, CDRH staff, and their mentors. Following the assessment, DETD incorporated relevant material into the RCP curriculum and the hands-on, interactive RCP Capstone exercise. Efforts were also made to incorporate cross-functional skill sets to facilitate a TPLC approach, such as four online and three classroom courses to address postmarket functions (e.g., Medical Device Corrections and Removals, Establishment Inspection Reports, and Quality System Reviews).

Finally, CDRH established the RCP Working Group, a rotating team of SMEs and senior leaders, to regularly update the RCP curriculum to ensure it provides consistent, high-quality training that meets reviewer needs. The RCP Working Group uses a standard implementation model that includes evaluating Kirkpatrick data, identifying necessary updates to the RCP curriculum, and sharing its findings and recommendations. When appropriate, matters discussed in the RCP Working Group are presented to CDRH's senior leadership for review and, if approved, incorporated into the RCP courses.

4.3.1.2 IMPROVED EXPERIENTIAL LEARNING PROGRAM (ELP)

The ELP offers experienced CDRH reviewers formal one- to three-day training visits to research, clinical, manufacturing, and healthcare facilities.[9] These site visits allow staff to remain abreast of industry practices and changes to the medical device development process by informing their understanding of the products they review and closing the knowledge gap between technological innovations and premarket review of the resulting devices. Twice per year during the ELP Training Solicitation Periods, CDRH managers list Training Areas of Interest (e.g., device development, innovation, incorporating patient perspective) on the FDA public website and invite stakeholders from the medical device industry, academia, and health care facilities to submit proposals for participation in the program.

[9] "CDRH's Experiential Learning Program," FDA https://www.fda.gov/science-research/fda-science-jobs-and-scientific-professional-development/cdrhs-experiential-learning-program – accessed 9/24/2021

DETD has partnered with industry to host over 2,900 review staff for 224 ELP site visits since ELP's inception in FY 2013. During MDUFA IV thus far, there was a total of 95 site visits and 1,259 participants, shown in Table 4-14. The COVID-19 PHE significantly impacted the number of site visits in FY 2020, although FDA continued to offer site visit opportunities. Virtual ELP sessions represent an important enhancement of the program that facilitated participation during the PHE. DETD also adjusted the Training Areas of Interest to accommodate emerging staff learning needs, such as understanding the effects of the TPLC reorganization on medical device review (e.g., medical device usability testing, digital health, agile software development).

Table 4-14. ELP Site Visits and Participants

Program Fiscal Year	Number of Site Visits	Number of Participants
FY 2018	52	692
FY 2019	38	474
FY 2020	5	93

4.3.1.3 CROSS-CENTER COORDINATION TO IMPROVE TRAINING

Coordination with the QMOE Program

DETD and the QMOE Program worked together on: 1) training process improvement; 2) identification of training needs though the Quality Management System (QMS); and 3) development of quality-related training.

First, DETD partnered with the QMOE Program on the staff training PIP project to streamline several DETD processes. The goals of the process improvement effort were to increase involvement of SMEs in curriculum development and improve trainee satisfaction. The effort spanned the training continuum, including establishment of business process time frames, creation of a metrics dashboard framework and a new Training Request SOP pilot.

Second, to help identify training needs, DETD and the QMOE Program leverage information gathered through the QMS, which relies on several components (e.g., Feedback✓CDRH, audits) for monitoring quality and consistency across CDRH's operations. DETD and the QMOE Program collaborate to develop tailored training when the QMS detects potential issues (e.g., nonconformities, risks) where training is needed. For example, staff input received via Feedback✓CDRH resulted in development of two trainings on the Document Control System (DCS), and audit findings prompted training to improve reviewer understanding for use of Four-Part Harmony (4PH) in deficiency letters.

Third, DETD and the QMOE Program also work together on the development of quality-related trainings. In addition to the DCS training mentioned above, DETD and QM also collaborated to develop, deliver, and assess training on LB principles. A Kirkpatrick Level 3 evaluation of this training was conducted and is discussed below in Section 4.3.2.

Coordinated with Other Offices, Programs, and Divisions

OPEQ established the Professional Development Program (PDP) during the TPLC reorganization to "provide guidance, information, and resources to develop an exceptional OPEQ workforce." DETD coordinates with PDP staff to support mission-critical behaviors and quality reviews by gathering and implementing changes based on Kirkpatrick data, meeting reviewer needs by identifying content gaps in the RCP curriculum, and supporting integration of CDRH's premarket and postmarket offices. PDP staff and DETD have addressed challenges identified by CDRH employees, such as reducing RCP learning commitments and converting classroom training to online training. DETD and PDP staff have also supported the learning needs of new staff involved in medical device regulation by developing a program where tenured staff members serve as mentors and learning resources for their colleagues. Executed differently by each OPEQ sub-office, mentors are assigned to new staff members based on their areas of technical expertise.

DETD also works with SMEs at the Office, Division, and Team levels to coordinate opportunities for reviewers to stay informed of updates to internal processes and procedures and regulatory issues across the TPLC through the OPEQ Rounds and TPLC Grand Rounds programs. The OPEQ Rounds program offers trainings on guidance issuances, SOPs, WIs, forms, tools, and templates to keep reviewers up-to-date on the Center's premarket and postmarket regulatory actions and review processes. DETD also uses feedback gathered from attendees and recommendations from other Centers across the Agency to inform topics of future rounds (e.g., including

presentations by CBER SMEs on relevant knowledge areas that impact medical device reviews). TPLC Grand Rounds presentations provide employees across the Center another opportunity to share interesting and challenging issues related to review activities across the TPLC and seek feedback from senior management and Center staff. Table 4-15 provides additional details on DETD's coordination with OPEQ.

Table 4-15. DETD Coordination with Other Offices

OPEQ Partners	Description
Professional Development Program	• Reduced RCP learning commitments from 10 days to six days • Converted classroom learning to online learning, as appropriate • Supported learning needs of new staff members in policy, process, and legislative knowledge with a mentorship program implemented by each OHT and monitored by staff supervisors • Modified the Reviewer Training Program to support mission-critical behaviors and quality reviews by implementing feedback from Kirkpatrick data
Subject Matter Experts	• Provide tailored and relevant on-the-job training opportunities that address reviewer needs through OPEQ Rounds and TPLC Grand Rounds • Gather feedback from attendees to inform topics of future rounds
OHT Employees	• Develop and deliver TPLC Grand Rounds, which cover topics on complex and innovative medical device technologies • Share challenges and insights across the TPLC • Participated in 39 TPLC Grand Rounds sessions reaching over 1,325 staff

4.3.2 ASSESS IMPACT OF CURRICULUM-BASED PREMARKET TRAINING USING THE KIRKPATRICK FRAMEWORK

This section describes how FDA met each of the commitments shown in Table 4-16. The findings are described in the following two sections:

- 4.3.2.1 Implemented Kirkpatrick Level 3 Evaluation of Behavior Change; and
- 4.3.2.2 Implemented Kirkpatrick Level 4 Evaluation.

Table 4-16. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• FDA will achieve Kirkpatrick Level 3 for curriculum-based premarket training through an assessment of work performance behavior change by the end of FY 2020. • FDA will evaluate the effectiveness of the impact of curriculum-based premarket training activities on relevant premarket program metrics and goals (Kirkpatrick Level 4) by the end of FY 2020.

4.3.2.1 IMPLEMENTED KIRKPATRICK LEVEL 3 EVALUATION OF BEHAVIOR CHANGE

Assessed RCP

FDA has used the Kirkpatrick Model [10] to gauge the impact of training received through the RCP since 2011 and for the ELP since 2012. DETD consulted with Kirkpatrick Partners to develop its implementation plan to evaluate training programs using the Kirkpatrick 4-level framework, shown in Table 4-17.

Table 4-17. Description of the Four Levels of Kirkpatrick Evaluation

Kirkpatrick Level	Description of Kirkpatrick Level
Level 1: Reaction	The degree to which participants find the training favorable, engaging, and relevant to their jobs.
Level 2: Learning	The degree to which participants acquire the intended knowledge, skills, attitude, confidence, and commitment based on their participation in the training.
Level 3: Behavior	The degree to which participants apply what they learned during training when they are back on the job.
Level 4: Results	The degree to which targeted outcomes occur as a result of the training and the support and accountability package.

DETD administered Kirkpatrick Level 3 evaluations to explore how RCP training has led to changes in work performance and critical behaviors across four areas: 1) Use of 4PH in the preparation of deficiencies; 2) Use of the SMART templates for 510(k)s; 3) Appropriate use of interactive review); and 4) Appropriate use of RTA review.

Surveys were administered post-training to RCP participants and staff supervisors to assess the transfer of knowledge, skills, and opinions on participants' work performance after completing training. In the FY 2020 survey,

[10] "The Kirkpatrick Model," Kirkpatrick Partners https://www.kirkpatrickpartners.com/Our-Philosophy/The-Kirkpatrick-Model – accessed 7/19/2021

approximately 30 reviewers and 10 supervisors were surveyed. Three to four questions were posed on each critical behavior and participants were asked to rank their answers on a six-point scale: Never, Rarely, Occasionally, Often, Always, and Not Applicable. Reviewers' self-assessment indicated that they applied the critical behaviors more frequently and consistently, as compared to the supervisors' assessment, shown in Table 4-18. DETD plans to conduct its next assessment in October 2021 and will conduct an in-depth review of the critical behaviors during MDUFA V.

Table 4-18. Key Takeaways from Kirkpatrick Level 3 Survey of Critical Behaviors

Critical Behavior	Key Takeaway: Reviewer Perspective	Key Takeaway: Supervisor Perspective
Use of 4PH: Explains the Scientific Rationale for Requesting Additional Information or, When Appropriate, Correctly Cites the Basis of the Rationale	• 81% indicated they "always" explain the scientific rationale • When "always" and "often" are combined, the rate rises to 93%	• 64% indicated staff "always" explain the scientific rationale • When "always" and "often" are combined, the rate rises to 91%
Use of SMART Template: Prepares an Accurate Review Summary	• 52% indicated that use of SMART provides prepares an accurate review summary • When "always" and "often" are combined, the rate rises to 70% • 23% indicated the question was not applicable	• 40% indicated that use of SMART prepares an accurate review summary 40% often • When "always" and "often" are combined, the rate rises to 80% • 10% indicated the question was not applicable
Use of Interactive Review: Use for Appropriate Deficiencies	• 31% indicated that interactive review is "always" used only for appropriate deficiencies • When "always" and "often" are combined, the rate rises to 76% • 14% indicated the question was not applicable	• 30% indicated that interactive review is "always" used only for appropriate deficiencies • When "always" and "often" are combined, the rate rises to 60% • 30% indicated the question was not applicable
Use of RTA Review: Use Reviewer Discretion to Conduct Interactive Review during RTA Review Correctly	• 31% indicated that they "always" use reviewer discretion to conduct interactive review during RTA correctly • When "always" and "often" are combined, the rate rises to 59% • 24% indicated the question was not applicable	• 20% indicated that staff "always" use reviewer discretion to conduct interactive review during RTA correctly • When "always" and "often" are combined, the rate rises to 60% • 30% indicated the question was not applicable

Assessed ELP

DETD also administered post-training surveys to 155 ELP participants in 2020 to evaluate the impact of the site visits on their learning and behavior. ELP is intended to provide CDRH staff with an opportunity to understand the policies, laboratory and manufacturing practices, and the challenges addressing patient perspective/input, quality system management, and other concerns that impact the device development lifecycle. These goals are directly linked to CDRH's strategic priorities of "Partnering with Patients," "Promoting a Culture of Quality and Organizational Excellence," and "Simplicity and Collaboration."

The Kirkpatrick survey asked ELP participants to self-assess their level of confidence in demonstrating 11 critical behaviors (e.g., provide industry with predictable, consistent, transparent, and efficient regulatory pathways; enhance communication and facilitate the premarket review process; understand current industry practices, innovative technologies, regulatory impacts and needs) before and after the site visit). Results showed participants felt they had increased their knowledge in all critical behaviors after the site visit. The largest increase in confidence was in the ability to "understand the challenges of quality systems design and management as they contribute to the success of the device development life cycle," with 65% of respondents indicating "I am confident I can do it: with assistance or with more practice; on my own; and help others to do it as well confidence" before the ELP, increasing to 92% after the ELP. Another notable increase was in respondents' confidence in their ability to "describe how patient perspective and quality systems management advances the development and evaluation of innovative devices, and monitor the performance of marketed devices," increasing from 76% prior to the ELP to 95% after the ELP.

4.3.2.2 IMPLEMENTED KIRKPATRICK LEVEL 4 EVALUATION

A Kirkpatrick Level 4 evaluation of the Center's training measured the impact of training activities on prespecified and relevant premarket program metrics and goals at the Center level. CDRH deployed post-course surveys with CDRH supervisors and industry, as applicable, to assess reviewer success applying the critical behaviors after visiting a site, from training on LB principles and the impact that training had on requests for additional information (i.e., deficiencies). The Center also surveyed industry to gauge their experience with FDA's review process after reviewers had completed LB training. The Center plans an additional Level 4 evaluation on the organizational impact of reviewer participation in ELP.

Evaluated Training Impact on Organizational Outcomes

FDA has conducted Level 4 evaluations for LB training and the RCP. In 2018, CDRH surveyed supervisors regarding the impact of LB training on deficiencies. Approximately one-third of supervisors indicated that reviewers were writing fewer overall deficiencies following completion of the LB training. Supervisors also noted that the need for revisions during supervisory review of deficiency letters decreased. In 2020, a survey was administered to supervisors to assess whether RCP training and tools supported application of the critical behaviors. Supervisors believed that RCP contributed to new reviewers' consistent application of each critical behavior. The RCP and "help from peers/mentors" were ranked by supervisors as having the most impact (compared to SharePoint resources, assistance from supervisors, and TPLC Grand Rounds) on the critical behaviors. While further data on program or organizational metrics and goals are currently not available, FDA plans to continue the development and implementation of Level 4 evaluations. FDA is also considering expanding the evaluations to measure the impact of ELP on review submission workload and efficiency.

4.3.3 CONCLUSION

Overall, FDA met its MDUFA IV commitments by enhancing training for new and existing reviewers, providing further targeted and personalized training to staff, and evaluated training using the Kirkpatrick framework. To improve training, CDRH implemented the RCP Revamp, which streamlined training allowing for quicker onboarding of review staff. DETD also coordinated with the QMOE Program and other offices (e.g., PDP staff, OHTs) to identify training needs and implement Kirkpatrick Levels 3 and 4 training evaluations.

4.4 Quality Management Program

CDRH leadership has demonstrated its commitment to quality principles in the Center's Strategic Priorities, including to "Promote a Culture of Quality and Organizational Excellence" in 2016-2017[11] and throughout its 2018-2020 Priorities.[12] Quality efforts have focused on developing consistent structures, processes, standards, metrics, and a culture committed to quality and continuous improvement.[13] The MDUFA IV commitments for QM are largely focused on implementation of a centralized QM organization, establishment of a QM Framework, and the development of an audit program. Booz Allen evaluated the QM efforts underway and CDRH's progress and status in terms of the evolution and maturity of the QMOE Program.

Booz Allen found that CDRH met its MDUFA IV commitments by establishing both a dedicated QM Program and QM Framework for the Center, and developing and implementing a QMS, which includes an audit program.

The assessment findings are presented in two sections:

- 4.4.1 Establish a Quality Management Program and Framework; and
- 4.4.2 Build an Audit Program.

[11] "CDRH 2016 – 2017 Strategic Priorities," FDA https://www.fda.gov/media/95317/download – accessed 9/19/2021
[12] "CDRH 2018 – 2020 Strategic Priorities," FDA https://www.fda.gov/media/110478/download – accessed 9/19/2021
[13] "CDRH 2016 – 2017 Strategic Priorities – Accomplishments," FDA https://www.fda.gov/media/110481/download – accessed 9/19/2021

4.4.1 ESTABLISH A QUALITY MANAGEMENT PROGRAM AND FRAMEWORK

This section describes how FDA met each of the commitments shown in Table 4-19. The findings are described in the following three sections:

- 4.4.1.1 Establish Quality Management Program;
- 4.4.1.2 Establish a Quality Management Framework; and
- 4.4.1.3 Establish a Quality Management System.

Table 4-19. MDUFA Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• The Agency will establish a dedicated QM Unit that reports directly to the CDRH Director or Deputy Director and establish a quality management Framework for the premarket submission process in CDRH. • The Framework will include infrastructure, senior management responsibility, resource management, lifecycle management, and quality management system evaluation.

4.4.1.1 ESTABLISH QUALITY MANAGEMENT PROGRAM

As part of the TPLC reorganization, CDRH established a central QMOE Program inside the Office of the Center Director (OCD) focused on enhancing the consistency and predictability of high-quality premarket review of medical devices. The QMOE Program is guided by key tenants of quality, including transparency, customer focus, standardization, and predictability. The QMOE Program developed and oversees the Quality Policy, the QM Framework, and the QMS to support quality assurance. Since 2018, the QMOE Program has been International Organization for Standardization (ISO) 9001:2015 certified for the provision of QM and organizational excellence (OE) services and tools to quality initiatives in the Center. CDRH Leadership governs the QMOE Program through Center- and Office-level QM Reviews (QMRs). QMRs examine alignment of the QMOE Program with the strategic direction of the Center. Included in the QMRs are an assessment of the Center's Quality Policy and objectives, analysis of QM services, discussion of customer feedback and satisfaction ratings, and improvement areas in CDRH products and services to be addressed using QM tools.

The QMOE Program began with seven FTEs and is projected to grow to 23 FTEs to coordinate quality and process improvement activities across CDRH. Under MDUFA IV, there were 20 QM positions allocated through FY 2021: 16 are allocated to the OCD QMOE Team and four to OPEQ. FDA intends for these four employees to function as dedicated support to help OPEQ cultivate a culture of quality and connect to the Center-wide QMOE Program in OCD. QMOE staff include scientists, engineers, healthcare, and business professionals with QM expertise to engage with both Center staff and industry stakeholders. There are also opportunities available for all employees to gain knowledge through quality training and certifications. Table 4-20 lists the OCD QMOE Team's certifications, representing an investment in quality-related professional development, and Table 4-21 lists quality management certifications achieved Center-wide through opportunities provided by the QMOE Program.

Table 4-20. Certifications Held by QMOE Program Team Members

Certification	Number Held
ISO 9001:2015 A to Z	16
Certified Quality Auditor	7
Lean Six Sigma Green Belt	6
Certified Quality Improvement Associate	5
Lean Six Sigma Yellow Belt	4
ISO 9001:2015 Lead Auditor	3
ISO 17025:2015 Trained	3

Table 4-21. Center-Wide Quality Management Certifications

Certification	Number Held
Certified Quality Improvement Associate	149
Certified Quality Auditor	64
Lean Six Sigma Yellow Belt	41
Lean Six Sigma Green Belt	18

4.4.1.2 ESTABLISH A QUALITY MANAGEMENT FRAMEWORK

The QM Framework, developed by the QMOE Program, outlines the scope and requirements of the QMS based on the ISO 9001:2015 standard. The QMOE Program drafted the first iteration of the QM Framework in 2013 and the Center Science Council's QM Subcommittee finalized the Framework one year later. In 2018, CDRH revised the Framework to bring it into full alignment with ISO 9001:2015 requirements and updated QMS processes. Table 4-22 shows how the QM Framework addressed the commitments by including the components specified.

Table 4-22. Mapping Commitment Letter Requirements to the QM Framework

MDUFA IV QM Framework Requirement	Section(s) of QM Framework
Infrastructure	**Infrastructure:** Addresses facilities, utilities, hardware, software, and other resources to allow staff to perform their tasks (e.g., device review)
Senior Management Responsibility	**Leadership and Commitment:** Addresses key responsibilities of senior management for system design, implementation, maintenance, and improvement
Resource Management	**Resources, Monitoring and Measuring Resources, Organizational Knowledge:** Addresses resource requirements for implementation and improvement of the QMS as well as customer satisfaction
Lifecycle Management	**Planning of Changes, Production and Service Provision:** Addresses management of all aspects of quality, reliability, and risk throughout the product lifecycle, including information exchange and flows throughout the QMS
QMS Evaluation	**Performance Evaluation:** Addresses scope, methods, and schedule for evaluating the QMS's performance and effectiveness (e.g., establishing metrics, management review, customer satisfaction, and audits)

4.4.1.3 ESTABLISH A QUALITY MANAGEMENT SYSTEM

A QMS is a formalized system that documents processes, procedures, and responsibilities for achieving quality policies and objectives. CDRH developed its QMS following the roadmap laid out in the QM Framework, which outlines the scope and requirements of the QMS. CDRH implemented the QMS to help ensure that quality objectives are met in accordance with the ISO 9001:2015 standard, surpassing the MDUFA IV commitments. An ISO-compliant system certifies that organizations use robust, formal processes to manage quality control. Figure 4-8 depicts the individual components of CDRH's QMS, with arrows depicting information flow from one component leading to an action in the next (e.g., internal feedback received leading to a document update, or audit findings leading to process improvements). The remainder of this section will focus on certain QMS components, including Feedback✓CDRH, the Customer Service Survey, PIP, the DCS, and Audits—interconnected elements that are critical in meeting CDRH's key tenants of quality.

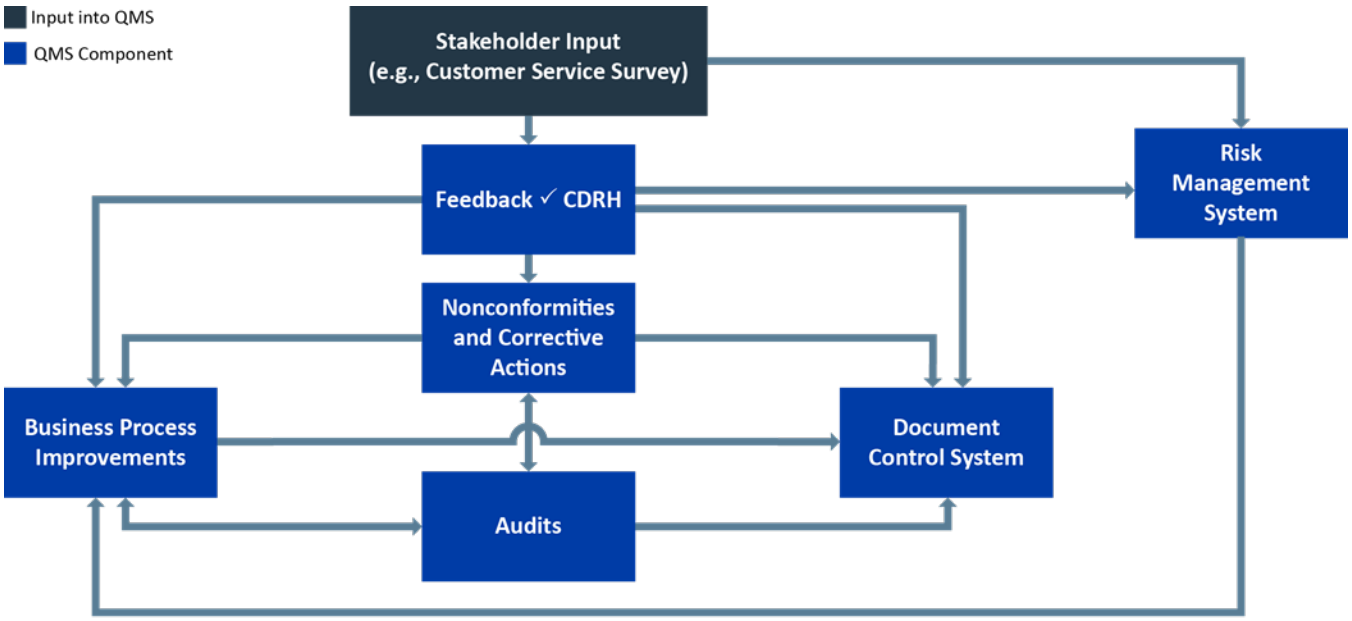


Figure 4-8. Components of the CDRH QMS

Collect Internal Input Through Feedback✓CDRH

Customer service is a core tenet of ISO 9001:2015 and CDRH's QMS, as well as one of the Center's 2014-2015 Strategic Priorities. The QMOE Program manages multiple sources of customer feedback including SharePoint and email submissions, and anonymous suggestion boxes located throughout the Center, and Feedback✓CDRH system, which is a voice-of-customer (VOC) tool used since 2015 to capture, prioritize, and address employee feedback on quality issues. These issues range from relatively simple concerns, such as broken hyperlinks within DCS-controlled

documents, to more substantive process changes. These feedback data have multiple uses, including for case collection, trend analysis, and identification of opportunities for continuous improvement.

After receiving Feedback✓CDRH submissions, the QMOE Team reviews and distributes submissions to the relevant office to address the customer's issue. An exception to this exists for critical issues, which the team triages immediately upon submission. For transparency, the internal CDRH Public Page publishes all Feedback✓CDRH submissions. CDRH also uses Feedback✓CDRH submissions to inform its reporting to the Center Director. Since the MDUFA IV Phase 1 Assessment report, Feedback✓CDRH has continued to evolve. Several new process improvements include easy reporting via links in the header of all SOPs and WIs; access via shortcuts from the desktop, intranet, and SharePoint; and the ability to request expedited processing of urgent feedback.

Defined metrics demonstrate the emphasis on VOC. For example, the QMOE Team has set performance goals of reaching a decision for 80% of submissions within 30 days and closing 80% of cases within 90 days. These metrics are monitored and displayed for CDRH employees on the QMOE Team's Tableau dashboard. In 2019, the QMOE Team exceeded these goals, with an 89% rate for both metrics. The QMOE Program is similarly on track to surpass the goal, with rates of 88% and 86%, respectively, as of November 2020.

Collect External Input Through Customer Service Survey

The QMOE Program also collects feedback from external stakeholders through its Customer Service Survey. This provides the Center with the opportunity to: 1) track and identify opportunities for continuous process improvement projects; 2) use the data for trend analysis and follow-up with specific Offices; and 3) collect input on customer satisfaction with QMS products and services. As part of the Center-wide focus on customer service, all employees receive training on customer service principles (e.g., active listening, problem solving, and process improvement techniques) to meet the Center's goal of 90% customer satisfaction. The survey provides the opportunity for CDRH QMOE and each Office to actively monitor customer satisfaction using unique codes for each Office. CDRH customer service satisfaction rates are consistently at an overall high rate with both internal and external stakeholders (e.g., 92% within CDRH and 95% with industry stakeholders between January and July of 2020).

The QMOE Program also uses the survey data to monitor customer satisfaction of its internal interactions with CDRH employees. The QMOE Team has consistently received positive customer service reviews, earning an 88% satisfaction rate between October 2017 and July 2020. QMOE training efforts received an 88% satisfaction rate in 2019 from staff, which increased to 97% as of November 2020. The QMOE Program's tool and service offerings (i.e., components of the QMS including the DCS, Feedback✓CDRH, PIP, and the Customer Service Survey) received an overall satisfaction rate of 83% for FY 2020.

Implement CDRH's Process Improvement Program

In 2018, FDA started a multi-year process improvement effort that aligned with CDRH's Strategic Priority of Simplicity to streamline processes, programs, and approaches to effectively, efficiently, and quickly achieve its mission.[12] Known as the PIP, individual teams employ Lean Six Sigma methodologies to "lean" (i.e., simplify) processes to improve repeatability, efficiency, and effectiveness, support harmonization to increase standardization, and improve clarity of processes and supporting documents (e.g., SOPs and WIs).

A Lean Six Sigma Practitioner leads each PIP effort and collaborates closely with a sponsor and a process owner. Project teams consist of team members who work or have experience in the specific area of focus for the project. The QMOE Program oversees and coordinates many PIP efforts across CDRH, monitors progress, and provides expertise as needed. The QMOE Program has developed the infrastructure for PIP teams and provided initial Lean Six Sigma training and assistance throughout all phases of each project. For example, CDRH developed the PIP Playbook, which guided teams throughout the PIP lifecycle. In addition to providing oversight and facilitating the process, QM staff can also provide subject matter expertise and participate as members of the team. Engagement efforts organized by the QMOE Program, such as Gallery Walks and presentations during CDRH All-Hands meetings, provide a mechanism to promote awareness across CDRH and facilitate conversation around the PIP projects.

CDRH identified its core business processes that were well-suited for a PIP project, 26 of which were priorities for a PIP project in the first year of the effort. During the second year of the PIP, the QMOE Team supported 18 additional PIP projects. As of June 2021, 48 PIP projects were completed, with some paused due to CDRH's response to the COVID-19 PHE. CDRH succeeded in "leaning" 86% of its core business processes and achieved its internal 80% goal slated for the end of calendar year 2020. Table 4-23 lists a select group of PIP projects relevant to other areas of the MDUFA IV Phase 2 Assessment (including one focused on the DCS described in the next section), demonstrating how the QMOE Program is integral to the Center and its core operations.

Table 4-23. Select List of PIP Projects Relevant to Other MDUFA IV Phase 2 Assessment Areas

PIP Project Name (Year)	Category	Assessment Area	Outcomes
Consults (Year 1)	TPLC	Premarket Review Efficiencies	• Defined consult review sub-process and scope, documented in SOP
510(k) (Year 1)	Premarket	Deficiencies	• Added two possible interaction points to reduce rework after sponsors respond to Additional Information Letters • Updated SOP to reflect Center-wide changes
Pre-Submission (Q-Sub) (Year 1)	Premarket	Pre-Submissions	• Standardized process to improve employee experiences • Shifted appropriate tasks towards other staff and created supporting tools (i.e., WI and checklist)
Staff Training (Year 1)	Operations/ Support	Training and Alignment	• Developed an integrated SOP in a standardized format • Created a dashboard of Key Performance Indicator metrics for better performance insight
De Novo (Year 1)	Premarket	Premarket Review Efficiencies	• Removed 20% of administrative steps • Harmonized ODE and OIR processes to support standardization and consistency
Third Party Review (Year 1)	Premarket	Third Party Review Program	• Developed a simple checklist to assist staff in determining the necessity of re-review, with a goal of reducing the number of re-reviews
Premarket Review Harmonization (Year 2)	Premarket	Premarket Review Efficiencies	• Created a lean, harmonized overall premarket process and SOP • Reduced the number of handoffs between staff for certain reviews • Harmonized taxonomy variations
Team Review (Year 2)	Premarket	Premarket Review Efficiencies	• Developed a model to streamline submission evaluation and communication • Defined a common memo structure and process to facilitate collaboration
DCS (Year 2)	Quality	QM	• Ongoing as of November 2020 • Examined challenges to locating, accessing, and using documents within CDRH Docs • Developing potential solutions to DCS pain points, including an updated template, a standardized cover sheet, and clarified document definitions

Continuously Improve the DCS

Document control is a key component of CDRH's QMS. The DCS houses and manages all controlled documents, with document content tightly regulated and updated systematically through managed revisions. This includes all SOPs, WIs, Forms, and Templates (collectively referred to as "SWIFT" documents). CDRH implemented its DCS in 2016 to promote consistency in the use of standardized documents across the Center. The DCS received an update in 2018, incorporating QM components to comply with ISO 9001:2015 requirements, shown in Table 4-24.

Table 4-24. Quality Principles Built into the DCS

Quality Principle	Key Features of DCS
Standardize and Centralize	• DCS is designed to house only the most up-to-date versions of documents (e.g., processes, instructions, forms, and templates), which are stored within CDRH Docs • Each document lists the version number, control history with dates, and a brief description of changes for consistency, version control, and tracking • Tags and smart identifiers are also used to enhance identification and searchability • SOPs and WIs guide the use and maintenance of DCS
Eliminate Redundancies and Increase Consistency	• Designed to ensure that outdated and duplicate versions of documents are removed • The OCD QM and OPEQ conduct yearly reviews as an additional safeguard for version control • Relevant documents are cross-referenced via embedded links to facilitate navigation; links are designed to lead users to the most current versions of documents • Strict version control means the correct documents are used to guide review
Continuously Maintain	• Development of new or updated procedures is documented and uploaded to the DCS • DCS creates and stores all notices whenever a document is created, revised, or withdrawn, allowing CDRH to keep track of any changes to the document • All versions of a document, throughout the document's lifecycle, are retained in the SWIFT Docs database for thorough record-keeping and preservation of institutional knowledge • Restricted access to SWIFT Docs prevents accidental dissemination of older document versions
Continuously Improve	• All documents contain a link to Feedback✓CDRH, allowing employees to easily flag issues with the document • Staff appear to take an active role in the quality improvement of DCS, with 33% of Feedback✓CDRH submissions from OPEQ related to a document issue • Tools and Services Requests (TSR) also play a role in DCS maintenance; since 2018, OPEQ staff have submitted 11 DCS-related requests such as support in formatting and uploading batches of new or revised documents and updating external links

The QMOE Program has continued to encourage use of the DCS and has added new features. The original components of DCS include CDRH Docs, which contains the single most up-to-date version of each controlled document, and SWIFT Docs, a repository of all previous versions of documents that are either out-of-date or no longer used. Newer functions include: Transmittal Notices (TN) to update staff on document revisions and withdrawals; Document Change Requests (DCR) to allow employees to request development of a new document, as well as modifications or withdrawal of existing documents; and CDRH Pilot Docs to allow rapid changes to documents in development, avoiding the layers of permission normally required for controlled documents in CDRH Docs. As of September 2020, CDRH Docs contained 1,038 unique SWIFT documents, a reduction from the 1,218 documents in April 2018,[5] demonstrating the impact of quality harmonization and simplification efforts.

In April 2020, CDRH initiated a DCS PIP effort, prompted by feedback from CDRH staff indicating that documents can be challenging to locate and may require workarounds for access and use. The PIP team identified and consolidated pain points, including unclear DCS nomenclature, inconsistent DCR use, and confusion around responsibilities of various parties in the document development process. The DCS PIP team is in the process of developing potential solutions to these DCS pain points, which include standardizing naming conventions and creating Document Development Guidelines and a standardized Document Cover Sheet for easier searching.

4.4.2 BUILD AN AUDIT PROGRAM

This section describes how FDA met each of the commitments shown in Table 4-25. The findings are described in the following four sections:

- 4.4.2.1 Develop Audit Processes and Solicit Industry Input;
- 4.4.2.2 Identify and Share Best Practices Identified During Audits;
- 4.4.2.3 Perform Required Audits; and
- 4.4.2.4 Expand Audits.

Table 4-25. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• At least once per year, the Agency will discuss with industry the specific areas it intends to incorporate in its ongoing audit plan. • FDA will identify, with industry input, areas to audit, which will include the effectiveness of CDRH's Corrective and Preventive Action (CAPA) process. • As part of these ongoing audits, high-performing premarket review processes utilized in one division will be identified and shared accordingly with other divisions to improve efficiencies and effectiveness. • At a minimum, FDA audits in the following areas will be completed by the end of FY 2020: Deficiency Letters and Pre-Submissions. Additional audits in the following areas will be completed by the end of FY 2022: Submission Issue Meetings, Interactive Review, Withdrawals, Special 510(k) Conversions.

4.4.2.1 DEVELOP AUDIT PROCESSES AND SOLICIT INDUSTRY INPUT

The QMOE Program identifies and prioritizes areas to audit according to its Audit SOP, which delineates the scope, roles, and procedures for conducting audits. The QMOE Team has conducted two evaluations of its audit system and both found that the audit system was in compliance with ISO 9001:2015 requirements. The audit process is subject to continuous improvement with refinements made to the process as audit experience increases.

Any CDRH internal activities may be subject to audit, including QMOE Program activities and the QMS, as well as review processes and programs. Suggestions for audits can come from CDRH Offices, CDRH employees via Feedback✓CDRH, and from industry stakeholders. Figure 4-9 provides an overview of CDRH's audit process.

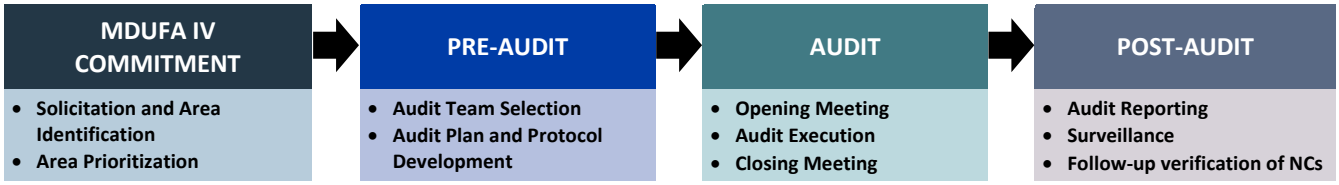


Figure 4-9. Overview of Audit Process

In 2019, the QMOE Program solicited input on the proposed 2020 Audit Schedule from internal stakeholders (e.g., OPEQ, Office of Science and Engineering Laboratories (OSEL), and CDRH senior leadership) and from industry groups (i.e., AdvaMed, MDMA, MITA, and the American Clinical Laboratory Association [ACLA]) as required in the MDUFA IV Commitment Letter. The solicitation notice included the name of the audit areas (e.g., Focal Point Program – Biocompatibility), a list of required audits under MDUFA IV, and a list of completed audits from 2019. CDRH received one response from an industry group requesting additional information about the scope of each audit and recommending three additional audit areas.

After soliciting input, CDRH prioritizes the audits and develops an Audit Schedule based upon several criteria, including QMS conformance data, process importance and risk, recent changes, and outcomes of previous audits. CDRH also develops Audit Plans and Audit Protocols to describe the purpose, methodology, and the scope, which centers on adherence to SOPs and the SOPs' adherence to ISO 9001:2015. An Audit Team, comprised of qualified auditors, works with the audited party to execute the audit. Review of documents and data, as well as observation of work practices, may be conducted to inform the audit. Upon completion, the Audit Team holds a Closing Meeting to communicate findings in a final presentation (the Closeout Report) to the Auditees. If requested by the Auditees, the QMOE Program may assist in addressing any Nonconformances (NCs) and Opportunities for Improvement (OFIs) identified, including solution development and monitoring. The Audit Team logs NCs in accordance with the CDRH NC and Corrective Action (CA) Management policy, rated by risk, and adds to the CDRH NC Records SharePoint. A root cause analysis is conducted, and the Auditee develops and implements Improvement Actions. The Closeout Report highlights any Best Practices (BP) identified during the audit, which are then presented in the Closing Meeting and added to the BPs List SharePoint site maintained by the QMOE Program.

Figure 4-10 illustrates how the findings from audits, along with other components of the QMS (i.e., Feedback✓CDRH, NCs, CAs, and DCS), enabled ongoing process improvements. Beginning in 2019, FDA conducted a series of audits of deficiency letters for 510(k) submissions. The first audit, which assessed for adherence to the 2017 Deficiency Guidance (per the MDUFA IV commitment), identified an NC, which was logged in the QMS; a subsequent root cause analysis identified inconsistent instructions across resources as a contributing factor. In response, FDA undertook various CAs, including clarifying its internal deficiency policy and procedural document, training staff on the updated policy, and conducting a second audit. Following the second audit, further CAs included updates to staff training, targeted staff outreach, and the release of an internal deficiency resource with examples for staff. A third audit, conducted in 2020, prompted further clarifying updates to the internal deficiency procedural document, additional rounds of staff training and outreach, and updates to the review template deficiencies which staff may use as a starting point when writing their own deficiencies.

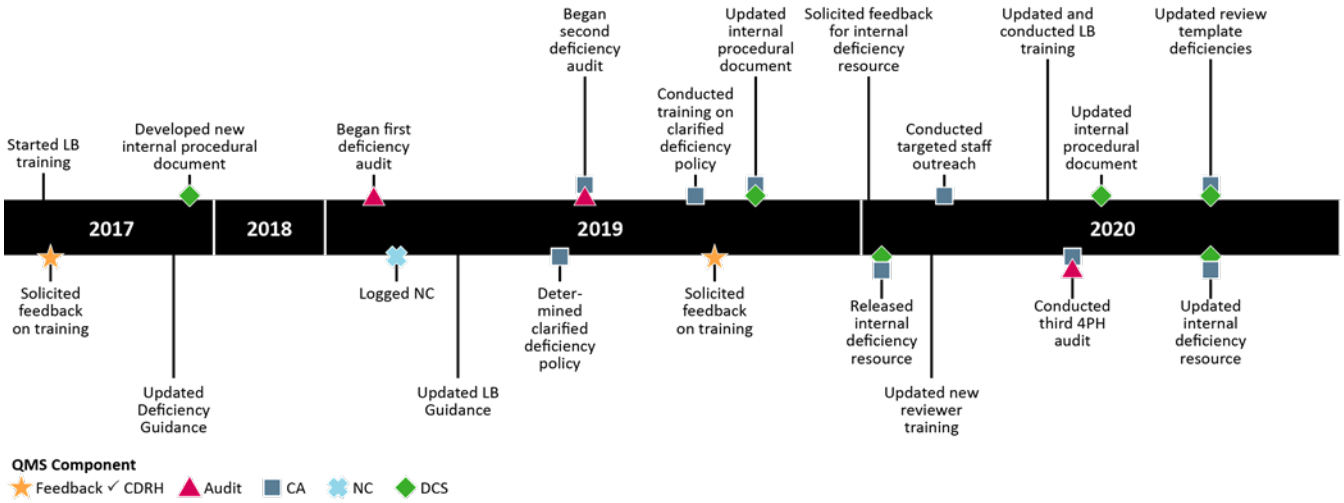


Figure 4-10. QMS Synergy: Four-Part Harmony and Deficiencies Audit Example

4.4.2.2 IDENTIFY AND SHARE BEST PRACTICES IDENTIFIED DURING AUDITS

Audits are one of the vehicles for driving change within the Center by providing a mechanism to identify OFIs and BPs. The audit program defines BPs as "procedures or practices that are accepted or prescribed as being correct or most effective." To address the MDUFA IV commitment to identify "high-performing premarket review processes utilized in one division and share accordingly with other divisions," the BPs identified during audits were included in the Closeout Report during the Closing Meeting and posted on the QMOE Program's Best Practices List SharePoint site, where they are accessible to all CDRH staff. In its first year, the Audit Program focused on assessing aspects of the QMS, limiting the ability to identify best practices related to premarket review. The third year (2020) reflects an expanded scope, with increased focus on premarket review processes, widening the opportunity to identify and share high-performing premarket review processes.

4.4.2.3 PERFORM REQUIRED AUDITS

FDA completed audits of Deficiency Letters and Pre-Submissions by FY 2020, as specified by the MDUFA IV Commitment Letter. The QMOE Program has also conducted an audit of its NC and CA system (ISO 9001:2015 terminology), referred to in the MDUFA IV Commitment Letter as CAPA. In addition, FDA has committed to completing further audits in other areas by FY 2022, as shown in Table 4-26.

Table 4-26. Required Audits from the MDUFA IV Commitment Letter

Audit Topic	MDUFA IV Commitment Letter Submission Date
Deficiency Letters	FY 2020*
Pre-Submissions	FY 2020*
Risk, NC, and CA System	At FDA's discretion*
Submission Issue Meetings	FY 2022
Interactive Review	FY 2022
Withdrawals	FY 2022
Special 510(k) Conversions	FY 2022

*Completed

4.4.2.4 EXPAND AUDITS

FDA conducted several activities to expand audit scope. The QMOE Team has 15 auditors with various certifications shown in Table 4-20, including seven American Society for Quality Certified Quality Auditors and three ISO 9001:2015 Lead Auditors, representing the QMOE Program staff's dedication to further build auditing capability. The number of audits conducted, and the breadth of topic areas, also reflects increased capacity. The number of audits has increased each year, with four initiated in 2018 (the first year for audits by the QMOE Program), 10 in 2019 that required substantial staff time, and 13 scheduled to occur in 2020, although not all were completed as scheduled due to FDA's COVID-19 response. In 2018, the QMOE team largely focused audits on the QMS, with three of four audits involving QMS-related processes (e.g., DCS, Feedback✓CDRH, Risk/NC/CA systems, the Audit Management System, QM Program). Audits have since expanded into other areas, including premarket

review processes (i.e., adherence to review process SOPs), shown in Figure 4-11. In 2019, two audits involved premarket review processes and in 2020, four of the 13 scheduled audits involve premarket review processes.

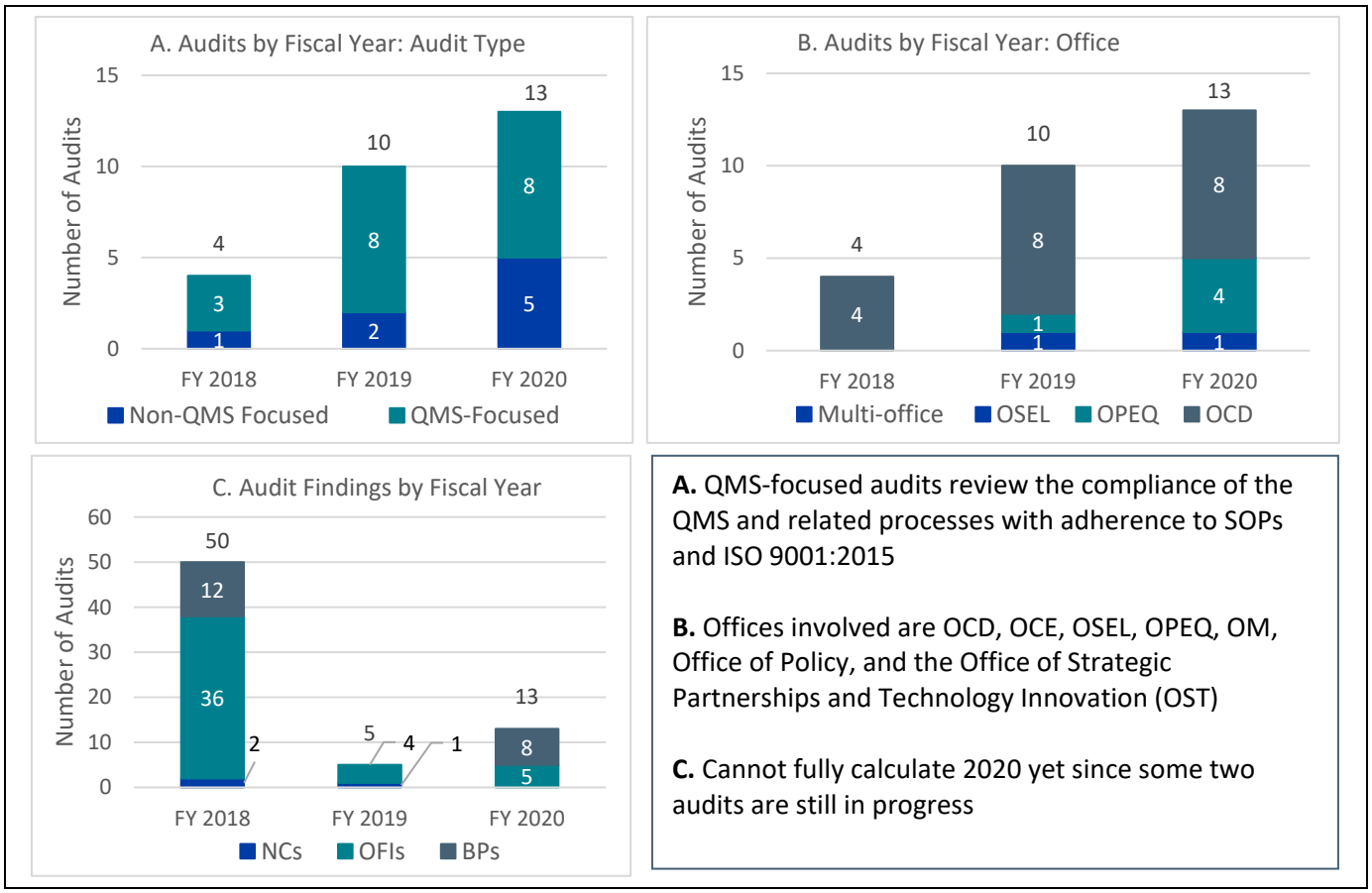


Figure 4-11. Annual Audit Overview (A-C)

The 2020 Audit Schedule, outlined in Table 4-27, demonstrates the range of audit topics, including four audits of premarket review processes, one of training, and eight of QMS processes. The table also presents the status of each audit and the available results to illustrate the nature of any NCs, BPs and OFIs identified.

Table 4-27. FY 2020 Audit Schedule and Preliminary Results

	Audit Title and Purpose	Status	NCs, OFIs, BPs Reported
Review Processes	Deficiency Letters for Adherence to Four-Part Harmony Criteria (MDUFA IV commitment) **	Complete	None
	Pre-Submissions Program Relative to MDUFA IV Requirements (MDUFA IV commitment)**	Complete	None
	Withdrawals Program**	In progress	(None at this time)
	LB Provisions Training and Guidance**	In progress	(None at this time)
Training	Training, Competence and Awareness Conformance to ISO 9001:2015*	Complete	None

	Audit Title and Purpose	Status	NCs, OFIs, BPs Reported
QM Systems and Processes	OPEQ Usage of Feedback✓CDRH, DCS, and QMR as Defined in SOPs and Conformance to ISO 9001:2015**	Complete	BP: Conducts weekly review of all QM processes to ensure all metadata are present and serves as a refresher training to staff
	DCS Conformance to ISO 9001:2015*	Complete	OFI: DCS Admin should consider linking TN to corresponding DCR BP: TN history is listed in metadata and is automated
	Internal Audit Program Implementation as Defined in SOP and Conformance to ISO 9001:2015*	Complete	None
	Design, Development, Verification and Validation (DDVV) as Defined in SOP and Conformance to ISO 9001:2015*	Complete	OFI: Attach a copy of the completion email to the customer in the DDVV record BP: Nintex Workflow file serves as a back-up if something goes wrong with workflow in production
	QMR Implementation as Defined in SOP and Conformance to ISO 9001:2015*	Complete	OFI: Streamline SOP to allow a clearer understanding of the roles and requirements of the process BP: All files discussed in the QMR are easily retrievable and are linked to the final QMR report
	Risk, NC, and CA Implementation as Defined in SOP and Conformance to ISO 9001:2015*	Complete	OFI: Risk Mitigation Plan should be approved by the Associate Director for QM BP: Records are attached to NC/CA and are easily retrievable
	Feedback✓CDRH Implementation as Defined in SOP and Conformance to ISO 9001:2015*	Complete	BP: The feedback lead provides detailed comments when addressing feedback resolutions. The customer is informed of the feedback resolution. The survey link is provided annually to measure customer's satisfaction
	TSR Implementation as Defined in SOP and Conformance to ISO 9001:2015*	Complete	OFI: Completion of the WI and review of Doc 01204 and 01205 to streamline process BP: Automation is used in the form to allow for initial and final approval by the Associate Director for QM

*QMS-focused audit; assesses compliance of the QMS and related processes with adherence to SOPs and the ISO 9001:2015 standard.
**Premarket review-focused audit; assesses compliance with SOPs.

4.4.3 CONCLUSION

FDA met the MDUFA IV commitments to establish both a dedicated QM Program and QM Framework for the Center. To apply the Framework, the QMOE Program developed and implemented an ISO 9001:2015-certified QMS, which includes an audit program. CDRH met additional audit requirements, including the execution of predefined audits, solicitation of industry input, and expansion of audit scope.

The QMOE Program has grown its staff and quality management capacity, developing and coordinating quality practices at the Center level. The QMOE Program and QMS are growing and evolving, with different components of the Program and QMS at different stages of maturity. Quality has matured in phases, with the initial focus on establishing the infrastructure (i.e., the QMS) needed to implement foundational quality management practices and encourage use of the QMS components across the Center. Currently, a major focus is on expanding and improving the QMS (e.g., Feedback✓CDRH, DCS) and measuring Program and QMS performance to ensure that the QMS is running smoothly (i.e., audits). In the next phase of maturation, CDRH could explore how best to continue to grow and support the Center in its advancement of Quality, which may include enhanced data visualizations and analytics, facilitation of process improvements, enhanced audit and assessment capacity, and investment in infrastructure.

4.5 Deficiencies

FDA review staff often identify the need for additional information to make a decision on a marketing application; these requests for additional information needed to complete the review are also known as deficiencies. FDA may convey deficiencies via interactive review or through a deficiency letter. In general, FDA uses interactive review to resolve minor deficiencies with the applicant by phone or email without putting the submission officially on hold. Deficiency letters are delivered through email, generally include at least one major issue, and place the marketing application on hold pending FDA's receipt of the requested additional information. Minor deficiencies may still be included in deficiency letters when related to the resolution of substantive issues (e.g., modification of the proposed IFU may lead to revisions in labeling and administrative items), or if they were still unresolved following interactive review attempts.

FDA undertook a series of deficiency improvement efforts throughout the MDUFA IV timeframe to improve deficiencies in premarket deficiency letters. As demonstrated in Figure 4-12, these efforts include six types of activities: 1) updating guidance; 2) implementing training; 3) developing resources; 4) integrating feedback; 5) conducting outreach; and 6) performing audits. After meeting its deficiency commitments in 2019, FDA made a concerted effort to continue to improve its deficiencies-related processes using an iterative approach. These activities, detailed in the following sections, demonstrate how FDA met the MDUFA IV Deficiency commitments to improve consistency and clarity in deficiency letters.

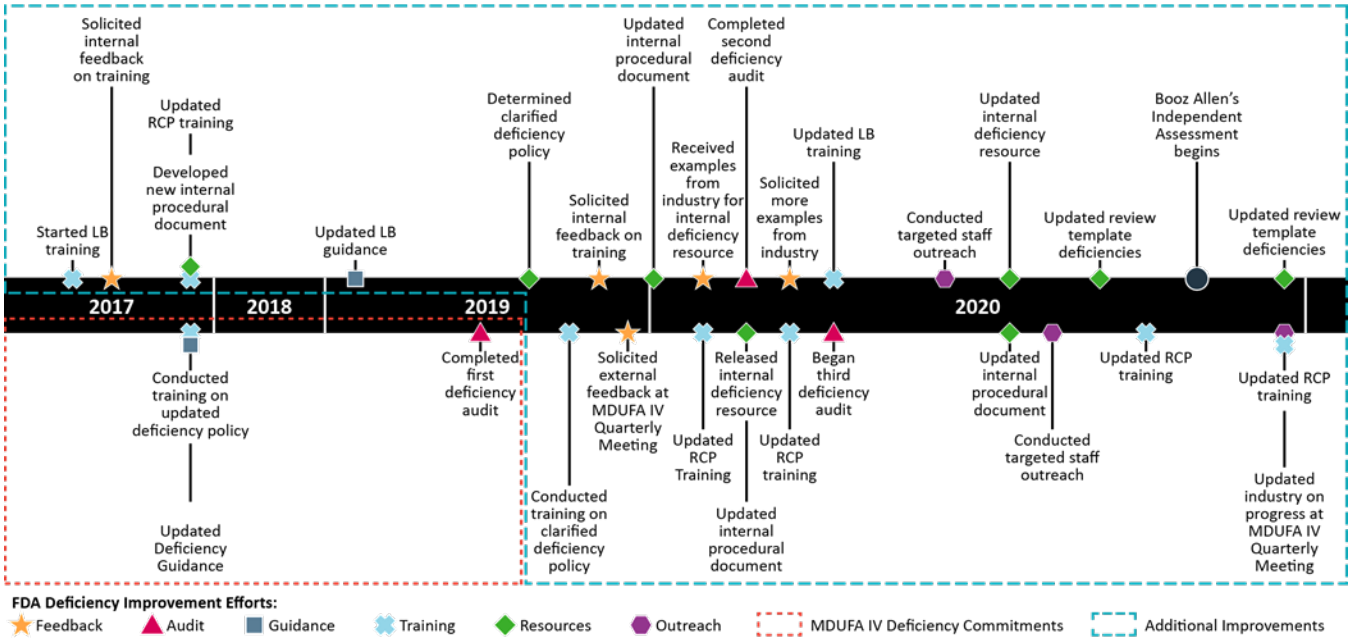


Figure 4-12. Timeline of FDA's Deficiency Improvement Efforts

The assessment findings are presented in five sections:

- 4.5.1 Phase 1 Improvements: Publish and Implement Updated Deficiency Guidance;
- 4.5.2 Audit Deficiency Letters to Assess Impact of Phase 1 Improvements;
- 4.5.3 Implement Additional Improvements to Address Audit Findings;
- 4.5.4 Assess Impact of FDA's Improvement Efforts; and
- 4.5.5 Update Deficiency Guidance with Best Practices.

4.5.1 PHASE 1 IMPROVEMENTS: PUBLISH AND IMPLEMENT UPDATED DEFICIENCY GUIDANCE

This section describes how FDA met each of the commitments shown in Table 4-28.

Table 4-28. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• By October 1, 2017, the Agency will publish a level 2 update to the final guidance "Suggested Format for Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions of FDAMA; Final Guidance for Industry and FDA Staff" to reflect the following: ○ All deficiency letters will include a statement of the basis for the deficiencies (e.g., a specific reference to applicable section of a rule, final guidance, recognized standard unless the entire or most of document is applicable). ○ In the instance when the deficiency cannot be traced in the manner above and relates to a scientific or regulatory issue pertinent to the determination, FDA will cite the specific scientific issue and the information to support its position. ○ All deficiency letters will undergo supervisory review prior to issuance to ensure the deficiencies cited are relevant to a marketing authorization decision (e.g., 510(k) clearance, PMA approval, and de novo classification). • FDA will train staff and managers on this process improvement and the updated guidance.

4.5.1.1 UPDATED 2017 DEFICIENCY GUIDANCE

History and Holistic Approach

Given the importance of this topic and the need for clear criteria and procedures for deficiency letters, FDA first published the relevant Guidance, "Suggested Format for Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions of FDAMA," in 2000 (hereinafter referred to as the 2000 Deficiency Guidance). The purpose of this guidance was to help FDA reviewers develop complete deficiencies in accordance with the LB provisions when requesting additional information and to provide industry a suggested format for responding to these requests for additional information. During this time, FDA first introduced its four-part approach to deficiency writing (also referred to as "Four-Part Harmony"). The 4PH content policy provides a framework for communicating and documenting the reviewer's thought process behind each deficiency. By using the 4PH format, FDA intends to promote clarity and consistency in deficiency letters and provide applicants with the necessary information to respond to the listed deficiency.

Statement of Basis for the Deficiency

As part of its MDUFA IV Deficiency commitments, FDA updated the Deficiency Guidance in 2017[14] to include revised language regarding what to include in a statement of basis for the deficiency (i.e., Part 3, which is the primary focus of the MDUFA IV Commitment Letter and this report), reflected in Figure 4-13. In addition to explaining the request's relevance to the regulatory decision (which was part of the 4PH content policy described in the 2000 Deficiency Guidance), Part 3 was expanded to also include a reference to either a final rule, final guidance, FDA-recognized standard, or specific scientific or regulatory issue and information to support FDA's position. FDA met its commitment by incorporating this language from the MDUFA IV Commitment Letter directly into the 2017 Deficiency Guidance.

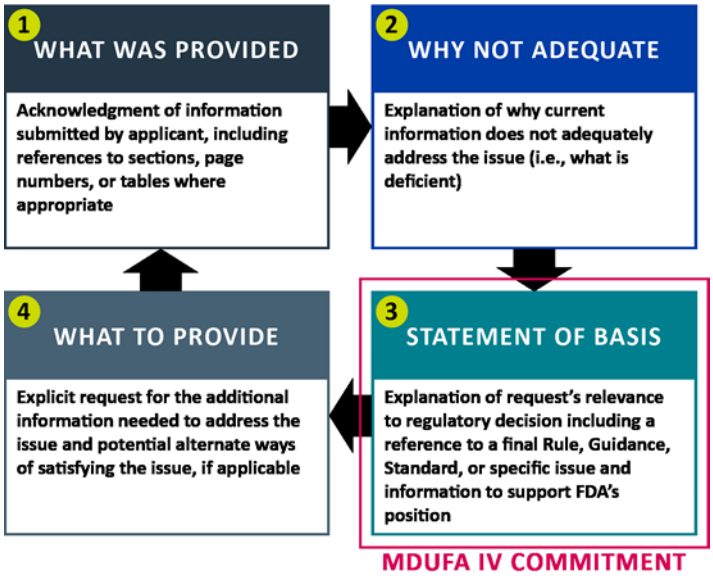


Figure 4-13. Four Elements of an Effective Deficiency

Supervisory Review

Consistent with the MDUFA IV Deficiency commitments, the 2017 Deficiency Guidance states all deficiency letters should undergo supervisory review prior to issuance to confirm that deficiencies cited are relevant to a marketing decision. Both prior to and during the MDUFA IV timeframe, FDA's workflow required supervisory concurrence on

[14] "Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/71735/download – accessed 3/2/2021

all deficiency letters for marketing applications. Once the appropriate manager provides concurrence, an auto-generated email is sent to the submitter from the LR's email address.

The 2017 Deficiency Guidance further expanded on this requirement beyond what was stated in the Commitment Letter in several ways, including the integration of the explanation of the request's relevance to the marketing decision into the statement of basis (i.e., Part 3) language, emphasizing the importance of this element for both reviewers and managers alike. The Guidance also noted that managers should consider the totality of all deficiencies listed in a letter to determine whether each individual request is still appropriate and aligned with LB principles. Finally, the 2017 Deficiency Guidance states managers should check that deficiencies include the four elements described above (including the statement of basis) and prioritized according to the Agency's view of their significance, with the most significant deficiencies (e.g., most challenging for the sponsor to address in terms of resources or time) listed first.

Additional Guidance Updates

In addition to the deficiency format and content policy described above, FDA included additional updates to the 2017 Deficiency Guidance that go beyond the MDUFA IV commitments, demonstrating their holistic approach to deficiency letters. For example, in accordance with FDA's LB Guidance[15] (initially published in 2002) that all premarket regulatory activities (including deficiency letters) are subject to LB provisions, the 2017 Deficiency Guidance emphasizes the importance of following LB provisions when considering requests for additional information. Review staff are instructed to request the minimum amount of information necessary to address the identified issue, as well as consider alternative approaches to resolve regulatory issues to optimize the time, effort, and resources of both review staff and submitters. The 2017 Deficiency Guidance also instructs review staff to separate deficiencies into major (i.e., deficiencies which, if not resolved, will preclude a favorable decision on the marketing application) versus minor (i.e., requests that can be resolved in a straightforward manner but should be addressed to meet regulatory requirements) deficiencies, as well as additional considerations (i.e., suggestions or requests that are not expected to preclude a favorable decision on the marketing application).

4.5.1.2 IMPLEMENTED DEFICIENCY GUIDANCE

Internal Procedural Document

Following the release of the updated 2017 Deficiency Guidance, FDA created a new internal procedural document to help staff implement this Guidance. This document reiterates the Guidance's focus on LB principles, separating major and minor deficiencies, the 4PH deficiency format including the statement of basis, and the role of supervisory review. The document also provides clarity on FDA staff roles and responsibilities, as well as letter format.

Staff Training

FDA provided specific training on the MDUFA IV commitments to all premarket staff prior to the start of MDUFA IV in 2017, including a required 15-minute online training that provided an overview of FDARA and the MDUFA IV commitments. As part of its RCP, the foundational training provided to new reviewers, FDA updated two modules: "Basics of Four-Part Harmony in Lead and Consult Reviews" and "Least Burdensome Provisions and Principles." The first module, previously implemented in March 2017, discussed the recent 2017 Deficiency Guidance update, emphasized the MDUFA IV commitment language (i.e., inclusion of a statement of basis for the deficiency and supervisory review to ensure the deficiencies cited are relevant to a marketing authorization decision), and provided examples of deficiencies which included a statement of basis. The second module, which launched in September 2017, builds upon concepts described in FDA's LB Guidance, emphasizing the importance of its provisions across CDRH's regulatory activities (including premarket). To augment this module, CDRH also offered an in-person course entitled "How to Make the Most of Least Burdensome: Case Study Practice" for staff in February 2018.

[15] "The Least Burdensome Provisions, Concept and Principles: Guidance for Food and Drug Administration Staff," FDA https://www.fda.gov/media/73188/download – accessed 3/2/2021

4.5.2 AUDIT DEFICIENCY LETTERS TO ASSESS IMPACT OF PHASE 1 IMPROVEMENTS

This section describes how FDA met its commitment to complete an audit of deficiency letters by the end of FY 2020 shown in Table 4-29.

Table 4-29. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• FDA will complete an audit of Deficiency Letters by the end of FY 2020 (i.e., before 10/01/2020).

4.5.2.1 AUDIT METHODOLOGY

To meet its MDUFA IV commitment, CDRH's QMOE Program conducted an audit of Traditional 510(k) Additional Information letters to assess the impact of the 2017 Deficiency Guidance update and its implementation. The QMOE Program led the audit and worked in conjunction with the Office of Regulatory Programs (ORP) in OPEQ, which offered assistance in developing the audit protocol, training auditors on 4PH principles, and providing expertise as needed. The audit took approximately 50 hours total (between training, active audit time, data analysis, and results reporting) and was completed over five months (between February and July 2019).

The audit sample was comprised of 20 Additional Information letters randomly selected from letters written between May 1, 2018 to September 30, 2018. Within each letter, FDA randomly selected up to 10 deficiencies, with lettered sub-parts of numbered deficiencies counting as individual deficiencies (e.g., sub-parts 1a, 1b, and 1c would be counted as three distinct deficiencies). In total, auditors assessed 194 individual deficiencies, marking each component as either "Present," "Not Present," or "Undetermined" in a data collection instrument (DCI). Although auditors assessed the deficiencies for the presence of all 4PH components (per the definitions outlined in the 2017 Deficiency Guidance), this report focuses only on aspects of the audit that were relevant to the statement of basis. The audit team discussed deficiencies initially marked as "Undetermined," which indicated that they were either difficult to identify or subject to interpretation, to determine whether the component was present before recording their answer in the DCI. However, FDA did not track the total number of deficiencies discussed nor the exact nature of the disagreements.

4.5.2.2 AUDIT RESULTS

The deficiency audit was the QMOE Program's first audit of a regulatory program, which the program completed over a year ahead of the MDUFA IV commitment (i.e., end of FY 2020). The audit results showed that inclusion of a reference to a final rule (FR), final Guidance (FG), FDA-recognized Standard (FS), or a specific scientific, clinical, or regulatory issue (SI) was present in 39% (75/194) of the deficiency samples, with FG (30) and SI (29) being the most prevalent reference types. In addition, an explanation of the request's relevance to the 510(k) regulatory decision was present in 49% (96/194) of the deficiency sample. Although both elements (i.e., reference and relevance statements) were present together in only 24% (46/194) of deficiencies, at least one of the elements was present in 64% (124/194) of deficiencies sampled. Due to varying interpretations of the criteria, there was uncertainty among auditors and reviewers whether both elements needed to be present in each deficiency, or rather if the presence of one element was sufficient. Recognizing the opportunity for improvement, FDA undertook a series of additional actions to clarify the criteria used to define the statement of basis, which are described in the following section.

4.5.3 IMPLEMENT ADDITIONAL IMPROVEMENTS TO ADDRESS AUDIT FINDINGS

The outcomes discussed in the following sections reflect activities that go beyond FDA's MDUFA IV commitments.

4.5.3.1 CLARIFY DEFICIENCY CONTENT POLICY

Given its importance in understanding the rationale behind the deficiency and the results of the first QMOE audit described above, FDA decided to clarify Part 3 (the statement of basis) of its 4PH content policy by splitting it into two sub-parts: a statement of reference (Part 3a) and statement of relevance (Part 3b), and emphasizing that except when referencing a final rule, both parts (Parts 3a and 3b) should be included.

4.5.3.2 RE-BASELINE 2018 DEFICIENCY LETTER SAMPLE WITH CLARIFIED DEFICIENCY POLICY

Audit Methodology

Following FDA's clarification of the criteria used to describe the statement of basis, the QMOE Team re-baselined the FY 2018 sample from the first deficiency audit described above. The key criteria updates included an expanded statement of relevance (Part 3b), which could include not only explanations of the request's relevance to the regulatory decision, but also relevance to understanding the device's benefit-risk profile or performance, the safe and effective use of the device, or an explanation that cited regulatory precedent (e.g., a 510(k) predicate). Additionally, FDA created a clarified key for when the statement of basis was considered Present, indicating that both a reference (Part 3a) and relevance (Part 3b) must be present. Using the 194 deficiencies that had been audited previously, FDA reassessed the rate of presence of Part 3b using the new definition for Part 3b in a second audit.

Audit Results

The results from the requalification audit showed that 62% (120/194) of the deficiencies contained Part 3b, an increase from 49% in the first audit. In addition, the percentage of deficiencies containing both elements (Part 3a and 3b) was 27% (53/194), according to the clarified policy that both be present, an increase from 24% in the first audit. This audit established an updated baseline for how frequently reviewers included a statement of basis in their deficiencies and facilitates the future assessment of the effect of additional process improvements, which are described below.

4.5.3.3 PHASE 2 IMPROVEMENTS: IMPLEMENT CLARIFIED DEFICIENCY CONTENT POLICY

Staff Training

ORP conducted training on the clarified 4PH content policy to all CDRH staff involved in marketing application reviews through 10 mandatory sessions for each OHT and supporting offices (ORP, Office of Clinical Evaluation and Analysis [OCEA], OSEL) in October 2019. FDA solicited feedback on these training sessions by encouraging staff to submit topic ideas and examples of good deficiencies to Feedback✓CDRH for inclusion in a new, future internal deficiency resource. ORP also provided the same training to relevant CBER review staff in January 2020.

Updated Internal Procedural Document and Added New Resource

FDA updated its internal procedural document with the clarified 4PH content policy (i.e., splitting the statement of basis definition into two sub-parts) in December 2020. Specifically, Part 3a was clarified to be a specific reference to a FR, FG, FS, or SI, while Part 3b was clarified to be an explanation that cites the relevance of the request to the regulatory decision, understanding of the device's benefit-profile profile, safe and effective use of the device, or regulatory precedent. The clarified policy also stated that deficiencies should have both elements (Parts 3a and 3b), except those that reference the statute or a final rule (e.g., in the Federal Food, Drug, and Cosmetic [FD&C] Act or in a section of the Code of Federal Regulations) because such is a regulatory requirement based in federal law or Agency rulemaking.

Additionally, FDA developed an internal deficiency resource document in February 2020, with examples of deficiencies that adhere to the clarified 4PH content policy, to help promote consistency in the writing of deficiency letters. This resource document indicates that the example language should be used as a starting point for reviewers to create their own deficiencies that include a clear statement of basis, modifying for the specific submission under review.

Additional Updated Training

In January 2020, FDA again updated its "Basics of Four-Part Harmony in Lead and Consult Reviews" RCP module to reflect the clarifications to the 4PH deficiency content policy and provide more thorough explanations for the provided examples. FDA also updated the "Master Four-Part Harmony" course, an optional RCP course, in March 2020, which provides review staff an opportunity to read, revise, analyze, and edit actual detailed deficiencies. FDA provided an online refresher of its "Least Burdensome Provisions and Principles" course in 2020.

4.5.3.4 AUDIT DEFICIENCY LETTERS TO DETERMINE IMPACT OF PHASE 2 IMPROVEMENTS

Audit Methodology

Following the implementation of additional staff training, updated internal procedural document, and new deficiency resource described above, FDA began an audit of a second sample of deficiency letters with the goal of assessing the implementation of these process improvements. FDA randomly selected 40 510(k) Additional Information letters from a sorted dataset of all Additional Information letters written in June 2020. Following the same methodology as in the first audit, FDA randomly selected 10 deficiencies within each randomly selected Additional Information Letter, with lettered sub-parts of numbered deficiencies counting as individual deficiencies (i.e., sub-parts 1a, 1b, and 1c would be counted as three distinct deficiencies). For letters with fewer than 10 deficiencies, all deficiencies were audited, for a total of 363 deficiencies.

Audit Results

The results of this audit showed that a reference to an FG, FR, FS, or SI (Part 3a) was present in 64% (234/363) of the sample while a relevance statement (Part 3b) was present in 74% (269/363), which both represent increases from the previous audit (39% and 62%, respectively). In addition, 50% (182/363) of the deficiencies in this cohort included both Parts 3a and 3b, an improvement from the 27% (53/194) of the 2018 sample during the previous audit. Overall, the audit series demonstrates that the inclusion rate of a statement of basis is trending positively as a result of the Phase 2 process improvements implemented during the MDUFA IV timeframe.

4.5.3.5 AUDIT DEFICIENCIES IN REVIEW TEMPLATES

Audit Methodology

FDA staff use SMART templates to guide their review of premarket submissions and as the basis of their internal review memos. Embedded within these review templates is a list of several hundred review template deficiencies across several topic areas, which can serve as a foundation for reviewers as they draft deficiency letters. These template deficiencies lay out a format for reviewers which follows the 4PH writing framework while also prompting reviewers to tailor the deficiencies to the particular file, attempting to strike a balance between consistency and specificity. Some of these deficiencies are more broadly applicable (e.g., administrative) or relate to a particular device review topic (e.g., biocompatibility), while others apply to more specific categories of devices (e.g., electrical stimulators).

As another part of the re-baseline audit described above, FDA also applied its clarified criteria to all review template deficiencies and determined how frequently a statement of basis, with both a statement of reference (Part 3a) and statement of relevance (Part 3b), was present.

Audit Results

FDA found that the review template deficiencies included statements of reference in 96% (217/225) and statements of relevance in 66% (149/225) of the sample, while both elements were present together 64% of the time (143/225).

4.5.3.6 PHASE 3 IMPROVEMENTS: INCORPORATE FEEDBACK AND IMPLEMENT TARGETED IMPROVEMENTS

Updated Review Template Deficiencies

Based on the audit results described above, ORP worked with SMEs from CDRH's FPPs to improve the review template deficiencies in which the statement of basis was incomplete (i.e., either the reference or statement of relevance was not present). By September 2020, 38 review template deficiencies identified by the audit in two TAs (biocompatibility and "Reprocessing, Sterility, Shelf-Life, and Reuse") were updated to include a complete Part 3 statement of basis, and an additional 22 were updated for additional clarity and ease-of-use (for a total of 60 updated review template deficiencies).

Figure 4-14 compares an example of an updated review template deficiency to the prior version, demonstrating the addition of both a reference to a final Guidance as well as an explanation of the request's relevance to the

regulatory decision. While the process of updating these review template deficiencies is ongoing, ORP has encouraged reviewers to use the new review template deficiency language to save time and improve uniformity.

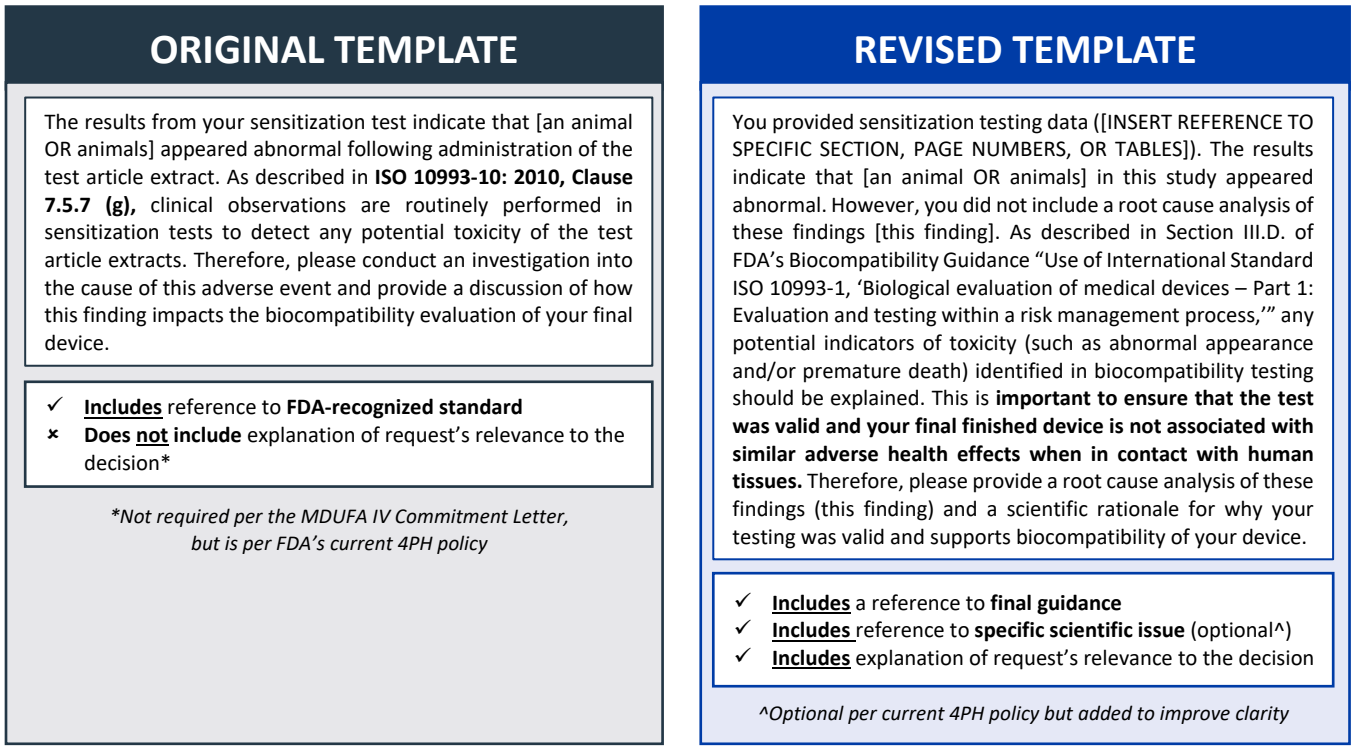


Figure 4-14. Review Template Deficiency Example

Updated Internal Procedural Document and Resources

After the release of the updated internal procedural document with the clarified 4PH content policy and new internal deficiency resource document described in the Phase 2 Improvements above, FDA continued to improve them by collecting and incorporating both internal and external feedback. Specifically, ORP requested example deficiencies from industry trade groups identified by their members as having a clear rationale or statement of basis to help inform improvements. FDA received 11 examples from one of these groups, the clearest of which were included in the internal deficiency resource. These examples clearly state what information is absent and why this information is important for a decision. ORP also collected multiple staff viewpoints (following the interactive outreach events) to gather feedback on how to better implement and improve the 4PH deficiency content policy and internal resources, which resulted in an expansion of the internal deficiency resource (in July 2020) to more than 80 example deficiencies, including both full deficiencies as well as specific examples of the statement of basis (i.e., both Parts 3a and 3b). It also was updated to emphasize that Part 3b statements should clearly and directly explain why the cited concern is a risk or why the reviewer not having the information could affect the device's benefit-risk profile. The document is now organized by common deficiency types that reviewers are likely to encounter, such as "test results inadequate" and "required element missing," and continues to note that the examples provided are a starting point that should be customized to the file under review.

Training Feedback

During the summer of FY 2020, FDA engaged with Kirkpatrick Partners to conduct an evaluation of the RCP training, including the 4PH modules mentioned above, demonstrating FDA's intention to measure progress as well as solicit feedback of staff who took the trainings. The evaluation included a survey of both reviewers, all of whom had completed the RCP training in either 2018 or 2019, and their supervisors. The majority of respondents in both groups (reviewers: 30/32; supervisors: 10/11) expressed their belief that deficiencies often or always "explain the scientific rationale for requesting additional information or…cite the basis of the rationale," although under half

(9/20) of supervisors surveyed indicated that the RCP courses made an impact in helping their staff formulate deficiencies in 4PH.

4.5.4 ASSESS IMPACT OF FDA'S IMPROVEMENT EFFORTS

Per the MDUFA IV Commitment Letter shown in Table 4-30, Booz Allen conducted an independent assessment of the proportion of deficiencies in which FDA references the basis for the deficiency determination.

Table 4-30. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Independent contractor will assess "proportion of deficiencies in which FDA references the basis for the deficiency determination," starting no earlier than 10/01/2020.

4.5.4.1 ASSESSMENT METHODOLOGY

Statement of Basis for the Deficiency

The objective of the independent assessment was to assess the proportion of deficiencies that include a statement of basis for the deficiency, which corresponds with the inclusion of Part 3 of 4PH. Thus, Booz Allen assessed the proportion of deficiency samples for the presence of a statement of basis (i.e., Parts 3a and 3b).

Booz Allen began its assessment of PMA and De Novo deficiencies by randomly selecting 100 PMA deficiencies (from 10 PMA Original and Panel-Track Supplement [PTS] deficiency letters) and another 100 De Novo deficiencies (from 17 De Novo deficiency letters) written in Q1 of FY 2021. This represents the first assessment of deficiency letters for these submission types, which offers a new dimension to understanding FDA's deficiency improvement efforts (i.e., those that had been implemented up to this point), as well as provides a baseline against which to compare the effect of future activities. For purposes of this assessment, PMA Original and PTS deficiencies were counted together. The samples were representative of their respective cohorts in terms of major versus minor deficiencies and breakdown by each OHT. Two analysts independently coded the deficiencies for Parts 3a and 3b using NVivo (QSR International, Release 1.4) qualitative analysis software and subsequently compared and discussed their individual results in order to reach consensus.

4.5.4.2 ASSESSMENT RESULTS

Statement of Basis for the Deficiency

De Novo deficiencies were more likely to include a statement of basis for the deficiency determination than PMA deficiencies, as shown in Table 4-31. This was largely attributable to the frequency of Part 3a in De Novos compared to PMAs, given that Part 3b was present at similar rates in both samples. Compared with the 510(k) results from FDA's most recent deficiency letter audit (which was completed prior to the Phase 3 improvements described above), De Novo deficiencies were more likely to include Part 3a and Part 3b, both individually and together, than 510(k) deficiencies. Although several factors could account for this, the novel nature of De Novo applications could lead to reviewers more clearly articulating a specific scientific, clinical, or regulatory issue with the device or data presented. PMA deficiencies were less likely to include Part 3a, slightly more likely to include Part 3b, and about as likely to include Part 3a and Part 3b together when compared with 510(k) deficiencies.

Table 4-31. Adherence to Part 3 by Application Type

	Type of Application		
Statement of Basis Component	PMA	De Novo	510(k)*
Part 3a	55%	81%	64%
Part 3b	81%	83%	74%
Parts 3a and 3b	48%	69%	50%

*From FDA's second deficiency letter audit.

As illustrated in Figure 4-15, a specific issue (SI) was the most common Part 3a reference type cited for both PMAs and De Novos, similar to the 510(k) deficiencies in FDA's most recent deficiency letter audit. However, De Novo deficiencies were significantly more likely (71%) to include an SI reference than PMA deficiencies (43%). Although PMAs were slightly more likely to reference a Final Standard and De Novos to reference a Final Guidance, these were not considered significant differences between the two submission types.

In addition to the evaluation described above, Booz Allen conducted a secondary analysis by also coding deficiencies for phrases that reviewers felt could function as both Part 2 and Part 3a. This was based on an observation made during the training exercise that there was not always a clear distinction between a statement of inadequacy (i.e., a Part 2) and a specific concern with data (i.e., a Part 3a) when the problem was that the manufacturer did not provide necessary data (e.g., a particular biocompatibility test report). Analysts felt that it may have been similarly difficult for reviewers to write deficiencies that included a Part 3a reference if the manufacturer omitted information that was essential for FDA to make a final decision, which coding these "Hybrid Part 2-3a" phrases could take into account.

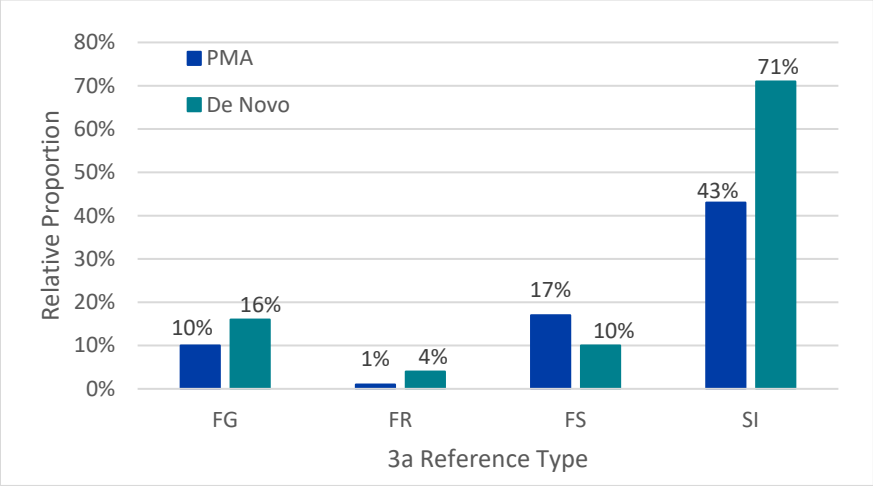


Figure 4-15. Relative Proportion of 3a Reference Types by Application Type

As seen in Table 4-32, adherence to Part 3a increases to 93% for both PMAs and De Novos when counting "Hybrid Part 2-3a" phrases in deficiencies with no other standalone 3a reference (i.e., no double-counting). In addition, counting these "Hybrid Part 2-3a" phrases increased the proportion of deficiencies that include both Parts 3a and 3b to 77%. These results demonstrate the impact that small changes in counting Part 3a or 3b can potentially have on the calculated rate of inclusion of a statement of basis for the deficiency.

Table 4-32. Impact of "Hybrid Part 2-3a" Phrases on Adherence to 4PH

Application Type	Part 3a	Part 3b	Part 3a with Hybrid Part 2-3a	Part 3a and 3b	Part 3a with Hybrid Part 2-3a and 3b
PMA	55%	81%	93%	48%	77%
De Novo	81%	83%	93%	69%	77%

As such, any modifications to the 4PH criteria, such as an update that makes the definitions of Part 2 and Part 3a more distinct from one another, may affect how reviewers write deficiencies in unintended ways. It should be noted that the 4PH criteria clarification (due to variable interpretation by reviewers and auditors, as demonstrated in the first QMOE audit) and subsequent implementation of process improvements like training and outreach efforts did not immediately lead to full adherence to 4PH criteria. Along those lines, it is reasonable to hypothesize that further updates to the 4PH criteria may present an initial challenge to reviewers until a full training program and outreach sessions are undertaken to confirm a shared understanding of the changes.

4.5.5 UPDATE DEFICIENCY GUIDANCE WITH BEST PRACTICES

Table 4-33. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• FDA will incorporate additional best practices identified by quality audits and/or the Independent Assessment in updates to the guidance, as appropriate.

FDA committed to incorporating additional best practices identified by quality audits and/or the Independent Assessment in updates to the 2017 Deficiency Guidance, as appropriate. As shown in Table 4-33, work on this commitment is contingent upon completion of this independent assessment; therefore, FDA has not yet published an updated Guidance. Nonetheless, Booz Allen has observed FDA's ongoing efforts to incorporate best practices on writing deficiencies. This iterative process begins with evaluating current practices (i.e., audits), followed by process improvement (e.g., clarifying criteria, developing/updating tools), which FDA implemented (e.g., training for staff and managers) and then audited again to evaluate the impact of the first set of

improvements. In addition, FDA has continued to take further action to improve deficiencies since Booz Allen's independent assessment began, including additional revisions to review template deficiencies and updated deficiency examples in FDA's interactive staff training.

4.5.6 CONCLUSION

FDA has met the MDUFA IV commitment to update the 2017 Deficiency Guidance to reflect that deficiency letters should include a statement of basis for the deficiency and undergo supervisory review to confirm that the deficiencies listed are relevant to a marketing authorization decision, as well as trained review staff and managers on the updated Guidance. FDA also completed its first audit of Traditional 510(k) deficiency letters ahead of the FY 2020 due date, which allowed the Agency to measure progress in meeting the commitment and identify challenges in its implementation early-on. Finally, FDA took a proactive approach and developed several inter-related process improvements, including multiple training modalities as well as resources for reviewers and managers.

The independent evaluation of deficiency letters demonstrates that PMA deficiency letters include a complete statement of basis for the deficiency at about the same rate as Traditional 510(k) deficiency letters (i.e., approximately 50%), while De Novo deficiency letters include a complete statement of basis at a higher rate (69%). These results indicate that further opportunities for improving clarity and consistency remain.

4.6 Pre-Submission Program

Pre-Submissions are an important mechanism for submitters to request feedback from FDA regarding a potential or planned IDE or marketing application. This voluntary mechanism facilitates early interaction with FDA on planned studies and other key aspects of the device and submission development process. Since FY 2013[16] the number of qualified Pre-Submissions submitted has nearly doubled, with the number increasing every year, from 1,779 in FY 2013 in to 3,306 in FY 2020.[17]

The MDUFA IV commitments for Pre-Submissions are largely focused on: 1) whether CDRH is using Pre-Submissions appropriately; 2) whether CDRH is providing guidance specific to the questions asked; and 3) whether CDRH and Industry are adhering to the procedures specified in the Commitment Letter.

FDA met its MDUFA IV commitment for the Pre-Submission Program by engaging the independent contractor to evaluate the effectiveness and correspondence to the MDUFA IV Commitment Letter. The Pre-Submission Program, its activities, and its impact on premarket review at CDRH are described below.

The assessment findings are presented in three sections, which align to the MDUFA IV commitments:

- 4.6.1 Appropriate Use of Pre-Submissions;
- 4.6.2 Responsiveness to Pre-Submission Questions, and
- 4.6.3 Adherence to MDUFA IV Procedures.

4.6.1 APPROPRIATE USE OF PRE-SUBMISSIONS

This section describes how each of the commitments shown in Table 4-34 were met. Per the Commitment Letter Booz Allen conducted an analysis. The findings are described in the following two sections:

- 4.6.1.1 Updated Pre-Submission Guidance and Program; and
- 4.6.1.2 Analysis of Appropriate Use.

[16] "December 10, 2018 MDUFA III Performance Report," FDA https://www.fda.gov/media/120475/download – accessed 5/6/2021
[17] "May 26, 2021 MDUFA IV Performance Report," FDA https://www.fda.gov/media/149605/download – accessed 6/1/2021

4.6.1.1 UPDATED PRE-SUBMISSION GUIDANCE AND PROGRAM

Table 4-34. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)

• By October 1, 2018, the Agency will update the Guidance on "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff" to include:
  ○ Additional information to assist applicants in determining the need for a Pre-Submission
  ○ An enhanced Pre-Submission acceptance checklist
  ○ Examples of frequently asked Pre-Submission questions that lend themselves to productive Pre-Submission interactions
  ○ Edits to reflect the revised process outlined above
• FDA will provide an opportunity for the public to comment on the updated guidance. No later than 12 months after the close of the public comment period, the Agency will issue a final guidance. FDA will implement this guidance once final.
• Assess whether (a) CDRH is providing guidance specific to the questions being asked; (b) CDRH is using Pre-Submissions appropriately; and (c) CDRH and Industry are adhering to the procedural aspects as set forth in this agreement).

Updated Guidance

FDA issued draft Guidance in September 2017, final Guidance in 2019, and further revised the final Guidance in January 2021[18] (hereinafter referred to as the 2021 Q-Submissions Guidance) to reflect the changes laid out in the Commitment Letter and enhance the clarity of other Pre-Submission program elements. These changes were intended to focus both FDA and sponsor efforts on the relevant issues during product development and include:

- Administrative changes (e.g., addition of process timelines and performance goals)
- Enhanced Pre-Submission RTA Checklist to provide clarity on acceptance requirements
- Meeting minutes template to promote consistency
- List of review topics and example questions to guide development of Pre-Submission requests (e.g., request specific feedback on provided proposal, clearly articulate desired outcome for labeling, do not request decision regarding approval or clearance), ranging from clinical or animal studies and benchtop performance to cybersecurity, reprocessing and sterilization, and regulatory strategy

Updated Tools

FDA also updated its internal procedures and various internal tools/documents to implement the 2021 Q-Submissions Guidance, clarify roles and review procedures for staff, and support consistency in written feedback. This includes the SMART template, which reviewers use to document internal discussions that lead to the final feedback, as well as the CorGen to assist reviewers in generating their formal written feedback letter, tailored to the Pre-Submission questions asked.

4.6.1.2 ANALYSIS OF APPROPRIATE USE

Although the Commitment Letter requires an independent assessment of whether CDRH is using Pre-Submissions appropriately, "appropriate use" is not defined. The acceptance rate of Pre-submissions (i.e., meeting the criteria on the RTA checklist) is not an accurate reflection of appropriate use because acceptance reflects administrative completeness, not appropriateness. Booz Allen was also not able to address the origin of Pre-Submission requests (i.e., whether a suggestion from FDA prompted a Pre-Submission) nor whether FDA and industry could have communicated informally (e.g., via phone call or email) to resolve certain types of questions submitted via Pre-Submission.

Booz Allen analyzed 100 Pre-Submission requests selected at random from the 150 most recently closed requests, as of April 1, 2021. The sample included a total of 465 sponsor questions and represented all OHTs. As an indicator of appropriate use, Booz Allen examined alignment between the Pre-Submission questions posed and the list of review topics outlined in the 2021 Q-Submissions Guidance that FDA expects to lead to productive interactions. Figure 4-16 shows the distribution of topics of questions asked, with those on Clinical Studies being the most prevalent topic comprising 22% (102/465) of questions posed in the sample, followed by Regulatory Strategy (20%, 92/465) and Benchtop Performance Testing (19%, 89/465). In addition, analysts found a small number of questions where sponsors requested overall feedback or confirmation of the approach across several topics, shown as "Other" (3%, 16/465).

[18] "Requests for Feedback and Meetings for Medical Device Submissions, The Q-Submission Program: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/114034/download – accessed 5/6/2021

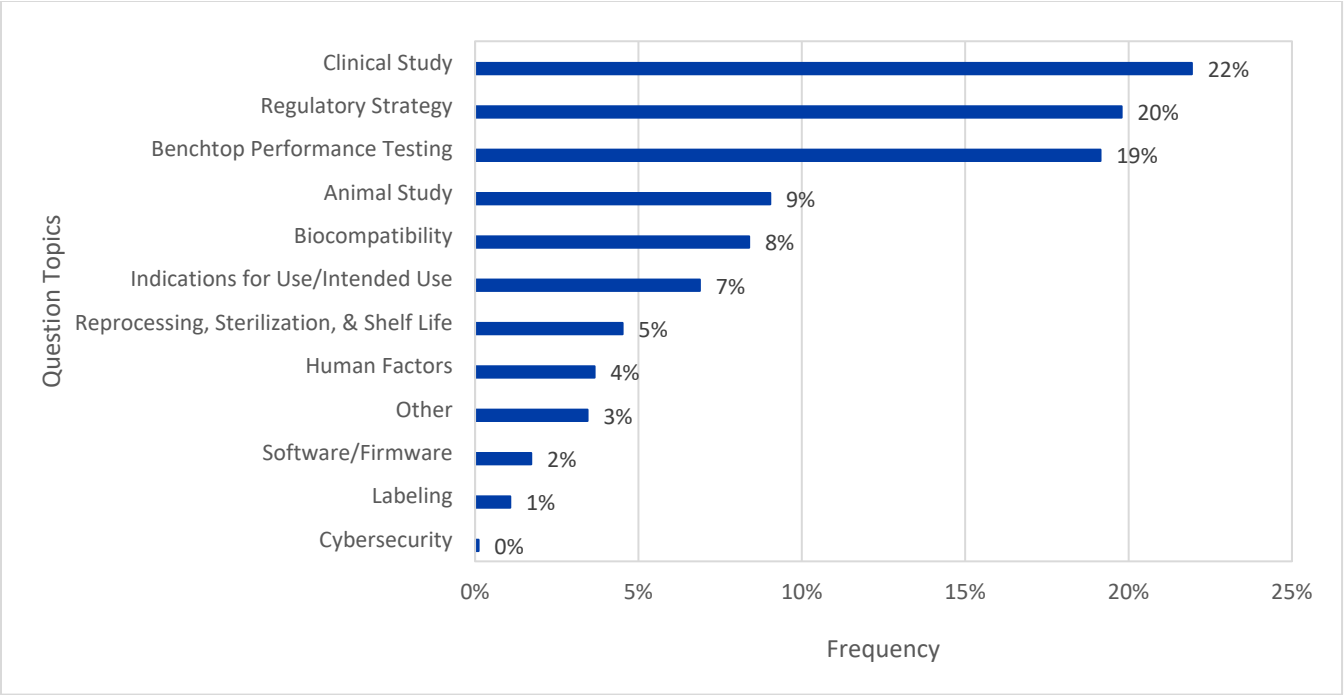


Figure 4-16. Pre-Submission Question Review Topic Frequency

Survey Findings on Appropriate Use

As part of program governance, the QMOE Program conducted an audit of the Pre-Submissions program in 2020, which included surveys of FDA reviewers (n= 242) and industry stakeholders (n= 129). The goal of the surveys was to gather perspectives on experiences using the Pre-Submission program to inform future improvements.

The surveys conducted measure both reviewers' and industry stakeholders' views on the use of Pre-Submissions. One element of this included questions asking whether applicants are submitting, as well as if reviewers are requesting, Pre-Submissions for questions that respondents' felt they could resolve through informal communications (i.e., an email or phone call). As shown in Figure 4-17, while most industry stakeholders and FDA reviewers surveyed believed that Pre-Submission questions could not be answered informally, FDA reviewers were somewhat more likely to believe this (70%, including "never" and "rarely") than were industry respondents (54%, including "never" and "rarely"). On the other hand, more industry respondents (17%) than FDA reviewers (8%) indicated that Pre-Submission questions could be answered informally "most" or "all of the time." When reviewers encountered these situations, approximately 20% indicated that they worked interactively with sponsors to address questions and recommend that the submitter contact FDA directly for similar questions in the future rather than

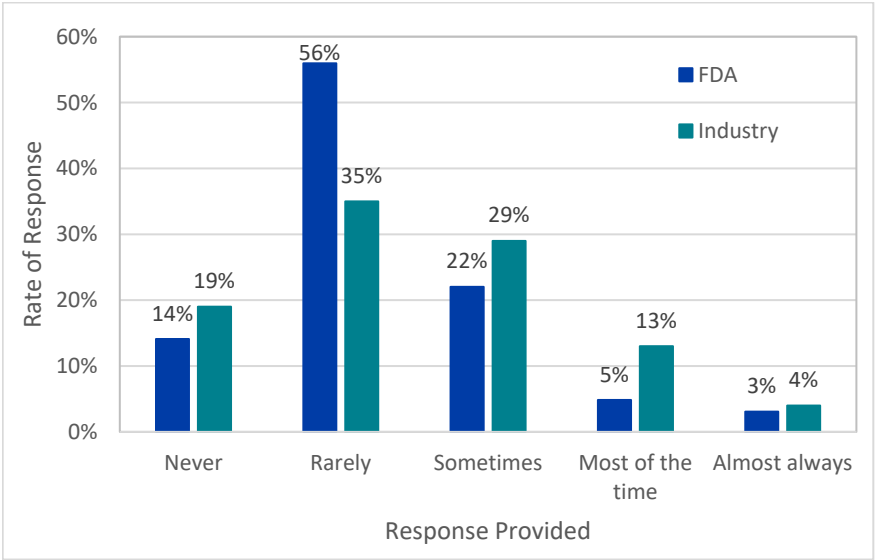


Figure 4-17. Perceptions on How Often Pre-Submission Questions Could Be Handled Informally

Note: Of the FDA respondents, approximately 12% (31/242) did not answer this question Never=0%; Rarely=1-25%; Sometimes=25-50%; Most of the time=50-75%; Almost always=75-100.

submit a Pre-Submission. Finally, when asked about the most significant challenges encountered during Pre-Submission review, submission quality was the most reported factor (76%), followed by the number of Pre-Submissions assigned to review simultaneously (47%).

4.6.2 RESPONSIVENESS TO PRE-SUBMISSION QUESTIONS

This section describes how FDA met the commitment shown in Table 4-35. The findings are described in the following section:

- 4.6.2.1 Providing Guidance Specific to Industry Questions.

Table 4-35. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Assess whether (a) CDRH is providing guidance specific to the questions being asked; (b) CDRH is using Pre-Submissions appropriately; and (c) CDRH and Industry are adhering to the procedural aspects as set forth in this agreement).

4.6.2.1 PROVIDING GUIDANCE SPECIFIC TO INDUSTRY QUESTIONS

To assess whether FDA provided guidance specific to the questions asked in Pre-Submissions, Booz Allen examined the length and nature of reviewers' responses both to industry requests as well as any Additional Considerations.

Length and Nature of FDA Responses

Booz Allen characterized various features of the sample to understand the amount of information received for FDA to review and ultimately respond to, shown in Table 4-36. Requests generally consisted of one page of questions, while the remaining contained key background information (e.g., device description, testing conducted to date, proposed premarket submission strategy). Pre-Submissions contained approximately five questions each on average, although the number ranged from one to 19, shown in Figure 4-18. The vast majority (87%) contained six or fewer questions, consistent with the recommendations in the 2021 Q-Submissions Guidance. FDA addressed all questions posed within the sample set reviewed, regardless of the number of questions posed and number of topics per Pre-Submission.

Table 4-36. Pre-Submission Characteristics

Pre-Submission Characteristics
• Median length: 31 pages (range: 2-545) • Mean number of questions per request: 5 (range: 1-19) • Mean number of review topics: 3 (range: 1-7) • Mean length of FDA response: 3.5 pages per Pre-Submission (range: 1-12)

The QMOE's survey results align with Booz Allen's findings, indicating that most industry respondents felt that FDA answered their questions "almost always" (68%) or "most of the time" (22%). In addition, both FDA reviewers (76%, 186/242) and industry (31%, 40/129) respondents reported "insufficient information was provided" as the leading reason they felt specific feedback was not provided to the questions posed. Finally, a large majority of industry respondents reported feeling that FDA follows the written feedback provided to the Pre-Submission (e.g., in the future marketing application) "almost all of the time" (48%) or "most of the time" (34%).

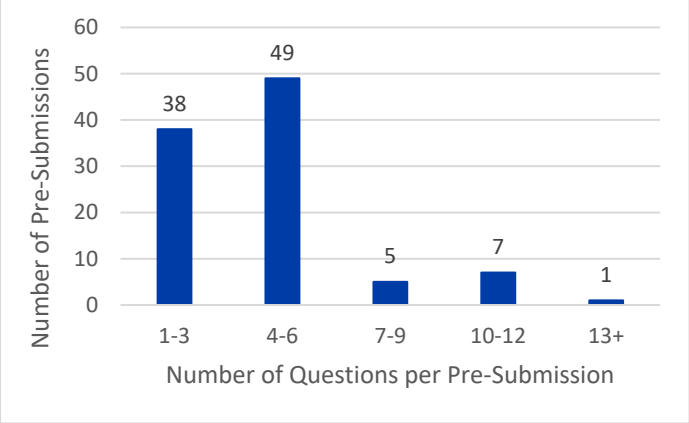


Figure 4-18. Range of Questions by Pre-Submission

Booz Allen also reviewed written feedback documents from the sample to analyze how CDRH communicates information to the submitter. Analysis found that reviewers used a consistent structure in their responses, providing: a direct answer to the question, an explanation of the answer, and recommendations for future actions the submitter could take (e.g., suggestions on modifying clinical study protocol).

Frequency and Nature of Additional Considerations

According to the Pre-Submission SOP, reviewers may provide additional feedback that goes beyond the scope of specific questions asked in a standalone section of the written response, referred to as additional considerations. This additional feedback allows reviewers to provide submitters with the opportunity to consider and correct potential issues (e.g., additional testing requirements) that may arise upon review of the future marketing submission. Booz Allen found that FDA provided additional considerations in 56% (56/100) of the Pre-Submission requests sampled, which included a total of 198 additional considerations that ranged from one page to 8 pages in length, with a median length of 1.5 pages. Reviewers wrote the additional considerations consistently, citing the specific information in the original request that prompted the additional considerations, the specific issue cited, and recommended changes or additional actions.

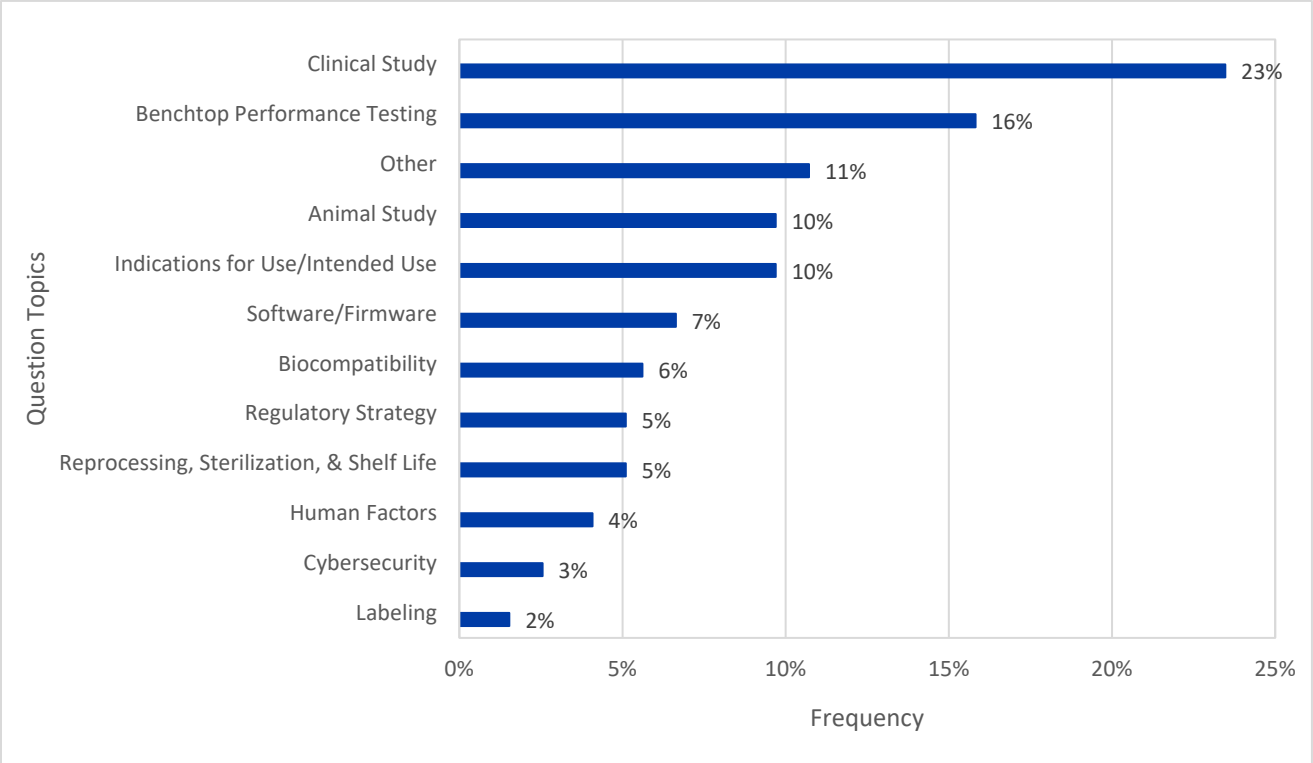


Figure 4-19. Frequency of Review Topics in Additional Considerations

Figure 4-19 shows the distribution of additional considerations, categorized according to the 11 review topics provided within the 2021 Q-Submissions Guidance. This distribution is similar to the questions asked in Pre-Submission requests, with Clinical Study (23%, 46/196) and Benchtop Performance Testing (16%, 31/198) comprising the two most common categories. One exception to this was the Regulatory Strategy topic, which comprised a relatively smaller percentage of additional considerations (5%) compared to questions posed (20%, as seen in Figure 4-16). Additional considerations that did not fall into the categories identified in the 2021 Q-Submissions Guidance were marked as Other (11%, 21/198), with most of these dealing with suggestions regarding the device's description and a few relating to manufacturing. In addition, Booz Allen analyzed the topics covered in additional considerations provided by FDA reviewers within a particular Pre-Submission and compared them to those of the questions posed by the applicant. Results showed that 92% (182/198) of additional considerations aligned with the sponsors' questions.

4.6.3 ADHERENCE TO MDUFA IV PROCEDURES

This section describes how FDA met each of the commitments shown in Table 4-37. To assess FDA's and industry's adherence to the MDUFA IV Pre-Submission procedures, Booz Allen analyzed performance metrics in the quarterly performance reports.[19] FDA and industry agreed to a series of Pre-Submission milestones in MDUFA IV, shown in Figure 4-20. Table 4-38 lists a series of Pre-Submission performance metrics between FY 2018 and FY 2020.

FDA's first goal is providing an Acceptance Review decision within 15 days following receipt of the Pre-Submission. During this review, FDA assesses the Pre-Submission's administrative completeness. Despite receiving an increasing number of Pre-Submissions every year,[20] only a small number (between 2-4%) failed to undergo an RTA review within 15 days. FDA also attempts to schedule a future feedback meeting if requested by the submitter during Acceptance Review. Each year, approximately 71% of the Pre-Submissions FDA receives include a request for a meeting, most of which FDA schedules (98-99%) within 30 days. For the small percentage that FDA did not schedule within 30 days, FDA met its MDUFA goal of resolving the issue by day 40 on average in FY 2018 (36 days) and FY 2019 (37 days) but missed this goal in FY 2020 (50 days).

Table 4-37. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Assess whether CDRH and Industry are adhering to the procedural aspects as set forth in this agreement: ○ Within 15 calendar days of receipt of a Pre-Submission, FDA will communicate with the applicant regarding whether the application has been accepted and, if applicable, regarding scheduling of the meeting or teleconference. ○ FDA intends to reach agreement with the applicant regarding a meeting date within 30 days from receipt of accepted submission. ○ For all requests for meetings or teleconferences that do not have such a meeting or teleconference scheduled by 30 days from receipt of an accepted submission, an FDA manager will contact the applicant to resolve scheduling issues by the 40th day. ○ FDA will provide written feedback that addresses the issues raised in the pre-submission request within 70 calendar days of receipt date or five calendar days prior to a scheduled meeting, whichever comes sooner, for at least 1,530 Pre-Submissions received in FY 2018, at least 1,645 Pre-Submissions received in FY 2019, at least 1,765 Pre-Submissions received in FY 2020, at least 1,880 Pre-Submissions received in FY 2021, and at least 1,950 Pre-Submissions received in FY 2022. • Applicants will be responsible for developing draft minutes for a Pre-Submission meeting or teleconference, and provide the draft minutes to FDA within 15 calendar days of the meeting.

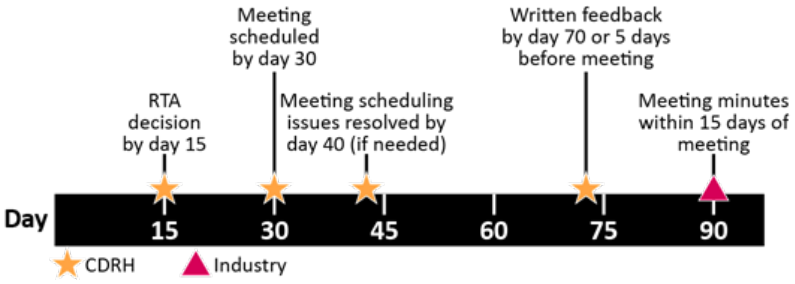


Figure 4-20. Pre-Submission Timeline and Associated Milestones

After RTA review and scheduling, FDA reviewers work to provide written feedback to submitter's questions within 70 days or five days before a requested feedback meeting, whichever comes first. FDA has surpassed its MDUFA IV commitment for the number of timely written responses by between 150% and 173% each FY, despite the increasing volume of Pre-Submissions received and the higher goal thresholds each year. In addition, reviewers also provided written feedback on average between 58 and 63 days after receipt, compared to the 70 days noted in the Commitment Letter. After receiving FDA's written feedback, sponsors may decide that a meeting is no longer necessary and cancel it; however, over 70% of sponsors elected to have the meeting. Following the meeting, applicants provided meeting minutes for FDA to review within 15 days after the meeting date only 64% of the time.

[19] "MDUFA Reports," FDA https://www.fda.gov/industry/medical-device-user-fee-amendments-mdufa/mdufa-reports – accessed 5/6/2021

[20] On 4/15/2021, CDRH announced that the Center will be declining In Vitro Diagnostic (IVD) Pre-Submissions that are not related to COVID-19, companion diagnostics, a breakthrough designation request, or have a significant public impact to prioritize the review of COVID-19 related IVD submissions. RTA acceptance rates in FY 2021 Q3 and Q4 data, when available, may decline based on this decision.

Table 4-38. Pre-Submission Procedural Metrics (Based on August 3, 2021 MDUFA IV Performance Report)

Metric	FY 2018	FY 2019	FY 2020
Number Received*	2,707	3,176	3,306
Number Accepted First Cycle; Number Not Accepted*	2,565 accepted; 66 not accepted	3,004 accepted; 60 not accepted	3,035 accepted; 39 not accepted
Number Without RTA Review Within 15 Days of Receipt*	2% (49/2,707)	2% (71/3,176)	4% (139/3,306)
Percentage (Number Meeting Requested/Number Received) Meetings Requested*	71% (1,921/2,707)	71% (2,245/3,176)	71% (2,362/3,306)
Percentage (Number) Meetings Scheduled within 30 Days*, **	98% (1,884/1,921)	98% (2,200/2,245)	99% (2,332/2,362)
Average Number of Days to Scheduling for Meetings Scheduled After 30 Days*	36	37	50
Number Provided Written Feedback by Day 70 or Five Days Prior to Meeting*	Actual: 2,439 Goal: 1,530	Actual: 2,848 Goal: 1,645	Actual: 2,652 Goal: 1,765
Average Number of Days to Written Feedback* (Goal: by Day 70 or Five Days Prior to Meeting)	58.86	59.94	62.95
Percentage (Number Meetings Held/Number Meetings Requested) Meetings Held*	78% (1,507/1,921)	78% (1,742/2,245)	73% (1,727/2,362)
Percentage (Number) Meeting Minutes Within 15 Days After Meeting Held*	64% (971/1,507)	64% (1,113/1,742)	64% (1,110/1,727)

*For all Pre-Submissions excluding those re-submitted after being closed without feedback due to reallocation of resources to COVID-19 activities.
**Calculated as: (Meetings Requested – Meetings Not Scheduled by Day 30) / Meetings Requested.

4.6.4 CONCLUSION

FDA met the MDUFA IV commitment to update its Guidance to include additional information for determining the need for a Pre-Submission, an enhanced Pre-Submission Acceptance Checklist, examples of frequently asked questions, and edits to reflect the revised Pre-Submission process. FDA then implemented the Guidance in May 2019 (with a further clarification in January 2021). FDA also met the commitment to adhere to Pre-Submission procedures by achieving the associated milestones consistently (i.e., providing an RTA decision by day 15, scheduling meetings by day 30) and exceeding the commitment to provide written feedback by day 70 for an increasing number of Pre-Submissions each year. FDA achieved these milestones despite receiving an increasing volume of Pre-Submissions each FY. Industry adhered to its meeting minutes milestone only 64% of the time between FY 2018 and 2020.

The independent assessment of Pre-Submissions provides evidence that reviewers consistently offer guidance specific to and address the questions asked. Additional considerations provide the opportunity for submitters to further enhance product development and correct potential review issues in a marketing application. The review topics of questions asked by submitters are consistent with the example review topics provided in the 2021 Q-Submissions Guidance, and additional considerations are usually within the scope of the Pre-Submission questions posed by the applicant.

4.7 Third Party Review Program

FDA's Third Party Review Program authorizes Third Party Review Organizations ("Third Parties") to review 510(k) submissions and recommend initial classifications for certain low-to-moderate risk devices. The purpose of the program is to create efficiencies that allow FDA to focus review resources on high-risk and high-complexity devices. Currently, submissions from the nine recognized Third Parties represent an average of 2% of all 510(k) submissions received from FY 2018 to FY 2020.

The MDUFA IV commitments for the Third Party Review program are largely focused on strengthening the recognition process and reducing FDA's re-review of Third Party submissions. Booz Allen found that FDA met its MDUFA IV commitments by defining consistent recognition standards and criteria, providing targeted training and tools, establishing communication channels, and focusing on monitoring and continuous improvement, which are collectively intended to result in reduced re-review. FDA also met its MDUFA IV commitment by engaging the

independent contractor to evaluate program efficiency, including the circumstances when FDA conducted re-reviews, and suggest process improvements, which is described below.

The assessment findings are presented in two sections:

- 4.7.1 Strengthen the Process for Recognition of Third Parties; and
- 4.7.2 Efforts to Eliminate Routine Re-Review.

4.7.1 STRENGTHEN THE PROCESS FOR RECOGNITION OF THIRD PARTIES

This section describes how FDA met each of the commitments shown in Table 4-39. The findings are described in the following four sections:

- 4.7.1.1 Issued Guidance Outlining Rerecognition Criteria for Third Parties;
- 4.7.1.2 Provided Training for Third Parties Seeking Recognition;
- 4.7.1.3 Established Communications Process for Updating Third Parties; and
- 4.7.1.4 Tailored Product Eligibility List.

Table 4-39. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)

• Strengthen the process for accreditation of Third Parties.
  ○ Provide training for Third Parties seeking accreditation by FDA. This training shall include the opportunity for Third Parties to have access to redacted review memos and other information as appropriate.
  ○ When FDA's expectations for a particular device type change, FDA will have in place a process to convey this information to the Third Parties and to industry.
• By the end of FY 2018, issue draft guidance outlining criteria for rerecognition, suspension, or withdrawal of recognition of a Third Party. Issue final guidance within 12 months of the conclusion of the public comment period.
• The Agency will seek greater authority to tailor the program. Specifically, FDA intends to expand the scope of the program to some product codes that require clinical data and to remove product codes from eligibility when appropriate, such as if/when safety signals arise.

4.7.1.1 ISSUED GUIDANCE OUTLINING RERECOGNITION CRITERIA FOR THIRD PARTIES

FDA revised the Third Party recognition process and recognition criteria for Third Parties by issuing draft guidance in September 2018, followed by final guidance in March 2020. [21] The guidance communicated FDA's expectations of Third Parties, including: 1) interactive consults; 2) factors used in determining device type eligibility; and 3) the processes for recognition, rerecognition, suspension, and withdrawal of a Third Party. The guidance leveraged international harmonization work with the IMDRF by aligning requirements for and referring readers to the Good Regulatory Review Practices and the Medical Device Single Audit Program working documents developed to promote core quality management principles. The guidance also noted that Third Parties in compliance with the IMDRF documents likely meet many of the requirements for FDA's Third Party Organization program, reducing FDA re-review of Third Party submissions by strengthening and standardizing the Third Party recognition process and increasing the consistency and quality of Third Party review.

Under the March 2020 Third Party Guidance, FDA expected all previously recognized Third Parties to apply for rerecognition by September 2020. The intent of the new guidance was to bring all Third Parties into alignment with the same recognition criteria, processes, and standards. In addition to the requirement to re-apply for recognition every three years, the guidance enables FDA to request documentation or inspect Third Parties at any time. These additional inspections promote effective document management and provide the opportunity to correct any issues that arise during the recognition window (e.g., revise outdated training records). Finally, FDA developed communication templates and processes to support FDA reviewers and facilitate consistent and clear communication on identified issues that require attention by the Third Party.

4.7.1.2 PROVIDED TRAINING FOR THIRD PARTIES SEEKING RECOGNITION

FDA offers training for Third Parties to gain relevant expertise conducting FDA-comparable 510(k) reviews that ranges from general policy and process topics that broadly impact 510(k) review quality to scientific topics. FDA

[21] "510(k) Third Party Review Program: Guidance for Industry, Food and Drug Administration Staff, and Third Party Review Organizations," FDA https://www.fda.gov/media/85284/download – accessed 2/11/2021

leverages a combination of informal (e.g., mentoring, in-person, webinars, workshops) and formal training via the online training platform CDRH Learn. Examples of CDRH Learn training modules are shown in Table 4-40.

Table 4-40. Third Party Review Training Modules on CDRH Learn

Training Module Title	Description
X-Ray Systems	How to review an X-Ray System to determine substantial equivalence (SE)
Third Party Review Program: Overview	Overview of the Third Party Review Program and the role of the Third Party reviewer
Deficiency Writing for Third Party Reviewers	How to write deficiencies when requesting additional information and a suggested format for responding to additional information requests
Deficiency Writing for Third Party Reviewers: Examples	Examples for writing deficiencies for Third Party submissions and responding to additional information requests
Overview of the 510(k) Process: Guide for Third Party Reviewers	Basic principles of the Third Party Review Program and review process and how to follow the 510(k) SE flowchart
510(k) Third Party Review Program: Final Guidance Webinar	Considerations for evaluating a Third Party submission and documenting the review and recommendation

The available training for Third Parties aligns to the content provided to FDA reviewers through the RCP. FDA develops tailored training based on feedback from Third Parties and on trends observed in the deficiency letters it issues to Third Parties and other reviewer feedback. The small number (nine) of Third Parties provides FDA with the opportunity to implement a flexible and tailored training approach. As appropriate, FDA develops content in partnership with FPPs, comprised of review topic SMEs (e.g., biocompatibility) across OPEQ.

4.7.1.3 ESTABLISHED COMMUNICATIONS PROCESS FOR UPDATING THIRD PARTIES

FDA established the Update Channel (i.e., a quarterly newsletter email) that they send to all recognized Third Parties to distribute important information related to the Third Party Review program. The emails include content such as notices and updates on device type changes, new and updated guidance, best practices, reviewer tools and checklists, upcoming events (e.g., conferences, workshops), and general advice. The Update Channel also distributes and socializes new training opportunities, as well as communicates cross-cutting feedback from audits of Third Party reviews to promote continuous improvement. FDA maintains historical emails and leverages the content to onboard new Third Parties.

4.7.1.4 TAILORED PRODUCT ELIGIBILITY LIST

In its March 2020 guidance, FDA tailored the criteria for device eligibility for Third Party review and updated the list of eligible devices. The guidance outlined six factors FDA considers when determining a device's eligibility for the Third Party program:

- Risk of the device type;
- Whether the device type (or subset of device type) is intended to be implanted in the human body or to sustain/support human life;
- Extent to which the device type is well understood;
- Extent to which information to support a well-informed decision is available to the Third Party;
- Extent to which the device does not require interdisciplinary expertise; and
- Availability of postmarket data suggesting that the device type is the subject of safety signals.

After releasing the final guidance, FDA updated the list of eligible devices to include low-to-moderate-risk, low-complexity devices, and removed high-risk, high-complexity devices. FDA intended the change in eligible devices to decrease the likelihood of FDA re-review by removing highly complex devices that are difficult for Third Parties to evaluate effectively, allowing them to focus on low-complexity and low-risk devices while enabling FDA to focus its resources on reviewing the high-risk, high-complexity devices.

4.7.2 EFFORTS TO ELIMINATE ROUTINE RE-REVIEW

This section describes how FDA met each of the commitments shown in Table 4-41. The findings are described in the following three sections:

- 4.7.2.1 Implemented Plan for Eliminating Routine Re-Review;
- 4.7.2.2 Published Performance of Third Parties with at Least Five Completed Submissions; and
- 4.7.2.3 Implemented a Program to Audit Reviews Conducted by Third Parties.

Table 4-41. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• By the end of FY 2018, establish a plan for eliminating routine re-review by FDA of Third Party reviews and implement the plan within 12 months. • Implement a program to audit reviews conducted by recognized Third Parties and provide tailored re-training to recognized Third Parties based on the results of audits. • Publish performance of individual recognized Third Parties with at least five completed submissions on the web. • Require the independent assessment of the Third Party Review Program to evaluate efficiency including the circumstances when FDA re-reviews were conducted; and suggest process improvements.

4.7.2.1 IMPLEMENTED PLAN FOR ELIMINATING ROUTINE RE-REVIEW

"Eliminating Routine FDA Re-Review of Third Party 510(k) Reviews," [22] released in September 2018, describes how FDA planned to improve the 510(k) Third Party Review program, reducing the time- and resource-intensive process of routine re-review and increasing the resources available to FDA for high-risk and high-complexity device reviews. This comprehensive plan set an ambitious goal to reduce re-review of Third Party 510(k) to 15% or fewer submissions by the end of FY 2021, and outlines five strategies for achieving that goal, described below:

- Established a Framework to Help Determine When Re-Review is Not Needed;
- Promoted Appropriate Device Types;
- Demonstrated Third Party Capability;
- Provided Third Party Reviewers with Tools; and
- Monitored and Facilitated Continuous Improvement of Third Party Performance.

Established a Framework to Help Determine When Re-Review is Not Needed

FDA initiates its review of a Third Party 510(k) submission upon receipt of a Third Party review memo and other review documentation (e.g., cover letter, original submission from the 510(k) submitter to the Third Party). The Third Party review memo provides the reasoning and steps that led to the Third Party's recommendation, including an explanation of the adequacy of each section of the submission, deficiencies identified, the submitter's response to deficiencies, and the Third Party's review of the response to the deficiencies, as appropriate. High-quality Third Party 510(k) submissions, in general, should only require a supervisory review of the Third Party review memo (i.e., does not review other review documentation) by FDA, unless FDA identifies deficiencies that cannot be resolved interactively and deems the Third Party review not FDA-comparable. When FDA deems the review not FDA-comparable, it conducts a substantive re-review of the full submission using the standard 510(k) procedure and issues Deficiency Letters to the Third Party, as appropriate. Re-review ultimately increases FDA resources needed to complete the review and the time to market for the product when compared with FDA-comparable Third Party reviews.

Prior to MDUFA IV, FDA did not have formal criteria for determining the need for re-review. In accordance with its plan to eliminate re-review, FDA developed an internal "Supervisory Memo Template for Third Party 510(k)" to support consistent review of Third Party review memos and identify whether re-review is necessary by determining whether the Third Party conducted an FDA-comparable review. The template outlines Third Party organizational, scientific, and regulatory considerations for determining whether the Third Party prepared an FDA-comparable review memo and whether it requires interactive review or a substantive re-review. These criteria include factors such as Third Party reviewer capability (e.g., previous review experience, general expertise), Third Party organizational capability, and adequacy of documentation in several review areas.

[22] "Eliminating Routine FDA Re-review of Third Party 510(k) Reviews," FDA https://www.fda.gov/media/116168/download – accessed 2/11/2021

Promoted Appropriate Device Types

The plan to eliminate routine re-review required FDA to provide guidance outlining device type eligibility criteria for the Third Party Review Program. As discussed above, FDA revised the list of eligible devices to focus on low-complexity and low-to-moderate-risk devices. By statute, the Third Party Review Program excludes more complex devices that increase the likelihood that re-review will be necessary and are therefore not appropriate for Third Party review. The criteria in the guidance, while applying to all devices, also respond to the statutory requirement to address when a permanently implantable, life sustaining, or life supporting device would be eligible for Third Party review. FDA maintains the list of eligible devices on its webpage, which contains the classification regulation numbers, classification regulation names, and links to applicable standards.[23]

Demonstrated Third Party Capability

The plan to eliminate routine re-review includes a multi-pronged approach for Third Parties to demonstrate their initial and ongoing capability to perform FDA-comparable regulatory reviews. Prior to conducting reviews, Third Parties must complete FDA's recognition process, which involves providing substantial documentation that demonstrates their capability in multiple key areas, including: 1) the qualifications and ongoing training of employees involved in review; 2) their knowledge of the relevant statutes and regulations associated with the device review areas; 3) information on the organization's quality management processes and procedures; and 4) the relevant records and documents related to those processes and procedures. To demonstrate ongoing capability, rerecognition is required every three years.

Provided Third Party Reviewers with Tools

The plan to eliminate routine re-review outlines four areas where CDRH will improve tools for Third Parties: 1) enhance both general and device-specific training and resources; 2) provide guided, tailored templates prompting Third Party reviewers for all required information; 3) establish an Early Interaction (EI) process, formerly "Ask the FDA Expert," for Third Party reviewers to ask questions; and 4) develop an Update Channel to communicate device type changes. Table 4-42 describes FDA efforts toward providing these tools.

Table 4-42. Third Party Tools Provided by FDA

Tool	Purpose
General and Device-Specific Training and Resources	• Provides orientation training to introduce the 510(k) Premarket Notification database, including how to access redacted review memos as examples to support performing FDA-comparable Third Party reviews • Provides general and device-specific CDRH Learn modules taught by review topic SMEs
Tailored Review Memo Templates	• Provides RTA checklist to help guide users through an administrative check of 510(k) completeness • Provides eSTAR to guide users through review and submission. The eSTAR template features help-text and embedded resources (e.g., links to FDA-recognized standards, guidances, product codes)
EI Process	• Enables Third Parties to communicate with FDA on current policies and processes early-on during review • Provides information on the EI process and provides example questions in guidance and on the FDA website
Update Channel	• Provides news, program updates, and information on upcoming events • Provides a centralized, archived resource for Third Parties (plan to create a webpage)

Monitored and Facilitated Continuous Improvement of Third Party Performance

In addition to quarterly performance reports, audits, and EIs, FDA also monitors and facilitates continuous improvement of Third Party performance through Third Party reviewer grades. FDA collects data to track the quality of individual Third Party reviews and issue grades based on factors such as whether the Third Party provided sufficient background and clear analysis. Developing and communicating reviewer grades provides FDA with the opportunity to highlight specific areas where Third Parties can improve review quality. FDA communicates reviewer grades to individual Third Parties through phone calls (e.g., Feedback Touchpoints) or follow-up emails. FDA also uses the reviewer grades to inform Third Party training needs based on areas where improvement in review quality exists.

[23] "List of Devices for Third Party Review," FDA https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfThirdParty/current.cfm – accessed 2/11/2021

4.7.2.2 PUBLISHED PERFORMANCE OF THIRD PARTIES WITH AT LEAST FIVE COMPLETED SUBMISSIONS

FDA monitors its own performance and the performance of recognized Third Parties across multiple efficiency and consistency measures as part of FDA's efforts to gain insight into the Third Party Review Program and identify opportunities for improvement and training. FDA publishes quarterly performance reports of all Third Parties with more than five completed submissions for each FY. The performance reports provide the opportunity for Third Parties to improve the quality of their submissions and perform consistent, FDA-comparable reviews. Table 4-43 highlights key efficiency and consistency measures captured in the report.

Table 4-43. Selected Third Party Program Performance Metrics

Selected Metrics	Definition
FDA Performance	The percentage of Third Party submissions that received MDUFA IV decisions by FDA within 30 days (see Total FDA Review Time)
Average Holds (Requests for AI)	The percentage (average number) of requests for additional information per submission
Initial Third Party Review Time	Elapsed time in calendar days for a Third Party to review the file and determine its recommendation (SE or NSE)
Third Party Hold Time	Elapsed time in calendar days for a Third Party to respond to a request from FDA for additional information.
Third Party Review Time	Elapsed time in calendar days for a Third Party to review a file from a 510(k) submitted, including the time it is on hold, if applicable
Total FDA Review Time	Elapsed time in calendar days for FDA to provide a MDUFA IV decision (30 days allowed by statute). The time does not include days that the submission is on hold while waiting for additional information from the Third Party
TTD from FDA Receipt	Elapsed time in calendar days between FDA's receipt of a Third Party submission and FDA's final MDUFA IV decision, which includes Third Party Hold Time
TTD from Third Party Receipt	Elapsed time in calendar days for FDA and the Third Party to provide a final MDUFA IV decision (SE or NSE) to a submitter. This metric spans the entire lifecycle of a Third Party submission

FDA has published quarterly performance reports on current and formerly recognized Third Parties since Q1 of FY 2018. Of the nine currently recognized Third Party organizations, three completed review of five or more submissions for FY 2020; submissions by these three Third Parties represent 96-100% of submissions to the Program.[24] As shown in Figure 4-21, the "Total Time to Decision from Third Party Receipt" has increased slightly between FY 2018 and FY 2020.[25] "Initial Third Party Review Time" takes the most time and its increase accounts for the overall increase in total time. The "Average Total FDA Review Time" decreased to 29 days in FY 2020, meeting the statutory requirement of 30 days. Progress was also made towards reducing re-review: the percentage of files placed on hold (i.e., due to requests for additional information, associated with re-review) steadily decreased from 57% in FY 2018 to 44% in FY 2019 and 35% in FY 2020. The average hold time decreased slightly from 36 days to 32 days.

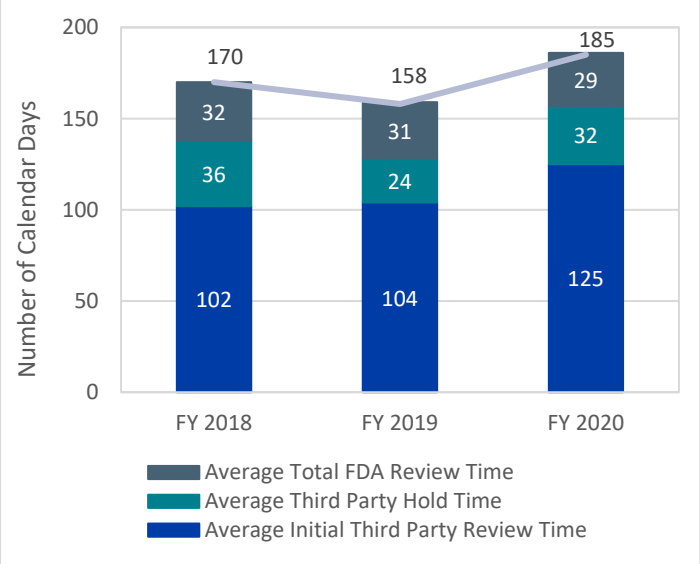


Figure 4-21. Initial and Total Third Party Review Time

[24] "FY 2021, Q3 Third Party Review Organization Performance Report," FDA https://www.fda.gov/media/150620/download – accessed 8/13/2021

[25] For comparison, the MDUFA IV goal for FDA review time for other 510(k)s is 90 days and the goal for TTD was 124 days in FY 2018, 120 days in FY 2019, and 116 days in FY 2020.

4.7.2.3 IMPLEMENTED A PROGRAM TO AUDIT REVIEWS CONDUCTED BY THIRD PARTIES

The Third Party Review Program implemented an audit program in 2018 to better understand the circumstances surrounding additional information requests (i.e., deficiencies) that led to re-review by CDRH. The audits examined deficiency letters sent from FDA to Third Party Organizations, focusing on Third Party submissions that received at least one additional information request during the first round of FDA review. The program conducted audits of 2018 and 2019 submissions, shown in Table 4-44.

Table 4-44. Comparison of 2018 and 2019 Audit Samples

Year	Number of Third Party Submissions that Received Deficiency Letter	Total Number of Deficiencies Represented
2018	(38/75)	231
2019	(23/78)	127

*Reflects submissions receiving at least one additional information request (i.e., deficiency letter) during the first round of FDA review.

The audits categorized each deficiency by topic to assess trends, determine the most common deficiency topics, and identify where to focus training efforts for Third Parties. Issues with labeling, performance testing, and the review memo were among the most common topics of deficiencies in 2018 and 2019, though deficiencies were widely distributed across all 15 possible topics, as shown in Figure 4-22. While the overall number of deficiencies across topics decreased in 2019, there were some TAs where the percentage of deficiencies increased, there is not sufficient information to determine causation in those specific areas.

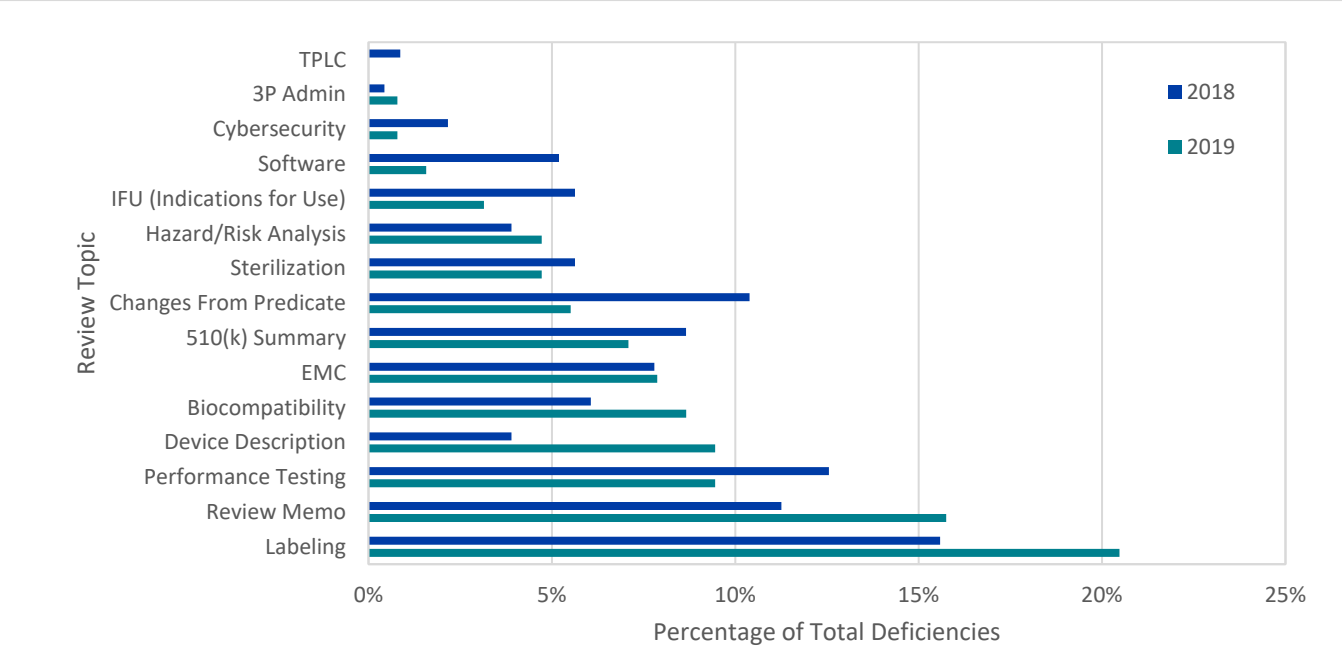


Figure 4-22. Distribution of Review Topics by Deficiency from Third Party Audits

The most common deficiency topics (e.g., labeling, performance testing, review memo) represent potential targets for additional training. Booz Allen observed that labeling and performance testing are also among the most common deficiency topics among Traditional 510(k) submissions, indicating challenges with these topics may not be specific to Third Parties. While training for Third Parties may be targeted to the most common deficiency TAs (e.g., labeling, performance testing, review memo), challenges remain across other topics given the broad distribution of reasons for re-review. Overall, the audit noted that many deficiencies were resolved through clarification or justification, rather than generation of additional information (e.g., did not require new data from studies nor updates to labeling), making overall Third Party Review Memo and submission quality potential targets for further training and engagement.

4.7.3 CONCLUSION

In accordance with the MDUFA IV Commitment Letter, FDA implemented a hands-on, tailored approach to promote the quality of Third Party reviews and reduce re-review. FDA achieved many of the commitments through activities outlined in the comprehensive plan, "Eliminating Routine FDA Re-Review of Third Party 510(k) Reviews." FDA activities included publishing Third Party guidance, tailoring the list of eligible devices, conducting audits, delivering training to Third Party Organizations, implementing the Update Channel, reporting Third Party performance, and other efforts to improve the exchange of information. These efforts resulted in fewer deficiency letters indicating improvement in Third Party review quality and progress towards FDA's goal of decreasing re-review.

4.8 Digital Health

The development of digital health products differs from other medical devices due to quicker and more iterative design, development, and validation processes. To accommodate new digital technologies, foster innovation, and meet its MDUFA IV commitments, FDA has engaged in the following activities: hire technical experts, participate in IMDRF's harmonization efforts, engage stakeholders, and explore innovative regulatory pathways through the Pre-Certification Pilot Program and development of the Artificial Intelligence (AI)/Machine Learning (ML) Framework. The commitments to publish guidance on "Deciding When to Submit a 510(k) for a Software Change" and on "Off-The-Shelf Software Used in Medical Devices" have been met. The commitment to publish guidance on "Content of Premarket Submissions for Software Contained in Medical Devices" has not been met, although it is prioritized for publication.

The assessment findings are presented in the following three sections:

- 4.8.1 Enhance Digital Health Review Capacity;
- 4.8.2 Explore Innovative Regulatory Pathways; and
- 4.8.3 Harmonize and Engage with Stakeholders.

4.8.1 ENHANCE DIGITAL HEALTH REVIEW CAPACITY

This section describes how FDA met each of the commitments shown in Table 4-45. The findings are described in the following five sections:

- 4.8.1.1 Establish the Division of Digital Health;
- 4.8.1.2 Develop Digital Health Expertise;
- 4.8.1.3 Encourage Training and Professional Development;
- 4.8.1.4 Develop Tools and Resources to Support Review; and
- 4.8.1.5 Provide Tools and Resources for External Stakeholders.

Table 4-45. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Establish a central digital health unit within CDRH's Office of the Center Director to ensure proper coordination and consistency across the Agency. The Agency will not reorganize staff such that existing review staff would be reassigned to the central digital health unit, while retaining and not disrupting the existing digital health talent within the reviewing divisions who have established, long-term therapeutic and device expertise. • Develop software and digital health technical expertise ("Technical Experts") to provide assistance for premarket submissions that include Software as a Medical Device (SaMD), Software in a Medical Device (SiMD), interoperable devices, or otherwise incorporate novel digital health technologies. • Utilize Technical Experts as appropriate or when requested by the manufacturer for submissions that include SaMD, SiMD, interoperable devices, or otherwise incorporate novel digital health technologies. • Incorporate appropriate metrics for digital health improvements to monitor, track, analyze and report the results of digital health premarket review timelines.

4.8.1.1 ESTABLISH THE DIVISION OF DIGITAL HEALTH (DDH)

CDRH established a digital health unit in the OCD in 2017, following the CDRH Digital Health Innovation Action Plan roadmap. As a result of the 2019 TPLC reorganization, the digital health unit became DDH within the newly established OST. The mission of DDH is to work across the Center to streamline and align regulatory processes, provide leadership on digital health issues, and develop a cohesive digital health strategy. DDH also addresses cross-cutting technical, human capital,

and regulatory policy needs in digital health for CDRH offices and external stakeholders. As part of the evolution of digital health efforts at CDRH, the Center launched the Digital Health Center of Excellence (DHCoE) in September 2020. The DHCoE serves as a centralized hub to promote coordination and the exchange of ideas and information across the Agency, as well as learning among digital health stakeholders.

Participate in the Digital Health Steering Committee (DHSC)

CDRH formed the DHSC to help meet its public health goals of facilitating innovation while assuring adequate patient protections. The DHSC is comprised of senior leadership (e.g., Associate Director of Digital Health, CDRH Center Director, Director of OPEQ, Deputy Center Director for Policy, among others) from across CDRH. The committee provides oversight of the Center's digital health policies and programs, consistent with CDRH's other ongoing efforts to improve coordination, consistency, transparency, and predictability in scientific and regulatory decision-making. The DHSC's goal is to enhance device safety, effectiveness, and quality, while fostering improved internal and external stakeholder communication. According to the DHSC's charter, the committee handles policy-related and product-specific issues unique to digital health technologies and devices.

The DHSC responds to and resolves complex policy issues and provides a forum for CDRH staff to raise digital health topics that require input from the Center's SMEs and senior leaders. During DHSC meetings, committee members and the DHSC Chair give the presenter(s) feedback and recommendations for future actions. The committee provides interpretations of digital health policy and guidance to foster consistent decision-making within the Center. The committee also gives DDH the opportunity to offer informative responses to stakeholder inquiries. On a case-by-case basis, the committee aims to resolve issues quickly and consistently during a submission's digital health review.

Monitor Digital Health Premarket Review Timelines

To monitor the results of digital health premarket review times, CDRH uses a tag in the Center Tracking System (CTS) to identify submissions containing digital health technologies. As of October 2020, CDRH received approximately 4,400 MDUFA IV submissions containing digital health technologies, shown in Figure 4-23. DDH has a process in place to monitor review time and TTD for digital health submissions on a quarterly basis. Based on monitoring of 510(k), De Novo, PMA submissions, and Q-Submissions, internal FDA analysis has determined that both FDA review times and TTD for digital health submissions are comparable to the broader respective MDUFA submission cohorts. CDRH also reviews metrics from the Feedback Library, Digital Health Inquiries Mailbox, and other sources to provide insight into trends in submission and review.

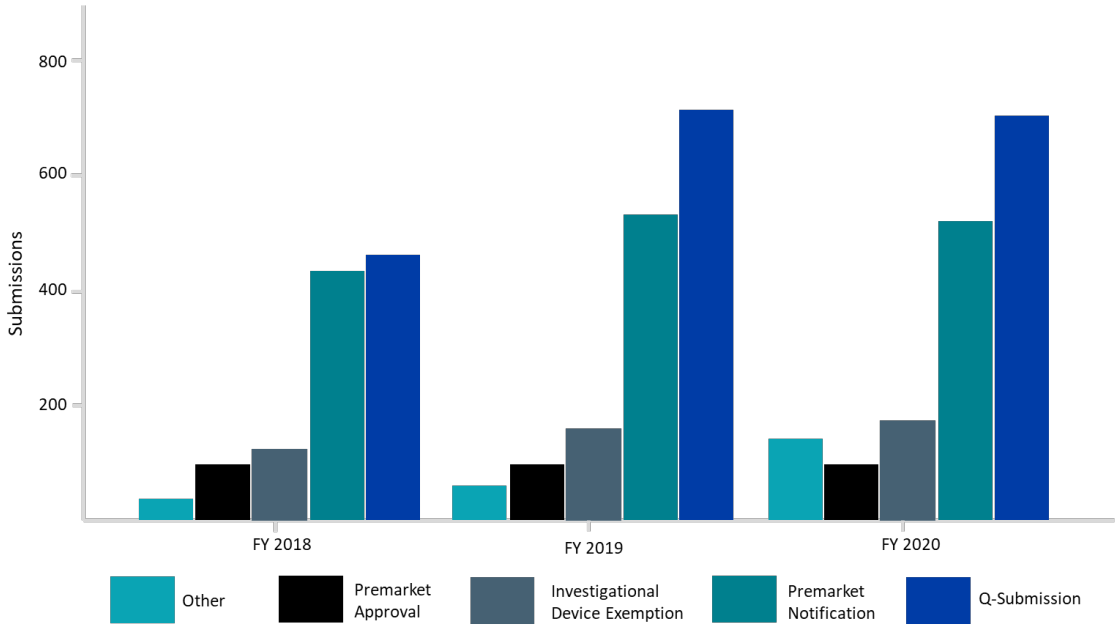


Figure 4-23. MDUFA IV Submissions Received with Digital Health Considerations as of October 2020

4.8.1.2 DEVELOP DIGITAL HEALTH EXPERTISE

Hire Staff with Digital Health Expertise

Hiring review staff within the DDH is a MDUFA IV priority to provide further leadership, policy support, and digital health expertise across CDRH. CDRH filled all seven of their allocated digital health FTEs in FY 2018 through FY 2019, eight out of 10 in FY 2020, and is targeting 13 digital health FTEs by the end of FY 2021.

DDH works to identify applicants with a comprehensive understanding of software development and digital health technologies. DDH designs job announcements to appeal to prospective applicants with a broad range of skills from a variety of diverse digital fields (e.g., mobile medical applications, AI, ML, cybersecurity) and posts announcements on federal jobs websites as well as professional networking platforms. Attracting highly qualified candidates—professionals with significant practical experience and up-to-date knowledge of digital health trends—has presented some challenges, including compensation (i.e., higher levels of compensation in the private sector) and relocation (i.e., greater concentration of needed expertise in technology hubs outside the Washington, District of Columbia metropolitan area).

Leverage Expertise Through Fellowships and Novel Programs

CDRH uses a variety of mechanisms to leverage external experts and innovators in digital health, including the NoE, Entrepreneurs in Residence (EIR), and Presidential Innovation Fellows (PIF). The NoE program enables collaboration and information exchange between CDRH and experts from over 40 scientific and professional organizations. These pre-vetted experts provide input on issues related to specific use cases that may affect a regulatory decision. In FY 2020, DDH expanded the existing NoE pool of traditional medical experts to include specialized expertise in digital health areas, forming the Network of Digital Health Experts (NoDEx). NoDEx experts often represent multiple specialty or TAs that follow different development patterns. NoDEx builds internal capacity by allowing CDRH to connect with recognized digital health leaders and experts in the field who are on the forefront of cutting-edge technologies and understand current best practices in various digital health subfields.

The EIR program allows CDRH to bring external experts and innovators to the Center to gain regulatory process perspectives from a traditional regulatory environment, while providing CDRH with perspectives from current industry expertise. Since 2018, DDH has welcomed three EIRs with varying, relevant backgrounds. EIRs have shaped and advised the SaMD Pre-Certification (Pre-Cert) pilot program and worked directly with DDH leadership to standup the infrastructure needed for multiple programs.

The PIF program, sponsored by the General Services Administration, is another way DDH leverages expertise externally. Beginning in 2012, the competitive, 12-month fellowship placed cohorts of diverse and multi-disciplinary fellows with senior government leaders. These fellows develop solutions for the nation's toughest challenges throughout the Federal Government by bringing data science, design, engineering, product, and systems thinking to existing digital capacities. Since January 2019, two PIFs supported work within DDH, responsible for helping develop the infrastructure and organization of DDH. Like their EIR counterparts, PIFs also coordinate and support the Division's work and FDA work groups on a variety of topics, including AI and ML.

4.8.1.3 ENCOURAGE TRAINING AND PROFESSIONAL DEVELOPMENT

FDA provides digital health information and professional development opportunities within CDRH and across the Agency through all-hands meetings, rounds, office-level presentations, journal clubs, and webinars. DDH hosts roundtable discussions to communicate Center policy, provide regulatory clarity surrounding digital health devices, and provide opportunities to stay up to date on DDH initiatives. Among the resources available to internal and external audiences, DDH provides presentations, slides, and transcripts on digital health programs to prompt discussion, provide updates on programs, communicate changes to policy and interpretation due to enacted legislation, and announce upcoming draft and final guidance.

DDH also collaborates with partners in industry, academia, research organizations, and other external stakeholder groups through the ELP. ELP is intended to provide CDRH staff with an opportunity to understand the policies, laboratory and manufacturing practices, and the challenges addressing patient perspective/input, quality system

management, and other concerns that impact the device development lifecycle. This program connects CDRH review staff directly to emerging and innovative technologies through two- and three-day events sponsored by external stakeholders including industry.[9] Table 4-46 lists examples of recent digital health ELP visits to foster collaboration.

Table 4-46. Recent Digital Health ELP Visits

Host Organization	Key Topics Covered
Verb Surgical (2019)	• Digital Surgery • Robotically-assisted surgical devices • Quantifying surgery and extracting insights from surgical data
Dassault Systèmes (2019)	• Managing quality and safety of digital health products • Personalized medicine and patient experience • Modeling/simulation for development of cardiovascular medical device • Modeling/simulation to validate early concepts including digital manufacturing
Intuitive AI (2019)	• Use, management, and quality assurance of AI • Safety mechanisms to mitigate unexpected AI behavior • Product-specific and non-product applications
Google Health (2020)	• Generalizability of AI algorithms • Assessment of AI algorithm performance and ways to eliminate bias • Deep learning and Continuous learning
Medtronic (2020)	• Personalized medicine • Closed-loop systems • Use cases with different risk profiles • Physician/patient perspectives on maturing AI/ML algorithms
Johnson & Johnson (2021)	• Advanced imaging, analytics/digital solutions • Vision for information management, learning & mentoring, and decision support tools including AI/ML • Digital surgery robotics and surgeon training

4.8.1.4 DEVELOP TOOLS AND RESOURCES TO SUPPORT REVIEW

Develop SaMD Decision Tool

DDH developed the SaMD Decision Tool, summarized in Table 4-47, to help users navigate digital health guidance and policies, facilitating access to and use of guidance documents relevant to a given regulatory decision. The decision tool consists of several flow charts that guide users through a range of questions to determine the potential scope of FDA oversight or likely review needed for a product. While not an official regulatory determination, the decision tool helps users obtain additional regulatory clarity.

Table 4-47. SaMD Decision Tool

SaMD Decision Tool Navigates Users Through Guidance by Answering:
1. Does this function have a potentially regulated medical purpose? 2. Is the function a Medical Device Data System software? 3. Does FDA's general wellness policy apply to the function in question? 4. Does FDA's mobile medical applications (MMA) and software functions policy apply to this function?

Implement Focal Point Programs

FPPs serve as a way for OPEQ to implement CDRH policy by promoting consistent and high-quality review practices through the identification of staff (i.e., focal points) with specific training and expertise in a TA. These focal points participate in discussion groups on their respective TAs and assist in the premarket review process by providing consultations and support to reviewers. Existing focal points also help OPEQ identify the core competencies needed by review staff, set a baseline for training programs, and identify additional competencies and TAs to develop additional focal points. DDH supports this program by having two representatives from each of the OHTs collaborate on emerging digital health topics and develop expertise within DDH and CDRH that crosses OHTs. The Digital Health FPP provides additional resources to FDA staff and external stakeholders in collaboration with DDH, including contributing to and providing early feedback on tools for review, such as the SaMD Decision Tool.

Provide Regulatory Consults

During the review process, CDRH reviewers may request a regulatory consult when they need additional digital health expertise. For functionalities and technologies in premarket submissions that may benefit from additional DDH expertise, a CDRH reviewer enters the digital health consult request in the CTS for assignment to digital health experts within DDH or the Center. Device sponsors may also request expertise from DDH on their device submissions. DDH has provided over 100 formal digital health consults during MDUFA IV and has engaged in other premarket issues and submissions using less-formal mechanisms as shown in Figure 4-24.

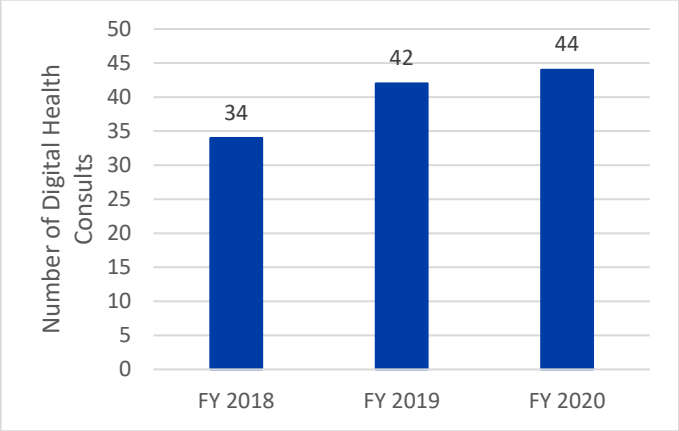


Figure 4-24. Digital Health Consults Requested Per FY

Develop and Maintain Feedback Library

DDH maintains a Feedback Library containing searchable records of stakeholder inquiries and DDH responses, and continually updates the library with new information and direct responses to stakeholder needs. The library is a valuable resource for Digital Health Mailbox Coordinators, discussed below, who field stakeholder inquiries and reviewers who seek clarity. The library creates efficiencies by reducing rework of responses. DDH intends for the library to enhance the consistency of CDRH feedback and review.

4.8.1.5 PROVIDE TOOLS AND RESOURCES FOR EXTERNAL STAKEHOLDERS

To respond quickly to external stakeholders and provide consistent messaging on CDRH policy and interpretation related to digital health technologies, DDH created the (electronic) Digital Health Inquiries Mailbox. This mailbox presents a low barrier to entry for external stakeholders to begin a conversation with FDA during any stage of product development. Digital Health Coordinators monitor the inbox and triage inquiries based on their content.

The mailbox also provides DDH with a platform to provide information and advice to stakeholders with questions on digital health technologies. When handling inquiries, Digital Health Coordinators choose from a variety of actions, which include: referencing the Feedback Library for previous resolutions related to an inquiry; requesting additional clarifying information from the stakeholder; providing specific guidance references when the guidance clearly addresses the question; coordinating with other offices to obtain a response when guidance does not clearly provide the answer; or forwarding more complex issues for resolution to the DHSC. As shown in Figure 4-25, Mailbox use has been steady, with inquiries increasing as awareness of this resource has grown. DDH monitors Mailbox metrics weekly to adjust resources as Mailbox volume fluctuates.

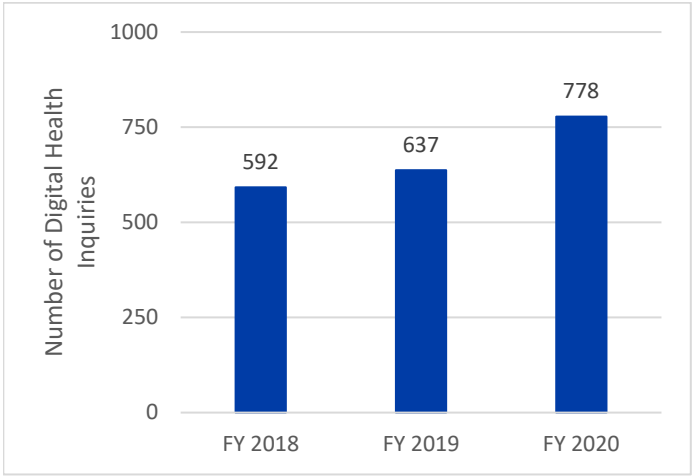


Figure 4-25. Digital Health Inquiries Received Per FY

4.8.2 EXPLORE INNOVATIVE REGULATORY PATHWAYS

This section describes how FDA met each of the commitments shown in Table 4-48. FDA met its MDUFA IV commitment to explore opportunities to establish pathways tailored to digital health technologies through the

Pre-Certification Pilot program and development of the proposed AI/ML Framework. In addition, commitments to publish guidance on "Deciding When to Submit a 510(k) for a Software Change" and on "Off-The-Shelf Software Used in Medical Devices" have been met. The commitment to publish guidance on "Content of Premarket Submissions for Software Contained in Medical Devices" has not been met, although it is prioritized for publication. The findings are described in the following three sections:

- 4.8.2.1 Establish Software Pre-certification (Pre-Cert) Pilot Program Working Model;
- 4.8.2.2 Propose a Regulatory Framework for AI/ML; and
- 4.8.2.3 Develop and Update Guidance Tailored to Digital Health Products.

Table 4-48. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Explore opportunities to establish premarket approval/clearance pathways tailored to SaMD, SiMD, and novel digital health technologies that take into account real world evidence while incorporating principles established through international harmonization. • Revise existing and/or publish new relevant guidance documents, including publishing a draft revised version of the "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" (issued in 2005) by the end of FY 2019, and within 12 months of the close of the comment period, publish the final revised version. The Agency will incorporate applicable concepts from its Guidance for "Off-The-Shelf Software Used in Medical Devices." • Publish final guidance addressing when to submit a 510(k) for a software modification to an existing device within 18 months of the close of the comment period.

4.8.2.1 ESTABLISH SOFTWARE PRE-CERTIFICATION (PRE-CERT) PILOT PROGRAM WORKING MODEL

The Pre-Cert Pilot program is one of CDRH's first major efforts to explore how best to align a future regulatory model with the modern software development process and digital health products. The intent of this pilot is to inform the development of a future regulatory model which can provide more streamlined and efficient oversight of digital health products. Unlike the traditional regulatory approach, the Pre-Cert Pilot program aims to include the appraisal of the developer of the product in addition to the product evaluation itself and use this additional piece of information to enhance regulatory efficiencies. Under this vision, FDA would conduct an excellence appraisal to "precertify" companies, followed by "review determination" to determine the appropriate premarket review pathway, as shown in Figure 4-26.[26] Finally, FDA considers how best to work with the company to collect and interpret real-world performance (RWP) information on the product's safety and effectiveness. Ultimately, the goal of the Pre-Cert Pilot is to demonstrate that the excellence appraisal and streamlined review yields the same quality of review compared to traditional approach.

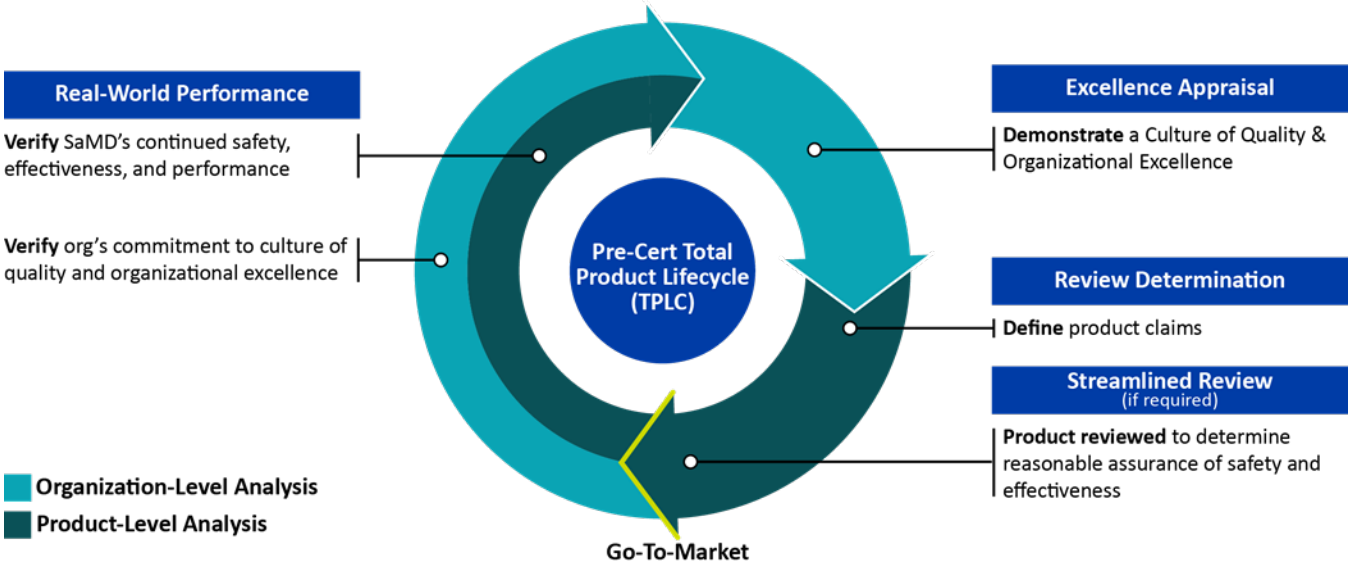


Figure 4-26. FDA TPLC Approach of Software Pre-Cert Pilot Program

[26] "Digital Health Software Precertification (Pre-Cert) Program," FDA https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-software-precertification-pre-cert-program – accessed 7/9/2021

The Pre-Cert Pilot program was developed by DDH leadership and its staff of advisors, EIR, PIF, with input from industry, academia, and other stakeholders. To develop the pilot, CDRH solicited public input on the continued development of the Pre-Cert Pilot program and version 1.0 of the Pre-Cert Pilot program Working Model. FDA introduced the model in CDRH's Digital Health Innovation Action Plan, followed by multiple presentations and webinars to disseminate the information to a wide audience.

CDRH is undertaking a phased approach to the Pre-Cert Pilot laid out in the Software Precertification Program 2019 Test plan.[27] The pilot is currently in the "Build and Iterate" phase as CDRH tests the proposed Pre-Cert Program framework in collaboration with manufacturers and software developers selected to participate in the pilot. For the test cases, participants submit a traditional package through existing regulatory pathways in parallel with a mock submission package for the pilot.[28]

As additional test cases are addressed and the pilot continues to evolve, CDRH is taking learnings into consideration to fully implement the Pre-Cert model and framework in a least burdensome way, including: identifying statutory authority, expansion to additional product/submission types, addressing potential challenges of the excellence appraisal (e.g., objective appraisal criteria), methodology and approach for continuous monitoring, and issues related to reliance on real-world data (RWD) (e.g., accuracy). Results from the pilot will help FDA determine the regulations and authorities needed to implement the program. In future phases, CDRH will be identifying plans for statutory authority, infrastructure and methodology, followed by a scaled-up beta testing phase and eventual program launch.

4.8.2.2 PROPOSE A REGULATORY FRAMEWORK FOR AI/ML

Prior to 2019, it was widely understood that developers of AI/ML technologies would lock their algorithms before providing a marketing submission to FDA, canceling out a significant benefit of many AI/ML algorithms—the ability to improve and adapt based on real-world use. FDA noted the need for a targeted regulatory pathway that ensures the safety and effectiveness of these devices but remains flexible enough to allow for the ongoing algorithm changes commonly found in AI/ML technologies. Leveraging TPLC practices explored in the Pre-Cert Pilot program, FDA released a discussion paper[29] and proposed an AI/ML framework in 2019, which may require additional statutory authority to implement fully. The discussion paper outlines FDA's exploration of targeted and flexible approaches to regulate evolving technologies by including a sponsor's quality management practices and postmarket RWP monitoring to get innovative products, beneficial to both patients and providers, to market. The discussion paper sought to engage stakeholders in a discussion on this proposed TPLC-based approach to AI/ML product regulation that recognizes the iterative and non-static nature of developing these devices. Due to the continuous changes possible in AI/ML algorithms, FDA based its discussion paper and proposed framework on the risk categorization harmonization efforts developed in collaboration with IMDRF.[30]

The TPLC approach outlined in the discussion paper would allow AI/ML SaMD to benefit from supervised learning during real-world use while maintaining a reasonable assurance of safety and effectiveness through managing and controlling risk from modifications using the principle of pre-determined change control plans. These plans include SaMD Pre-Specifications (SPS), a manufacturer's anticipated changes once the SaMD is in use, and Algorithm Change Protocol (ACP). ACP is the manufacturer's plan to appropriately control risk from changes specified in the SPS, both of which may necessitate individual consideration during FDA's premarket review. In addition, FDA would expect developers to commit to principles of transparency and RWP monitoring to improve the performance, safety, and effectiveness of the AI/ML SaMD, including providing periodic updates to FDA. The AI/ML discussion paper notes that FDA has successfully explored this voluntary approach to review device

[27] "Software Precertification Program: 2019 Test Plan," FDA https://www.fda.gov/media/119723/download – accessed 7/9/2021
[28] "Developing the Software Precertification Program: Summary of Learnings and Ongoing Activities," FDA https://www.fda.gov/media/142107/download – accessed 7/9/2021
[29] "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) – Discussion Paper and Request for Feedback," FDA https://www.regulations.gov/document/FDA-2019-N-1185-0001 – accessed 7/9/2021
[30] "Global Approach to Software as a Medical Device: Software as a Medical Device," FDA https://www.fda.gov/medical-devices/software-medical-device-samd/global-approach-software-medical-device – accessed 7/9/2021

modification plans, with several developers providing SPS and ACP that resulted in marketing authorizations and special controls in certain recent De Novo classifications involving IVD next generation sequencing products. Several examples are highlighted in "CDRH's Approach to Tumor Profiling Next Generation Sequencing Tests."[31]

The potential impacts of the proposed AI/ML framework include benefits from a consistent regulatory framework that align with the unique needs of AI/ML technologies and provide a clear pathway to create, expand, and adapt products for market. In January 2021, FDA described their intentions for further progress on the proposed AI/ML SaMD framework through planned issuance of guidance on the pre-determined change control plan.

4.8.2.3 DEVELOP AND UPDATE GUIDANCE TAILORED TO DIGITAL HEALTH PRODUCTS

FDA primarily uses guidance documents to communicate context around current regulatory requirements. In 2011, FDA published a notice on MMAs, marking a step toward an increased focus on digital health. CDRH is bound by the framework laid out in the Medical Device Amendments of 1976, which lagged massive shifts in the digital health landscape. CDRH has since issued multiple guidances on digital health, with a surge in draft and final guidances released during the MDUFA IV timeframe. The guidances on digital health, in addition to communicating regulatory expectations, address three important industry needs: 1) clarity on how FDA intends to regulate new types of digital health products; 2) defined boundaries of FDA's authority over digital health technologies (and what devices fall under that authority) introduced into the market; and 3) how FDA's thinking on digital health has evolved as a result of changes to the regulatory landscape. Providing clarity in these areas offers industry the consistent regulatory framework needed to encourage innovation, and it provides patients and healthcare providers confidence in the safety and efficacy of innovative digital health technologies.

Since 2017, CDRH has issued nine final guidance documents and two guidances in draft form on digital health. The intent of the guidance documents, listed in Table 4-49, is to create a consistent and holistic regulatory network, embrace risk-based approaches to reduce the evidentiary burden where appropriate, and enable paths to market for novel products. Of the guidances required by the MDUFA IV commitments, CDRH issued the final guidance "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" in 2017. However, the guidance "Content of Premarket Submissions for Software Contained in a Medical Device" has been delayed. Draft guidance was due by the end of FY 2019, with final guidance due within 12 months of the close of the draft comment period. CDRH has included the draft guidance on the list of priority guidance for completion.

Table 4-49. Planned and Recent Updates to Digital Health Guidance

Planned Draft Guidance	Status
Guidance for the Content of Premarket Submissions for Software Contained in a Medical Device (May 11, 2005)*	Priority Guidance (A-List) for FY 2021[32]
Pre-Determined Change Control Plan: Premarket Submission Considerations for Artificial Intelligence and Machine Learning software	Priority Guidance (B-List) for FY 2021
Risk Categorization for Software as a Medical Device: FDA Interpretation, Policy and Considerations	Priority Guidance (B-List) for FY 2021
Draft Guidance	**Purpose**
Clinical Decision Support Software (September 27, 2019) [33]	Intended to provide clarity on the scope of FDA's oversight of clinical decision support software intended for health care professionals, patients, or caregivers

[31] "FDA Fact Sheet: CDRH's Approach to Tumor Profiling Next Generation Sequencing Tests," FDA https://www.fda.gov/media/109050/download – accessed 9/18/2021
[32] "CDRH Proposed Guidances for Fiscal Year 2021," FDA https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/cdrh-proposed-guidances-fiscal-year-2021-fy-2021 – accessed 7/9/2021
[33] "Clinical Decision Support Software: Draft Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/109618/download – accessed 7/9/2021

Draft Guidance	Purpose
Content of Premarket Submissions for Management of Cybersecurity in Medical Devices (October 18, 2018) [34]	Intended to provide recommendations to industry regarding cybersecurity device design, labeling, and the documentation FDA recommends that sponsors include in premarket submissions for devices with cybersecurity risk
Final Guidance	**Purpose**
Multiple Function Device Products: Policy and Considerations (July 29, 2020)[35]	Addresses an important provision of the Cures Act related to multiple function device products that have a non-device software function
Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act (September 27, 2019)[36]	Includes interpretation of several software provisions of the Cures Act and details updates made to four other guidances to be consistent with the Cures Act, which removed certain software functions from the definition of device in Section 201(h) of the FD&C Act
Policy for Device Software Functions and Mobile Medical Applications (September 27, 2019)[37]	Updated to be consistent with the Cures Act, which removed certain software functions from the definition of device in Section 201(h) of the FD&C Act
Medical Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices (September 27, 2019)[38]	Updated to be consistent with the Cures Act, which removed certain software functions from the definition of device in Section 201(h) of the FD&C Act
General Wellness: Policy for Low-Risk Devices (September 27, 2019)[39]	Updated to be consistent with the Cures Act, which removed certain software functions from the definition of device in Section 201(h) of the FD&C Act
Off-The-Shelf Software Used in Medical Devices (September 27, 2019)[40]	Updated to be consistent with the Cures Act, removing certain software functions from the definition of device in Section 201(h) of the FD&C Act
Medical Device Accessories- Describing Accessories and Classification Pathways (December 20, 2017)[41]	Updated to be consistent with the FDA Reauthorization Act of 2017, which describes that the classification of accessory devices should reflect the risks of the device when used as intended and the level of regulatory controls necessary to provide a reasonable assurance of safety and effectiveness
Software as a Medical Device: Clinical Evaluation (12/8/2017)[42]	Adopts the internally converged principles agreed upon by the IMDRF for demonstrating the safety, effectiveness, and performance of SaMD
Deciding When to Submit a 510(k) for a Software Change to an Existing Device (October 25, 2017)[43]*	Provides clarification of key terms and how to use risk assessment to evaluate when to submit a 510(k) for a software change

*Guidance specified in the Commitment Letter

[34] "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices: Draft Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/119933/download – accessed 7/9/2021
[35] "Multiple Function Device Products, Policy and Considerations: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/112671/download – accessed 7/9/2021
[36] "Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/109622/download – accessed 7/9/2021
[37] "Policy for Device Software Functions and Mobile Medical Applications: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/80958/download – accessed 7/9/2021
[38] "Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/88572/download – accessed 7/9/2021
[39] "General Wellness, Policy for Low-Risk Devices: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/90652/download – accessed 7/9/2021
[40] "Off-The-Shelf Software Used in Medical Devices: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/71794/download – accessed 7/9/2021
[41] "Medical Device Accessories - Describing Accessories and Classification Pathways: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/90647/download – accessed 7/9/2021
[42] "Software as a Medical Device (SAMD): Clinical Evaluation," FDA https://www.fda.gov/media/100714/download – accessed 7/9/2021
[43] "Deciding When to Submit a 510(k) for a Software Change to an Existing Device: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/99785/download – accessed 7/9/2021

4.8.3 HARMONIZE AND ENGAGE WITH STAKEHOLDERS

This section describes how FDA met each of the commitments shown in Table 4-50**.** The findings are described in the following two sections:

- 4.8.3.1 Participate in the International Medical Device Regulator Forum (IMDRF); and
- 4.8.3.2 Hold Public Workshops and Collaborate.

Table 4-50. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Participate in international harmonization efforts related to digital health, including work on developing SaMD and other digital health convergence efforts through the IMDRF. • Engage through roundtables, meetings, and teleconferences. • Hold a public workshop.

4.8.3.1 PARTICIPATE IN THE INTERNATIONAL MEDICAL DEVICE REGULATOR FORUM (IMDRF)

FDA participates and provides leadership in international harmonization efforts related to digital health through the IMDRF, a group of global medical device regulators who work together to produce appropriate guidance and non-guidance documents that apply to their members. FDA's leadership in international harmonization efforts provides transparency, clarity, and predictability on an international stage that can help reduce the challenges inherent in regulatory oversight of devices on international markets. By harmonizing standards, products reach the market faster and consumers benefit from improved access and choice.

These international harmonization efforts hold increased importance in the context of the digital health landscape, where fast-paced development can take place independent of geographic location. FDA chairs the following IMDRF Working Groups: Cybersecurity, which provides recommendations on principles and best practices for medical device cybersecurity; Patient Registries, which develops common, shared principles for building patient registries; and SaMD, which seeks to establish common and shared principles for demonstrating SaMD's safety and effectiveness. After publishing "Key Definitions"[44] in 2013 and establishing the term "SaMD," in 2014, the SaMD working group released "Possible Framework for Risk Categorization and Corresponding Considerations,"[45] which outlined a risk-based approach and risk categorization schema for SaMD. Subsequently in 2015 and 2017, the working group also published "Application of Quality Management System"[46] and "Clinical evaluation"[47] respectively. FDA adopted these IMDRF SaMD documents and issued "SaMD: Clinical Evaluation" as a final Guidance in 2017.[48] Starting with these internationally harmonized principles CDRH has proposed the application of the SaMD risk categorization framework in several efforts, including the AI/ML discussion paper and the Pre-Cert Pilot Working Model. The Pre-Cert Pilot also uses IMDRF's proposed SaMD Definition Statement to help identify the risk level of devices.

4.8.3.2 HOLD PUBLIC WORKSHOPS AND COLLABORATE

FDA has engaged stakeholders through several channels including: hosting meetings, webinars, and town halls; participating in conferences with the broader digital health community; and providing hands-on training in intensive settings. These opportunities bring industry members together to advance best practices in digital health, work collaboratively to address challenges, develop solutions, and provide FDA perspectives and leadership.

FDA hosted 30 public meetings and webinars in FY 2018, 36 in FY 2019, and 24 in FY 2020 as of September 2020. These engagements covered a range of topics, including changes to guidance and updates on FDA's digital health activities (e.g., Pre-Cert Pilot program, evolving AI framework.) In addition, DDH collaborated with CDRH's PSE

[44] "Software as a Medical Device (SaMD): Key Definitions," IMDRF http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.pdf – accessed 09/16/2021
[45] "Software as a Medical Device (SaMD): Possible Framework for Risk Categorization and Corresponding Considerations," IMDRF http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf – accessed 6/17/2020
[46] "Software as a Medical Device (SaMD): Application of Quality Management System," IMDRF http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-151002-samd-qms.pdf – accessed 09/16/2021
[47] "Software as a Medical Device (SaMD): Clinical Evaluation," IMDRF http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170921-samd-n41-clinical-evaluation_1.pdf – accessed 09/16/2021
[48] "Software as a Medical Device (SaMD): Clinical Evaluation, Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/100714/download – accessed 09/24/2021

staff and hosts events, such as the Virtual CDRH Town Hall, to engage with patient needs in digital health devices. FDA also participated in conferences with the broader digital health community (e.g., Xavier Artificial Intelligence Initiative), providing leadership and collaborating to update the approach to regulating digital health technologies.

In addition to meetings and conferences, FDA provides hands-on training in a bootcamp setting for early-stage innovators. Through collaboration with the University of California San Francisco (UCSF)-Stanford University Centers of Excellence in Regulatory Science and Innovation (CERSI), the bootcamp emphasizes digital health technologies used to facilitate assessment of patient outcomes in clinical trials and offers participants a high-level understanding of the regulatory pathways for SaMD and the vocabulary used by FDA when communicating patient outcome measurements. This type of training has the potential to prepare innovators for more informed interactions with regulators, improve their evidence generation, and bring safe and effective medical technologies into the healthcare system in a timely manner.[49]

4.8.4 CONCLUSION

FDA met its commitments to hire technical experts, streamline and align review processes, explore innovative regulatory pathways, participate in international harmonization, and engage stakeholders. To support a consistent and holistic regulatory network, FDA published guidance on "Deciding When to Submit a 510(k) for a Software Change" and on "Off-The-Shelf Software Used in Medical Devices," as specified under the MDUFA IV commitment. Although it is prioritized for publication, FDA has not met its commitment to publish draft guidance on the "Content of Premarket Submissions for Software Contained in a Medical Device;" however, the overall policy and regulatory support provided by the program exceeded the MDUFA commitments. The infrastructure established by the program has positioned FDA to continue to stay abreast of current developments and to exercise the flexibility needed for incorporation of new data types and sources to enhance regulatory decision-making.

4.9 Patient Science and Engagement

CDRH emphasized their commitment to incorporating the patient perspective across the regulatory review process by including "Partnering with Patients" as a priority in their 2016-2017 Strategic Priorities. This priority outlined two primary goals: promote a culture of meaningful patient engagement by facilitating CDRH's interaction with patients, and increase use and transparency of patient input as evidence in CDRH's decision-making. These goals laid the foundation for the establishment of the PSE program and for many of the commitments in the MDUFA IV Commitment Letter.

In 2018, CDRH established the PSE program with the mission to engage with patients, understand their perspective, and proactively integrate their perspectives into the TPLC of medical devices to help protect and promote patient-centric public health. The MDUFA IV commitments for Patient Engagement and the Science of Patient Input focus on developing staff expertise and capacity, holding public meetings, and improving the regulatory predictability and impact of patient-reported outcomes (PRO).

Booz Allen found that FDA met its MDUFA IV commitments by developing clinical, statistical, and other scientific expertise and staff capacity; providing early consultation to industry; holding stakeholder engagement meetings; clarifying and modifying guidance; developing a model for bridging studies; and leveraging the dispute resolution process.

The assessment findings are presented in the following three sections:

- 4.9.1 Develop Expertise and Capacity;
- 4.9.2 Hold Public Meetings to Advance PPI, PROs, and Patient Engagement; and
- 4.9.3 Improve Regulatory Predictability and Impact of PROs.

[49] "IMPACT Bootcamp: Navigating the Journey from Digital Health Technologies to Meaningful Patient Outcomes," University of California San Francisco https://pharm.ucsf.edu/cersi/bootcamp – accessed 7/9/2021

4.9.1 DEVELOP EXPERTISE AND CAPACITY

This section describes how FDA met each of the commitments shown in Table 4-51**.** The findings are described in the following two sections:

- 4.9.1.1 Develop Clinical, Statistical, and Other Scientific Expertise and Staff Capacity; and
- 4.9.1.2 Provide Internal and External Consultations.

Table 4-51. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Develop clinical, statistical, and other scientific expertise and staff capacity to respond to submissions containing applicant-proposed use of publicly available and validated PPIs or PROs. • These staff will provide submission review and early consultation/advice to industry during study planning.

4.9.1.1 DEVELOP CLINICAL, STATISTICAL, AND OTHER SCIENTIFIC EXPERTISE AND STAFF CAPACITY

FDA committed to developing clinical, statistical, and other scientific expertise and staff capacity to respond to submissions containing applicant-proposed use of publicly available and validated voluntary Patient Preference Information (PPI) or voluntary PROs. The staff will provide submission review and early consultation/advice to industry during study planning. CDRH accomplished this through four mechanisms: 1) hiring new staff; 2) training existing staff; 3) leveraging expertise through internal consultations; and 4) participating in internal and external collaborations.

Hire Staff

To support the use of patient-centric medical device development and regulatory decision-making, CDRH targeted and hired six MDUFA IV FTEs through FY 2021. In addition, CDRH also hired three FTE and leveraged additional staff from other teams to establish the PSE program. Hires included people with expertise and experience in how patient input can influence regulatory decision-making; clinical study design, analysis, and interpretation; modern psychometric methods; health economics (including designing and evaluating patient preference studies); qualitative research methods; and experience working with patients and eliciting their feedback. CDRH also hired a manager for the Patient Engagement Advisory Committee (PEAC), an advisory committee comprised of patients, caregivers, and representatives of patient organizations to provide input on complex issues relating to medical devices.

Provide Training on Patient Science

CDRH has undertaken multiple efforts to develop training designed for expanding staff understanding of PROs. As part of CDRH's commitment to build capacity across the Center, the PSE program developed a course for the Advanced RCP to introduce PROs, provide background on PRO development, and explain how reviewers evaluate PROs in submissions. As part of the Advanced RCP, the PSE staff provide additional presentations on patient science and engagement.

To supplement the training content offered through the Advanced RCP, the PSE program staff also launched the Patient Science and Engagement Curriculum in February 2018. The curriculum, intended for reviewers, medical officers, team leads, and biostatisticians, aims to advance and promote the use of clinical outcome assessments (COAs) and PPI across the TPLC of medical devices. The course curriculum offers three tracks—PSE, COAs, and PPI—and provides introductory- and advanced-level training on a variety of topics, including the value of patient input, methods development, and validation. The Patient Science and Engagement Curriculum allows reviewers to develop in-depth knowledge and expertise on various patient science topics, including elicitation and evaluation of patient preferences and the use and evaluation of COAs. Between 2018 and 2021, there have been 785 enrollments in Patient Science and Engagement Curriculum courses, with 375 reviewers completing at least one course in the curriculum.

Beginning in May 2019, the PSE program conducted a Level 1, 2, and 3 Kirkpatrick evaluation of the Patient Science and Engagement Curriculum courses to assess the effectiveness of its training programs, shown in Table 4-52.

Table 4-52. Results from Kirkpatrick Evaluation of PSE Curriculum

Kirkpatrick Evaluation of Patient Science and Engagement Curriculum	
Kirkpatrick Level	**Key Findings**
1	Over 90% of learners indicated that they understood the learning objectives and felt challenged by the material
2	Learners indicated increased mastery of the topics in all five PPI-track and all 3 COA/PSE-track courses analyzed
3	• 100% of respondents expected positive results from their participation in the courses • 100% of respondents who had had the opportunity to apply what they learned, reported successfully applying those skills • Respondents also shared that the course deepened their understanding of clinical trial measures, improved their review and development of research studies, and supported them in discussing the advantages and limitations of PROs and PPI with review teams.

Participate in Collaborations to Build Capacity and Advance Patient-Generated Health Data (PGHD)

The PSE program works to advance the field of patient science through internal collaborations as well as external collaborations with academics, public-private partnerships, professional societies, and patient advocacy groups. Table 4-53 presents the partners and purpose for several of these internal and external collaborations.

Table 4-53. Examples of Collaborations Between PSE Staff and Internal and External Stakeholders

Internal Collaborations	
Partner	**Purpose**
FDA's Oncology Center of Excellence	Better understand how programs can use PGHD and how patients feel and function in their daily lives
FDA's Digital Health Center of Excellence	Consistent generation and evaluation of PGHD; harmonization of efforts to incorporate patient input into the regulatory process.
FDA's Office of Patient Affairs	Listening sessions with the National Organization for Rare Disorders to accurately capture and reflect the experiences of patients living with rare disease
CDER's Patient-Focused Drug Development (PFDD) program	Collaborate on PFDD guidance series to include LB and fit-for-purpose principles as well as internally and externally led meetings
External Collaborations	
Partner	**Purpose**
Johns Hopkins University CERSI, UCSF-Stanford CERSI, Veteran's Administration	Conducted a PPI study on upper limb prosthesis which helped inform the development of 2019 draft guidance[50]
Department of Defense and National Eye Institute at the National Institutes of Health	Developed the Patient-Reported Outcomes with LASIK (PROWL) questionnaire that was qualified as a Medical Device Development Tool[51]
UCSF-Stanford CERSI and the Yale/Mayo Clinic CERSI	Held bootcamps[49] in July 2020 and March 2021 to discuss considerations for COAs, PPI, and digital health technologies with stakeholders
Medical Device Innovation Consortium and Michael J. Fox Foundation	Developed and tested a method for incorporating PPI to set significance levels in clinical trial design for Parkinson's disease[52]
Medical Device Innovation Consortium	Examines how sponsors can use PPI to better understand tolerability of uncertainty and how patients weigh the benefits and risks associated with potential heart failure treatments[53]

[50] "Implanted Brain-Computer Interface (BCI) Devices for Patients with Paralysis or Amputation – Non-clinical Testing and Clinical Considerations," FDA https://www.fda.gov/regulatory-information/search-fda-guidance-documents/implanted-brain-computer-interface-bci-devices-patients-paralysis-or-amputation-non-clinical-testing – accessed 2/16/2021

[51] "Medical Device Development Tools," FDA https://www.fda.gov/medical-devices/science-and-research-medical-devices/medical-device-development-tools-mddt – accessed 9/24/2021

[52] "A novel method for incorporation of PCOR in clinical trial design," MDIC https://mdic.org/project/patient-centered-outcomes-research/ – accessed 9/20/2021

[53] "Heart Failure Study," MDIC https://mdic.org/project/heart-failure-study/ – accessed 9/20/2021

4.9.1.2 PROVIDE INTERNAL AND EXTERNAL CONSULTATIONS

The PSE program has liaisons in the OPEQ Immediate Office and each of the OHTs to help advance patient science, fill knowledge gaps, and build PPI, PRO, and other COA capacity within review teams (e.g., clinical reviewers and statisticians). PSE staff provide subject matter expertise to support review through internal consultations on a variety of patient science-related matters, including proper use and review of COAs in regulatory submissions. Since CDRH established the PSE program in 2018, the number of requests for internal consults has grown each year, reaching 84 requests in 2020, as shown in Figure 4-27. Figure 4-28 shows the distribution of consults, including both internal and external (i.e., Q-Submissions), by premarket submission type. Q-Submissions, which provide early consultation to industry, account for approximately half of the total number of consults. Q-Submissions topics involving PSE may include whether a COA is fit-for-purpose (i.e., well-defined, reliable, responsive, and appropriate for the context of use [COU]). Through this process, PSE staff confirm that new COAs accurately measure the intended concept and are easily interpretable and administrable to patients.

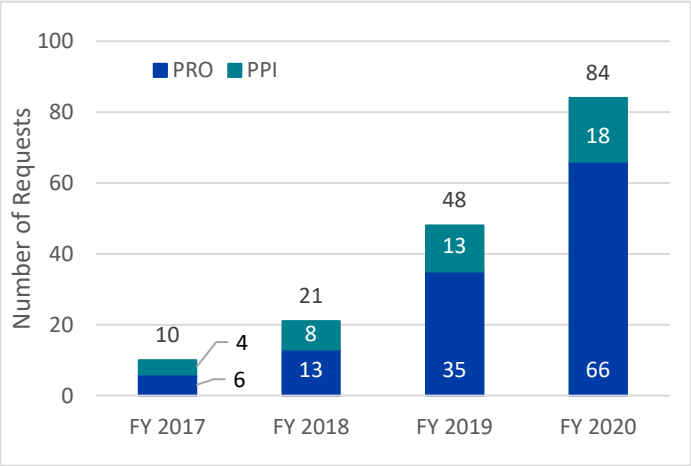


Figure 4-27. Number of Internal Consults on PROs and PPIs

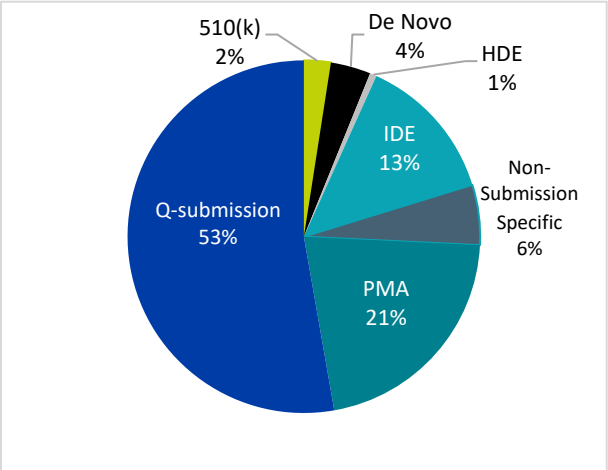


Figure 4-28. PSE Participation in Internal and External Consultations by Submission Type

4.9.2 HOLD PUBLIC MEETINGS TO ADVANCE PPI, PROS, AND PATIENT ENGAGEMENT

This section describes how FDA met each of the commitments shown in Table 4-54**.** FDA met its MDUFA IV commitment to hold a public meeting to discuss approaches for incorporating PPI and PRO as evidence in device submissions, and to discuss other ways of advancing patient engagement. Table 4-55 shows the approaches FDA used for incorporating PPI and PRO as evidence in device submissions and advancing patient engagement.

Table 4-54. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• By the end of FY 2020, hold one or more public meetings to discuss the topics below and publish the findings and next steps; • Discuss approaches for incorporating PPI and PRO as evidence in device submissions, as well as other ways of advancing patient engagement; • Discuss ways to use patient input to inform clinical study design and conduct, with a goal of reducing barriers to patient participation and facilitating recruitment and retention; • Public meetings should include specific examples and case histories for PPIs and PROs to ensure clarity and understanding by workshop attendees; and • Identify priority areas where decisions are preference-sensitive and PPI data can inform regulatory decision-making, in order to advance design and conduct of patient preference studies in high impact areas. Publish the priority areas in the Federal Register for public comment following the public meeting.

Table 4-55. Public Meetings Related to Patient Science

Approaches for Incorporating PPI and PRO as Evidence in Device Submissions and Advancing Patient Engagement	
Meeting Title	**Key Topics and Discussions**
2017 FDA-CERSI Workshop: Advancing Use of Patient Preference Information (PPI) as Scientific Evidence in Medical Product Evaluation[54, 55]	• Collection and use of PPI in regulatory decision-making • Patient preference-sensitive areas (e.g., high-risk/high-benefit, low-risk/low-benefit) • Future research capacity needs • Hypothetical case examples (i.e., pediatric cancer/rare disease and neurological degenerative disease)
Medical Devices Virtual Public Meeting – Patient-Reported Outcomes (PROs) and Medical Device Evaluation: From Conception to Implementation[56]	• Incorporating patient perspectives in regulatory decision-making and medical device design • Adapting PRO instruments to different use cases • PRO examples for kidney disease, cardiovascular care, mental health, plastic surgery, orthopedics, pediatric heart failure, and LASIK • Challenges with PROs (e.g., survey fatigue, using understandable language, adapting PROs across age groups, managing patient privacy)
Virtual ISPOR-FDA Summit 2020: Using Patient Preference Information in Medical Device Regulatory Decisions: Benefit-Risk and Beyond[57]	• Case studies for use of PPI in regulatory decision-making (e.g., emphysema, home hemodialysis) • Challenges in gathering and using PPI (e.g., patient vs caregiver preference, cost, return on investment) • Opportunities for future uses and acquisition of PPI
Use of Patient Input to Inform Clinical Study Design and Conduct	
Meeting Title	**Key Topics and Discussions**
2017 PEAC Meeting[58]	• Patient involvement in clinical trial design • Patient recruitment, enrollment, and retention • Dissemination of trial results • Recommendation to focus efforts on developing a framework for engaging patient advisors in the clinical investigation process
2018 PEAC Meeting[59]	• Discuss and make recommendations on e-platforms potentially expanding the definition of scientific evidence • Address how FDA can leverage patient-driven platforms to better engage patients and promote responsible innovation • Seek additional feedback from the PEAC on the questions reflected in the 2018 discussion document[60]

FDA used these meetings to inform development of discussion documents, draft guidance, and other publications. Related to patient engagement in clinical trials, FDA released a 2018 discussion document[60] followed by draft

[54] "Advancing the Use of Patient Preference Information as Scientific Evidence in Medical Product Evaluation," FDA https://www.fda.gov/science-research/advancing-regulatory-science/advancing-use-patient-preference-information-scientific-evidence-medical-product-evaluation – accessed 1/25/2021

[55] FDA and CERSI staff published a summary review of the workshop in The Patient – Patient Centered Outcomes Research in November 2019, which discussed the value of PPI and noted challenges in conducting PPI studies. The summary review also noted potential future opportunities for collaborative efforts between stakeholders to coordinate training, outreach, and scientific exchange to advance patient science.

[56] "Medical Devices Virtual Public Meeting – Patient-Reported Outcomes (PROs) and Medical Device Evaluation: From Conception to Implementation," FDA https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/medical-devices-virtual-public-meeting-patient-reported-outcomes-pros-and-medical-device-evaluation – accessed 1/21/2021

[57] "Virtual ISPOR-FDA Summit 2020: Using Patient-Preference Information in Medical Device Regulatory Decisions: Benefit-Risk and Beyond," ISPOR https://www.ispor.org/conferences-education/conferences/past-conferences/ispor-fda-summit-2020 – accessed 7/28/2021

[58] 2017 Meeting Materials of the Patient Engagement Advisory Committee, FDA https://www.fda.gov/advisory-committees/patient-engagement-advisory-committee/2017-meeting-materials-patient-engagement-advisory-committee – accessed 1/25/2021

[59] "2018 Meeting Materials of the Patient Engagement Advisory Committee," FDA https://www.fda.gov/advisory-committees/patient-engagement-advisory-committee/2018-meeting-materials-patient-engagement-advisory-committee – accessed 1/25/2021

[60] "Patient Engagement in Medical Device Clinical Trials Discussion Document: November 15, 2018," FDA https://www.fda.gov/media/117890/download – accessed 1/21/2021

guidance.[61] The final guidance has been identified as a CDRH priority for completion, as resources permit. Additionally, FDA identified and published priority patient preference-sensitive areas in May 2019 for public comment,[62] some of which were specific to diagnostics/therapeutics, while others were specific to a disease/condition. In response to feedback from stakeholders, PSE partnered with ISPOR to co-sponsor a one-day virtual summit in September 2020.[57] The PSE program has also collaborated with various stakeholder groups on case examples for a variety of conditions and research methodologies, including:

- Wayne State University on uterine fibroids;
- Medical Device Innovation Consortium (MDIC) on heart failure;
- Harms Study Group on pediatric idiopathic scoliosis;
- Kidney Health Initiative on end-stage kidney disease;
- Baylor College of Medicine and Stanford University on chronic pain; and
- Johns Hopkins University and the American Glaucoma Society on glaucoma.

4.9.3 IMPROVE REGULATORY PREDICTABILITY AND IMPACT OF PROS

This section describes how FDA met each of the commitments shown in Table 4-56. The findings are described in the following three sections:

- 4.9.3.1 Clarify the Voluntary Nature of PROs and Leverage the Dispute Resolution Process;
- 4.9.3.2 Modify Guidance to Outline a Flexible Framework for PRO Validation Evidentiary Thresholds; and
- 4.9.3.3 Develop a Model for Bridging Studies.

Table 4-56. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)

• FDA will undertake several activities to improve the regulatory predictability and impact of PROs, including:
  ○ Clarify to device review divisions that use of PROs is voluntary and may be one potential way of demonstrating safety or effectiveness (or elements of either or both, such as in a composite endpoint). Consistent with least burdensome principles, applicants may use alternative approaches.
  ○ Modify the guidance to outline a flexible framework for PRO validation thresholds. These thresholds may vary depending on the particular regulatory use of the PRO.
  ○ Work on developing a model for "bridging studies" to make efficient use of existing validated PROs which may be improved or adapted to other subpopulations or other regulatory uses in a more streamlined and expeditious manner than creating novel PROs.
• The existing dispute resolution process should be used in the event of disagreement between the applicant and the Agency on the need for PPI or PRO.

4.9.3.1 CLARIFY THE VOLUNTARY NATURE OF PROS AND LEVERAGE THE DISPUTE RESOLUTION PROCESS

In the 2020 PRO Draft Guidance,[63] CDRH noted that the use of PRO instruments is generally voluntary but may be specifically recommended for submissions where the most effective option for capturing data is through a PRO. CDRH also addressed the voluntary nature of PROs in the report, "Value and Use of Patient-Reported Outcomes (PROs) in Assessing Effects of Medical Devices,"[64] which notes PROs are one method, but not the only method, a sponsor can use to measure an outcome of interest. In addition, CDRH trains staff on the proper use and review of COAs (including PROs) and PPI through the RCP and PSE curriculums. Training continues to evolve to address the concerns most frequently encountered by reviewers, reinforce the voluntary nature of PPI, and encourage use of LB principles. Beyond guidance, documentation, and training, PSE staff are actively working with reviewers to develop a framework for clearly

[61] "Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations, Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders," FDA https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-engagement-design-and-conduct-medical-device-clinical-investigations – accessed 1/21/2021

[62] "List of Patient Preference-Sensitive Priorities; Establishment of a Public Docket; Request for Comments," Federal Register https://www.federalregister.gov/documents/2019/05/03/2019-09051/list-of-patient-preference-sensitive-priorities-establishment-of-a-public-docket-request-for – accessed 1/21/2021

[63] "Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments for Use in Medical Device Evaluation," FDA https://www.fda.gov/regulatory-information/search-fda-guidance-documents/principles-selecting-developing-modifying-and-adapting-patient-reported-outcome-instruments-use – accessed 1/27/2021

[64] "Value and Use of Patient Reported Outcomes (PROs) in Assessing Effects of Medical Devices," FDA https://www.fda.gov/media/109626/download – accessed 1/27/2021

articulating the voluntary nature of PROs in deficiency letters and provide clear direction on when patient input may be necessary.

In the event of a disagreement between the sponsor and FDA on the need for PPI or PRO data, FDA has committed to using its dispute resolution process to resolve differences of opinion regarding scientific, clinical, and/or regulatory issues. To date, there have been no disputes involving PPI or PROs; however, OPEQ agreed to engage PSE staff if any disputes specific to patient input should any arise.

4.9.3.2 MODIFY GUIDANCE TO OUTLINE A FLEXIBLE FRAMEWORK FOR PRO VALIDATION EVIDENTIARY THRESHOLDS

FDA published multiple documents to support sponsors in selecting, modifying, and developing PRO instruments, including guidance[65,66] and publicly available resources for using COAs.[64,67] FDA's 2020 PRO Draft Guidance provides recommended best practices for developing reliable PRO instruments based on a flexible, LB approach. The draft guidance included four considerations for incorporating PRO instruments into the evaluation across the TPLC of medical devices, which include: establishing and defining concept of interest (COI); identifying the role of the PRO (e.g., primary, key secondary, or exploratory) in the clinical study protocol and statistical analysis plan; providing evidence the PRO reliably assesses the COI; and effectively communicating results in product labeling to inform decision-making. FDA also detailed three factors that sponsors should consider when selecting a PRO instrument, including whether the COI being measured is meaningful to patients, what role the PRO will serve in the clinical study protocol and statistical analysis plan, and if evidence supports its use in measuring the COI. The 2020 PRO Draft Guidance also presented best practices for the LB selection, development, modification, and adaptation of PRO instruments. These best practices include the following: measure concepts important to patients; ensure PRO instruments are understandable to patients; be clear about the role of the PRO instrument in the clinical study protocol and statistical analysis plan; leverage existing PRO instruments and validity evidence; consider alternative platforms and parallel development for generating validity evidence for PRO instruments; and collaborate with others in the pre-competitive space.

4.9.3.3 DEVELOP A MODEL FOR BRIDGING STUDIES

In 2020, FDA published draft PRO Guidance,[63] stating that modifying or adapting an existing PRO instrument may be a LB approach for a new COU rather than developing a new instrument. To use this approach, a sponsor can conduct a "bridging" study to demonstrate that the modifications still result in a reliable instrument for the new COU (e.g., different population, disease severity). FDA encourages sponsors interested in modifying or adapting an existing PRO to engage with the Agency via the Q-submission process to discuss their approach. FDA also hosted a 2020 virtual public PRO meeting,[56] which included discussions and use cases on how bridging studies could determine the applicability of existing questionnaires for a different COU. In one example, the Kansas City Cardiomyopathy Questionnaire (KCCQ), used to quantify the patients' health status of heart failure patients, was adapted for adult patients of different races and ethnicities, as well as adolescent patients.

4.9.4 CONCLUSION

FDA has met its MDUFA IV commitments for Patient Science and Engagement by developing staff expertise and capacity, holding public meetings, and improving the regulatory predictability and impact of PROs. PSE leverages expertise through a variety of activities including training, consultations, stakeholder engagement, research, and by hiring staff experienced in the design and analysis of patient preference studies. The PSE program also

[65] "Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims," FDA https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims – accessed 1/27/2021

[66] "FDA Patient-Focused Drug Development Guidance Series for Enhancing the Incorporation of the Patient's Voice in Medical Product Development and Regulatory Decision Making," FDA https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical – accessed 1/26/2021

[67] "PRO Compendium," FDA https://www.fda.gov/media/109629/download – accessed 1/21/2021

developed external partnerships to conduct research in patient preference-sensitive areas and engage with industry on the use of patient data. The PSE program has made significant progress expanding the use of patient-generated data in regulatory decision-making. The progress in this assessment area is notable given the challenges associated with advancing innovation in science and technology, particularly within the regulatory environment. Incorporating new data types and sources to enhance regulatory decision-making requires flexibility and the wherewithal to adapt while maintaining standards of safety and effectiveness.

4.10 Real-World Evidence

As currently defined by FDA, RWD are data related to patient health status and/or the delivery of health care and can come from a variety of sources (e.g., electronic health records (EHR), administrative data, data from product and disease registries, patient-generated data, device-generated data). RWE is the clinical evidence derived from analysis of RWD regarding the usage and potential benefits or risks of a medical product. Given that RWD are often collected for non-regulatory purposes but can be used to further understand the performance and benefit-risk profile of a medical device as appropriate, RWE plays an increasing role in CDRH's regulatory decision-making process.

The MDUFA IV commitments for RWE include: streamlining Medical Device Reporting (MDR) requirements; using RWD sources in place of postmarket surveillance studies (i.e., 522 studies) where possible; hiring staff with RWE expertise; and establishing the National Evaluation System for health Technology Coordinating Center (NESTcc). Additional commitments related to the functions of NESTcc and its pilot projects are the subject of a separate independent assessment.

Booz Allen found that FDA met its commitments for RWE through signing a cooperative agreement to establish the NESTcc, hiring RWE staff, streamline MDR, and developing guidance on using RWD in place of postmarket surveillance studies, as appropriate.

The assessment findings are presented in the following four sections:

- 4.10.1 Establish NESTcc;
- 4.10.2 Build RWE Expertise;
- 4.10.3 Streamline Medical Device Reporting; and
- 4.10.4 Use RWD in Place of Postmarket Surveillance Studies, as Appropriate.

4.10.1 ESTABLISH NESTCC

Table 4-57. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• The Agency will use user fee revenue to support the NEST by providing funding for NESTcc and hiring FDA staff with expertise in the use of RWE. • FDA will contract with an organization to serve as NESTcc to facilitate use of real world evidence to support premarket activities.

This section describes how FDA met each of the commitments shown in Table 4-57. In August 2016, FDA addressed its MDUFA IV commitment to establish NESTcc by signing a cooperative agreement with and providing funding to the MDIC, a public-private, nonprofit organization with the objective of advancing approaches that promote patient access to medical technologies. MDIC launched NESTcc in September 2016. NESTcc provides governance, oversees infrastructure building, promotes standards, and monitors progress of its mission by leveraging RWE to accelerate the development of new and safe health technologies. NESTcc serves a dual role in the medical device ecosystem; it provides a collaborative community for teams of diverse stakeholders (e.g., FDA, device sponsors, registries, researchers) to work together around common RWE needs and initiatives, and it offers services to organizations seeking to sponsor medical device research based on RWD.

FDA holds a seat on the NESTcc Governing Committee, which provides leadership for the NESTcc membership community and establishes subcommittees. NESTcc members include diverse stakeholder groups such as patients, clinicians, manufacturers (including one representative each from AdvaMed, MDMA, MITA, and ACLA), regulators,

health systems, and payors. FDA staff also participate on NESTcc subcommittees and provide expertise on data quality and research methods frameworks. OCEA supports collaboration and interaction regarding methods development and test case project discussions by serving as liaisons that connect test case sponsors to OHTs, so the appropriate OHT can provide regulatory feedback.

4.10.2 BUILD RWE EXPERTISE

This section describes how FDA is on track to meet the MDUFA IV hiring commitment shown in Table 4-58. Under MDUFA IV, 10 RWE FTE were allocated for FY 2018 through FY 2021: five in 2018, one in 2019, one in 2020 and three in 2021. As of May 2021, CDRH added five FTEs within OPEQ.

Table 4-58. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• The Agency will use user fee revenue to support NEST by providing funding for the NESTcc and hiring FDA staff with expertise in the use of RWE.

The specialized skills and expertise of RWE staff provide leadership, support policy development, and further promote the growth of RWD and collaboration between external stakeholders (e.g., researchers, registries, industry). To support these FTEs and further strengthen FDA's review capacity, CDRH offers multiple training opportunities as shown in Table 4-59.

Table 4-59. RWE Training Opportunities

Training Opportunities	Description
Reviewer Certification Program	Condensed, curriculum-based training that new reviewers complete within their first 60 days of employment. Example RWE topics include RWE review practices, case studies, quiz questions and more
Internal Webinars, Workshops, Presentations	Opportunities to share challenging issues and highlight opportunities related to the use of RWE across the TPLC with senior management and staff
CDRH Learn	Publicly available learning platform. Example RWE topics include guidance information and MDR
Example RWE submissions	Identified examples where RWE has been used and case studies on its use to enhance the expertise of review staff and increase organizational knowledge within CDRH and the Agency

4.10.3 STREAMLINE MEDICAL DEVICE REPORTING

This section describes how FDA met the commitment shown in Table 4-60 by establishing the Voluntary Malfunction Summary Reporting (VMSR) program. FDA announced a proposed program in December 2017, [68] followed by a notification in 2018[69] granting an alternative for certain device malfunction MDRs and describing the overarching principles for the VMSR program. The VMSR allows sponsors to submit a single summary report on a quarterly basis, instead of multiple reports on an ongoing basis. This reduces the volume of reports that manufacturers need to submit, provides FDA with a more efficient way to understand malfunction issues, and facilitates greater understanding and identification of malfunction trends by the public. The VMSR program replaced the Alternative Summary Reporting program and permits eligible manufacturers to report device malfunctions in summary format on a quarterly basis for certain, well-known, and well-established risks associated with eligible Class I and II device product codes. Under VMSR, manufacturers submit a malfunction summary report and narrative for each unique combination of brand name, device model, and product code. The summary report and narrative, available in the Manufacturer and User Facility Device Experience (MAUDE) database, identifies the total number of reportable malfunctions. While summary malfunction reports submitted under the program may change the format in which the information is

Table 4-60. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• The Agency will establish criteria for streamlining MDR requirements.

[68] "Center for Devices and Radiological Health; Medical Devices and Combination Products; Voluntary Malfunction Summary Reporting Program for Manufacturers," Federal Register https://www.federalregister.gov/documents/2017/12/26/2017-27650/center-for-devices-and-radiological-health-medical-devices-and-combination-products-voluntary – accessed 9/19/2021

[69] "Medical Devices and Device-Led Combination Products; Voluntary Malfunction Summary Reporting Program for Manufacturers," Federal Register https://www.federalregister.gov/documents/2018/08/17/2018-17770/medical-devices-and-device-led-combination-products-voluntary-malfunction-summary-reporting-program – accessed 9/19/2021

presented (i.e., summary report versus individual report), the content of information provided should not be affected.

CDRH lists the eligibility status of a given device product code for the VMSR program in the publicly available Product Classification Database, which includes a list of all medical devices and their associated classifications, product codes, FDA Premarket Review organizations, and other regulatory information.[70] CDRH also established an email address where manufacturers can request FDA to consider a device code's eligibility for the VMSR program. The VMSR program requires individual reporting for malfunctions that represent a variety of public health issues such as reusable devices with a high risk of infection, malfunction events potentially attributed to complex failure modes, devices with ongoing safety signals or other safety-related investigations, or for manufacturers with a history of failing to comply with reporting requirements.

4.10.4 USE RWD IN PLACE OF POSTMARKET SURVEILLANCE STUDIES, AS APPROPRIATE

This section describes how FDA met the commitment shown in Table 4-61 through publication of updated guidance. FDA has the authority under Section 522 of the FD&C Act to require manufacturers to conduct postmarket surveillance studies (i.e., 522 studies) on certain Class II and III devices. In updated draft Guidance on Postmarket Surveillance Under Section 522,[71] released May 2021, FDA noted it may be possible to meet a 522 order requirement using RWD, given increased access to RWD and improvements to methods of analysis. Where appropriate, a sponsor may conduct prospective or retrospective analysis of data from real-world sources, such as device registries and EHRs to meet a 522 order. In addition, FDA may decide not to issue a 522 order where RWD of sufficient relevance and reliability already exist and a timely prospective analysis can be performed by the device manufacturer.

Table 4-61. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• FDA will not require postmarket surveillance studies (i.e., 522 Studies) for devices for which registries and/or other RWD sources exist if FDA has access to the information/data in the RWD source and has determined that the information/data in the RWD source is sufficient to take the place of a postmarket surveillance study.

FDA also released RWE guidance in August 2017 that provides additional information on when a retrospective analysis of data may meet a Section 522 order.[72] The guidance outlines the criteria FDA uses to assess whether RWD is fit-for-purpose including data quality, completeness, and relevance. In addition to the guidances, FDA includes pre-522 screening questions in the Postmarket Surveillance Section 522 WI to prompt initiating reviewers to identify existing RWD sources and their adequacy to address the identified public health concerns. Booz Allen was unable to determine how frequently FDA permits the use of RWD in lieu of 522 studies or the influence of either Guidance on these submissions due to limitations in CDRH's ability to systematically tag RWE-containing submissions.

4.10.5 CONCLUSION

FDA met its commitments for RWE through signing a cooperative agreement to establish NESTcc, streamlining medical device reporting, and providing guidance on using RWD in place of postmarket surveillance studies, as appropriate. FDA is on track to meet its hiring commitments, filling 71% (i.e., five of seven) of positions allocated through FY 2020.

[70] "Product Classification Database," FDA https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm – accessed 4/28/2021

[71] "Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act: Draft Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/149346/download – accessed 6/1/2021

[72] "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/99447/download – accessed 4/28/2021

4.11 Special 510(k) Conversions

FDA introduced the Special 510(k) program in 1998 with the goal of creating an efficient review process for certain changes subject to 510(k) review requirements, providing an optional pathway for sponsors to submit certain well-defined modifications to their own legally marketed predicate device. By leveraging design control procedures—practices used during device design to demonstrate that the product conforms to users' needs and intended uses—FDA can reduce the amount of information that sponsors must submit to make a determination of substantial equivalence without compromising statutory requirements. As a result, FDA can review Special 510(k)s more quickly than Traditional 510(k)s, with FDA intending to process the file within 30 days of receipt compared to 90 days for Traditional 510(k) submissions. Only certain types of device modifications are eligible for the Special 510(k) pathway. If sponsors submit an ineligible change, FDA will, following management concurrence, convert the file to a Traditional 510(k). The MDUFA IV commitment focuses on an independent analysis of conversions from Special 510(k)s to Traditional 510(k)s. The decision to convert a submission may extend the review process given the differences in review timelines and data package requirements between Special and Traditional 510(k)s.

FDA met its MDUFA IV commitment for Special 510(k) conversions by engaging Booz Allen to evaluate implementation of process improvements. This assessment of Special 510(k) conversions examines the conversion rate and common themes of conversions in the context of the 510(k) program. The assessment findings are presented in the section below:

- 4.11.1 Assess the Conversion of Special 510(k)s to Traditional 510(k)s.

4.11.1 ASSESS THE CONVERSION OF SPECIAL 510(K)S TO TRADITIONAL 510(K)S

Per the MDUFA IV Commitment Letter shown in Table 4-62, Booz Allen conducted an independent assessment of conversions from Special 510(k) to Traditional 510(k). The findings are described in the following two sections:

- 4.11.1.1 Expanded Special 510(k) Eligibility; and
- 4.11.1.2 Implemented Updated Eligibility Criteria.

Table 4-62. MDUFA IV Commitment Letter (Excerpt)

MDUFA IV Commitment Letter Addressed in This Section (Excerpt)
• Analyze conversions of Special 510(k)s to Traditional 510(k)s.

4.11.1.1 EXPANDED SPECIAL 510(K) ELIGIBILITY

Since the authorization of MUDFA IV, FDA has completed a series of activities intended to clarify Special 510(k) program requirements and increase the number of eligible device changes. Figure 4-29 shows a timeline of these efforts, categorized as outreach, resources, or guidance efforts. A CDRH-led internal audit of the Special 510(k) Program, required by the end of FY 2022, has not yet occurred.

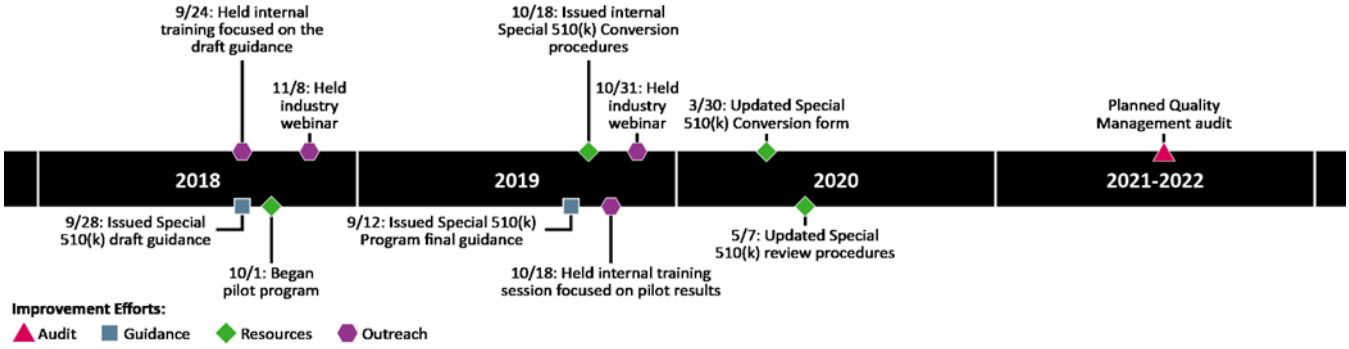


Figure 4-29. Key Special 510(k) Program Activities

Updated Guidance and Eligibility

The original 1998 Guidance limited Special 510(k) eligibility to 510(k)s describing modifications to a manufacturer's own legally marketed predicate device that did not have an impact on the device's intended use nor its fundamental scientific technology, defined as changes affecting the device's operating principle(s) or mechanism of action.[73] This meant that FDA frequently converted Special 510(k)s that included modifications to the design, IFU, or associated labeling changes.

FDA updated the Special 510(k) eligibility factors with new Guidance in 2019 (hereinafter referred to as the 2019 Special 510(k) Guidance),[74] to clarify the criteria and expand eligibility (i.e., increase the number of submissions that are eligible) for the Special 510(k) program. The previous eligibility criteria focused on the type of device modification (i.e., a change in fundamental technology or IFU), while the updated criteria shifted the focus to the methods and data used to evaluate the modification (i.e., lack of a well-established method), as shown in Figure 4-30. First, manufacturers determine whether they need performance data to evaluate the modification based on their internal design control procedures. If performance data are not needed, sponsors may submit these modifications as a Special 510(k) with rationale describing their reasoning. If performance data are needed, sponsors should use "well-established methods" to evaluate the change, as well as provide data in a summary or risk-analysis format (e.g., a table describing any risks identified, verification and validation activities, and summary-level results). The Guidance provides examples of well-established methods, allowing for some deviation. If a sponsor is uncertain about the significance of a potential deviation from a well-established method, they can use the Pre-Submission process to obtain feedback.

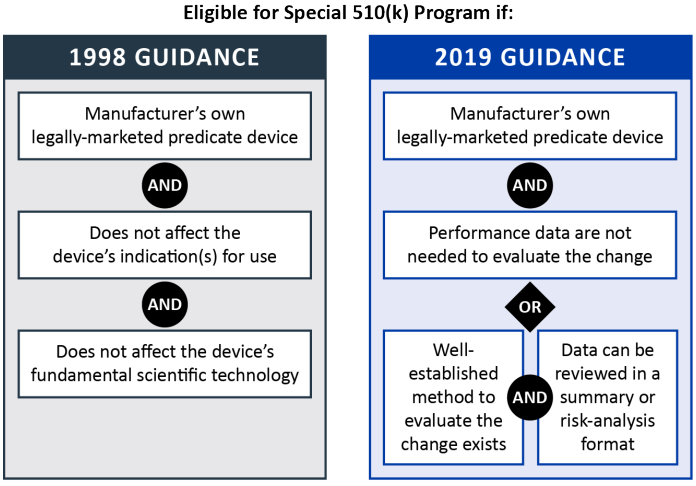


Figure 4-30. Special 510(k) Guidance Comparison

Updated Reasons for Conversion

The decision to convert a submission received as a Special 510(k) to a Traditional 510(k) often occurs early in the review process during Acceptance Review, which serves as a check that the file is eligible for the Special 510(k) program and that it is administratively complete (i.e., contains the information needed to undergo a substantive review). The update in eligibility criteria was accompanied by an update to the RTA checklist[75] (used during Acceptance Review), including the reasons for conversion used by FDA during review of Special 510(k) submissions. If a reviewer believes that a file is ineligible for the Special 510(k) program, it is documented in the Conversion Form, which contains a standardized list of conversion reasons and comment boxes to provide an explanation or additional details. FDA revised the possible reasons for conversion after the 2019 Special 510(k) Guidance update to reflect the updated eligibility criteria. The update introduced one new conversion reason, "lack of a well-established method" and removed two old reasons, "change in indication for use" and "change in fundamental scientific technology."

FDA also revised its internal procedures to mirror the eligibility factors in the 2019 Special 510(k) Guidance, outlining the Special 510(k) review process and providing instructions for reviewing performance data (with examples). They also defined specific staff roles during the conversion process and provided recommendations

[73] "The New 510(k) Paradigm: Alternative Approaches to Demonstrating Substantial Equivalence in Premarket Notifications," FDA https://qualomics.com/wp-content/uploads/2015/08/FDA-Guidance-The-New-510k-Paradigm.pdf – accessed 5/26/2021
[74] "The Special 510(k) Program: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/116418/download – accessed 5/26/2021
[75] "Refuse to Accept Policy for 510(k)s: Guidance for Industry and Food and Drug Administration Staff," FDA https://www.fda.gov/media/83888/download – accessed 5/26/2021

for communicating the conversion reason with sponsors. When explaining the conversion reason, FDA recommends that reviewers provide an explanation for why the submission failed to meet the eligibility criteria. For example, if there is no well-established method, FDA should explain why (e.g., developed a new protocol) instead of stating only that a full review of data is necessary.

4.11.1.2 IMPLEMENTED UPDATED ELIGIBILITY CRITERIA

Conducted Stakeholder Outreach and Pilot Program

To support implementation of the new eligibility criteria, FDA held an internal staff training session in September 2018 to explain the new policies outlined in the draft Special 510(k) Guidance. CDRH also updated its webpage with information regarding the proposed eligibility for the draft Special 510(k) program, the content and format of a Special 510(k), and how to submit a Special 510(k), providing links to the new draft Special 510(k) Guidance and other useful resources.

On October 1, 2018, FDA launched a pilot program to evaluate the impact of the updated eligibility criteria and conversion reasons on 510(k) submission review efficiency. FDA introduced and communicated the pilot program to industry through a variety of outreach events, including publishing details on the pilot website and holding a public webinar to explain the updated eligibility criteria. As part of the roll-out, FDA automatically enrolled all Special 510(k)s submitted between October 1, 2018 and July 1, 2019 in the pilot. To assess the effects of the updates, FDA tracked the number of Special 510(k)s received, the average TTD for the cleared files, the average FDA Day on which conversion occurred (if applicable), and the conversion rate of the submissions received.

FDA presented the results of the pilot compared to the same nine-month period from the previous year during an October 2019 webinar,[76] also shown in Table 4-63, suggesting progress, particularly with a decrease in the conversion rate from 34% to 25%. While the average number of FDA days to conversion remained similar, the slight reduction (16 days to 15 days) is notable because day 15 marks the end of Acceptance Review when the files proceed to substantive review. For cleared files, the average FDA Day reviewers placed a file on hold remained about the same (27 vs. 28 days), indicating that the updated eligibility criteria did not prevent FDA from reaching its 30-day goal. The average TTD for cleared files decreased from 49 to 43 days, suggesting that the changes to the program may facilitate a more efficient review.

Table 4-63. Pre-Pilot and Pilot Comparison of Key Special 510(k) Metrics

Metric*	Pre-Pilot (10/2017 – 7/2018)	Pilot (10/2018 – 7/2019)
Total number of Special 510(k)s received	464	476
Conversion Rate of Special 510(k)s	34% (158/464)	25% (119/476)
Average FDA days to Conversion	16 days	15 days
Average FDA Day cleared file placed on hold	Day 27	Day 28
Average TTD for cleared file	49 days	43 days

*Data from "Special 510(k) Program" presentation slides on October 31, 2019[76]

Reasons for Conversion Shifted with Updated Eligibility Criteria

The reasons for conversion of Special 510(k)s to Traditional 510(k)s were also analyzed to understand the impact of the updates to the eligibility criteria. FDA analyzed the reasons for conversion during the pre-pilot and pilot periods, while Booz Allen conducted an independent analysis (using the Conversion Forms) of all conversions from FY 2020. The Booz Allen analysis encompassed 139 conversions out of 533 (26%) total Special 510(k) submissions received, consistent with the 25% conversion rate during the pilot.

As anticipated, the distribution of the eligibility factors shifted between the pre-pilot and pilot periods because of the new eligibility criteria and reasons for conversion, with the distribution remaining relatively consistent between the pilot and post-pilot periods, shown in Table 4-64. The leading reason for conversion during the pre-pilot period was "change in fundamental scientific technology" (61%); however, during the pilot and post-pilot

[76] "Webinar - The Special 510(k) Program: Final Guidance," FDA https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/webinar-special-510k-program-final-guidance-10312019-10312019 – accessed 5/26/2021

periods, the leading reason was "lack of a well-established method," at 59% and 54%, respectively. The second most common reason for conversion was "can't be placed into a summary or risk-analysis format," at 23% during the pilot and 32% during the post-pilot period.

Table 4-64. Comparison of Reasons for Conversion

Reason for Conversion	Pre-Pilot* (FDA Analysis)	Pilot* (FDA Analysis)	Post-Pilot (Booz Allen Analysis)
Not the manufacturer's own device	1% (2/158)	5% (6/119)	4% (6/139)
Lack of well-established method	N/A	59% (70/119)	54% (75/139)
Can't be placed into a summary or risk-analysis format	13% (21/158)	23% (27/119)	32% (45/139)
Change in IFU	21% (33/158)	N/A	N/A
Change in fundamental scientific technology	61% (96/158)	N/A	N/A
Other**	4% (6/158)	13% (16/119)	9% (13/139)

*Data from "Special 510(k) Program" presentation slides on October 31, 2019[76]

**Reflects conversions for other reasons, such as those outlined in the "Additional Considerations" section of the 2019 Guidance (e.g., greater than three scientific disciplines, use of clinical or animal data).

Although the Conversion Form only allows reviewers to specify one of the four conversion reasons, there are comment boxes for additional explanations and details from reviewers. Booz Allen's examination of reviewer comments on the Conversion Forms revealed that many converted submissions contained multiple grounds for conversion. For example, "lack of well-established method" and "can't be placed in summary or risk-analysis format" were present in the same submissions 30% of the time. Similarly, 41% (57/139) of converted submissions met grounds for conversion beyond the four reasons listed in the Conversion Form, based on the circumstances outlined in the Additional Considerations section of the 2019 Special 510(k) Guidance (e.g., included or would require review of clinical, animal, or cadaver data).

Consistency of Communication

Booz Allen also conducted an analysis to examine how FDA communicated conversion decisions to sponsors and adherence to its internal procedures. Booz Allen reviewed the conversion communication emails for 25 of the 139 conversions from FY 2020, randomly selected from those available in CDRH's IT system. All 25 conversion decision emails followed a consistent structure and aligned with FDA's procedures to convey the specific, necessary information to the sponsor. Each email stated that FDA was converting the submission and provided the reason and explanation for the conversion.

4.11.2 CONCLUSION

FDA introduced updated eligibility factors intended to expand the number of 510(k) submissions eligible for the Special 510(k) Program, updating its internal and external documentation to reflect these updates to eligibility, and conducting outreach to sponsors. An analysis of Special 510(k) conversions in FY 2020 shows a similar distribution of conversion reasons as the pilot program in FY 2019, with "lack of a well-established method" as the most cited reason for conversion. The decreased conversion rates since 2018, coupled with decreased TTD during the pilot, suggest that updates have made some improvements to the efficiency of Special 510(k) review.

5. ADDITIONAL OPPORTUNITIES

Booz Allen identified one recommendation for CDRH to fulfill the remainder of its commitments in the assessment areas outlined in the MDUFA IV Commitment Letter. We also discuss several opportunities identified during the assessment for CDRH to build on recent progress and successes to further strengthen the premarket review process; however, Booz Allen did not identify any practices that rose to the level of a best practice appropriate for broader application or sharing across offices.

5.1 Recommendations

To fulfill FDA's obligations in the specified assessment areas of the MDUFA IV Commitment Letter, one action is pending under Digital Health. In this case, Booz Allen recommends publishing the outstanding draft guidance to fully satisfy the commitment. Table 5-1 below describes the key findings and recommendation.

Table 5-1. Key Findings and Recommendations

Assessment Area	Commitment Excerpt	Key Finding	Recommendation
Digital Health	Revise existing and/or publish new relevant guidance documents, including publishing a draft revised version of the "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" (issued in 2005) by the end of FY 2019, and within 12 months of the close of the comment period, publish the final revised version. The Agency will incorporate applicable concepts from its Guidance for "Off-The-Shelf Software Used in Medical Devices."	• Draft guidance, "Content of Premarket Submissions for Software Contained in a Medical Device" is pending • Publication is prioritized	Publish draft guidance

5.2 Additional Considerations

Continuous improvement and growth of CDRH's premarket review program is priority for both FDA and Industry. Building on the successes of MDUFA IV Commitment Letter, Booz Allen identified opportunities that have the potential to support growth. These additional considerations, described in Table 5-2 below, may support FDA as each assessment areas continues to mature.

Table 5-2. Additional Considerations

Assessment Area	Key Observation	Additional Considerations	Intended Impact
Deficiencies	OPEQ/ORP conducted a multi-year, multi-pronged continuous improvement effort around Deficiencies. There appears to be differing perceptions of the criteria/threshold for the statement of basis and how best to communicate them between CDRH and industry; specifically, weighing of benefit-risk and uncertainty. In addition, the QM audit shows that the statement of basis is present in 50% of the deficiencies sampled, indicating challenges interpreting and/or applying the existing criteria.	To inform further improvement efforts, CDRH could explore additional engagement with industry to align expectations for the statement of basis and identify best practices.	• Clarify and/or simplify deficiencies criteria • Increase alignment on the statement of basis • Improve communication of deficiencies • Inform reviewer training, audits, and other improvement efforts

*There may be resource implications associated with this activity.

Assessment Area	Key Observation	Additional Considerations	Intended Impact
Pre-Submission Program*	The Pre-Submissions program continued to grow (i.e., increasing volume each year). If this trend continues, it will be difficult to sustain current performance.	CDRH could explore options for sustainable growth, either through identification of additional resources or strategies for controlled growth, which may include enhancing the quality of Pre-Submissions to reduce pre-work and reducing the number of Pre-Submissions (i.e., creating informal communication mechanisms, although these are resource-intensive).	• Increase quality of Pre-Submissions • Enhance efficiency and sustainability of the Pre-Submissions process
Infrastructure and FTE Allocations	Improvements have been made to tracking of MDUFA positions (i.e., implementation of the PBM Tracker) and allocation of FTEs (i.e., implementation of Insight Time Reporting [ITR]), and FDA has begun to communicate available data to industry stakeholders.	As PBM and ITR mature and reliable data become available (e.g., appropriate use of codes) allowing for accurate analysis, CDRH could explore providing targeted updates to industry stakeholders specifically regarding the number of external hires for MDUFA positions, rates of attrition in these positions, and time spent on MDUFA-related activities.	• Inform workforce planning • Enhance retention efforts • Increase transparency
Quality Management Program*	CDRH implemented all core components of an ISO 9001:2015 compliant QMS at the level of the OCD, serving all of CDRH. QMOE is working with Offices that are currently ISO-conforming to facilitate their progression to ISO-compliance and full integration into the QMS.	CDRH could explore expanding current QMS capabilities and infrastructure to increase continuity and connectivity across CDRH. By enabling enhanced monitoring through additional premarket review and MDUFA performance goal data, the capabilities and infrastructure could better inform updates to training, reduce reliance on employee reporting of risks and challenges, facilitate incorporation of broader informational inputs, and introduce automatic triggers to facilitate preventive action.	• Increase the responsiveness of the QMS • Greater integration and coordination between Offices to promote quality • Increase the range of informational inputs • Enhance ability to quantify progress using additional indicators of functional outcomes at the Office-level beyond compliance
Training and Alignment*	Kirkpatrick Level 3 and 4 evaluations are starting to provide insight into the effectiveness of certain training courses, although data collection is limited.	CDRH could explore further refinements to Kirkpatrick Level 3 and 4 evaluations to include more frequent assessment intervals, additional data sources (e.g., external stakeholders, QMS data), indicators of impact at the program/organizational level, and integration with the QMS (e.g., indicators audit program for validation and verification of survey data).	• Enhance understanding of training outcomes in terms of individual behavioral changes and program/organizational impacts • Optimize training effort • Greater integration of Training and the QMS, focusing on functional outcomes at the organizational level beyond compliance
Premarket Review Efficiencies*	CDRH has incorporated premarket review process improvements to encourage interactive review and add touchpoints between reviewers and sponsors both during the review and while the file is on hold. Current IT capabilities do not allow for straightforward capture and tracking of these activities.	CDRH could explore enhancing infrastructure and connectivity of the submission and review systems to facilitate tracking of premarket communications (e.g., interactive review, informal communications).	• Improve tracking of premarket communications (e.g., use of informal and interactive mechanisms), identify potential trends, and further improve the quality of the customer experience • Enhance ability to assess effectiveness of communication process improvements

APPENDIX A. MDUFA IV COMMITMENT LETTER REQUIREMENTS BY REPORT SECTION

MDUFA IV Commitment Letter Requirements	Report Section
Premarket Review Efficiencies	**4.1 Premarket Review Efficiencies**
Evaluate FDA's premarket review program to identify efficiencies that should be realized as a result of the process improvements and investments under MDUFA III and IV.	4.1.1 Impact of Review Tools and Process Improvements on Consistency 4.1.2 Effect of Review Process Changes on Efficiency and Communication 4.1.3 Implementation of a Total Product Life Cycle (TPLC) Approach for Holistic Premarket Review
Develop electronic submission templates that will serve as guided submission preparation tools for industry to improve submission consistency and enhance efficiency in the review process.	4.1.1 Impact of Review Tools and Process Improvements on Consistency
By FY 2020, the Agency will issue a draft guidance document on the use of the electronic submission templates. FDA will provide an opportunity for public comment on the guidance. No later than 12 months after the close of the public comment period, the Agency will issue a final guidance. FDA will implement the guidance once final. In addition, the Agency will update the Guidance "eCopy Program for Medical Device Submissions" to reflect the respective changes to the technical standards and specifications.	4.1.1 Impact of Review Tools and Process Improvements on Consistency
Continue to incorporate an interactive review process to provide for, and encourage, informal communication between FDA and applicants to facilitate timely completion of the review process based on accurate and complete information.	4.1.2 Effect of Review Process Changes on Efficiency and Communication
CDRH will explore transitioning to a similar TPLC model building in the other device areas based on the lessons learned from its experience with OIR and taking into account the Center's mission, vision, strategic priorities, and development of a patient-centric benefit-risk framework for regulatory and non-regulatory decision-making across the TPLC. Because an essential element for the success of the Center's benefit-risk decision-making framework and approach to device regulation (particularly emerging and innovative technologies) is the incorporation of the clinical context and the impact of a decision on patient health and quality of life, CDRH will take steps to increase and enhance the integration of its clinicians into its TPLC activities, amongst themselves, and with the Center's scientists and engineers. Building on the success of considering and incorporating additional expertise and viewpoints into our decision-making, such as through the use of the Network of Experts and the leveraging of patient perspectives, CDRH will also explore ways in which to better learn from and leverage the expertise of clinicians in other parts of the agency and outside of the agency to inform its decision-making, enhance consistency, and assure a more holistic clinical perspective. Clinicians involved in device-related activities will have appropriate training on and make recommendations consistent with applicable device statutory provisions, regulations, guidances, and this Commitment Letter. In addition, CDRH will provide managerial oversight of clinician recommendations and device submission decisions, except for those devices subject to CBER oversight.	4.1.3 Implementation of a Total Product Life Cycle (TPLC) Approach for Holistic Premarket Review
Infrastructure and FTE Allocations	**4.2 Infrastructure and FTE Allocations**
The Agency will also apply user fee revenues to enhance and supplement scientific review capacity by hiring device application reviewers as well as leveraging external experts needed to assist with the review of device applications. To ensure such additional positions are filled by qualified experts, the Agency will apply user fee revenues to recruitment and hiring.	4.2.1 MDUFA III and IV Hiring Targets and Strategies to Enhance Review Capacity
CDRH intends to enter into an IAA with OPM to provide supplemental recruitment and staffing support throughout MDUFA IV to augment existing FDA Human Resources services.	4.2.1 MDUFA III and IV Hiring Targets and Strategies to Enhance Review Capacity

MDUFA IV Commitment Letter Requirements	Report Section
The Agency will apply user fee revenues to retain high-performing supervisors in the premarket review program.	4.2.2 Reduce Supervisory Ratio and Retain High-Performing Supervisors
The Agency will apply user fee revenues to reduce the ratio of review staff to front line supervisors in the premarket review program to improve consistency.	4.2.2 Reduce Supervisory Ratio and Retain High-Performing Supervisors
Training and Alignment	**4.3 Training and Alignment**
FDA will continue to improve training for new and existing reviewers under this agreement.	4.3.1 Improve Training for New and Existing Premarket Reviewers
FDA training efforts will be closely coordinated with the Quality Management Program to provide more targeted and personalized training to staff.	4.3.1 Improve Training for New and Existing Premarket Reviewers
FDA will achieve Kirkpatrick Level 3 for curriculum-based premarket training through an assessment of work performance behavior change by the end of FY 2020.	4.3.2 Assess Impact of Curriculum-based Premarket Training Using the Kirkpatrick Framework
FDA will evaluate the effectiveness of the impact of curriculum-based premarket training activities on relevant premarket program metrics and goals (Kirkpatrick Level 4) by the end of FY 2020.	4.3.2 Assess Impact of Curriculum-based Premarket Training Using the Kirkpatrick Framework
Quality Management Program	**4.4 Quality Management Program**
The Agency will establish a dedicated QM Unit that reports directly to the CDRH Director or Deputy Director and establish a quality management Framework for the premarket submission process in CDRH.	4.4.1 Establish a Quality Management Program and Framework
The Framework will include infrastructure, senior management responsibility, resource management, lifecycle management, and quality management system evaluation.	4.4.1 Establish a Quality Management Program and Framework
At least once per year, the Agency will discuss with industry the specific areas it intends to incorporate in its ongoing audit plan.	4.4.2 Build an Audit Program
FDA will identify, with industry input, areas to audit, which will include the effectiveness of CDRH's CAPA process.	4.4.2 Build an Audit Program
As part of these ongoing audits, high-performing premarket review processes utilized in one division will be identified and shared accordingly with other divisions to improve efficiencies and effectiveness.	4.4.2 Build an Audit Program
At a minimum, FDA audits in the following areas will be completed by the end of FY 2020: Deficiency Letters and Pre-Submissions. Additional audits in the following areas will be completed by the end of FY 2022: Submission Issue Meetings, Interactive Review, Withdrawals, Special 510(k) Conversions.	4.4.2 Build an Audit Program
CDRH is also required to expand the scope of its annual audits as it implements and builds up its auditing capability.	4.4.2 Build an Audit Program
Deficiencies	**4.5 Deficiencies**
By October 1, 2017, the Agency will publish a level 2 update to the final guidance "Suggested Format for Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions of FDAMA; Final Guidance for Industry and FDA Staff" to reflect the following: • All deficiency letters will include a statement of the basis for the deficiencies (e.g., a specific reference to applicable section of a rule, final guidance, recognized standard unless the entire or most of document is applicable). • In the instance when the deficiency cannot be traced in the manner above and relates to a scientific or regulatory issue pertinent to the determination, FDA will cite the specific scientific issue and the information to support its position. All deficiency letters will undergo supervisory review prior to issuance to ensure the deficiencies cited are relevant to a marketing authorization decision (e.g., 510(k) clearance, PMA approval, and de novo classification).	4.5.1 Phase 1 Improvements: Publish and Implement Updated Deficiency Guidance
Any additional best practices identified by quality audits and/or the Independent Assessment will be incorporated in updates to the guidance, as appropriate.	4.5.3 Implement Additional Improvements to Address Audit Findings
FDA will train staff and managers on this process improvement and the updated guidance.	4.5.1 Phase 1 Improvements: Publish and Implement Updated Deficiency Guidance
FDA will complete an audit of Deficiency Letters by the end of FY 2020 (i.e., before 10/01/2020).	4.5.2 Audit Deficiency Letters to Assess Impact of Phase 1 Improvements
Independent contractor will assess "proportion of deficiencies in which FDA references the basis for the deficiency determination", starting no earlier than 10/01/2020.	4.5.4 Assess Impact of FDA's Improvement Efforts

MDUFA IV Commitment Letter Requirements	Report Section
FDA will incorporate additional best practices identified by quality audits and/or the Independent Assessment in updates to the guidance, as appropriate.	4.5.5 Update Deficiency Guidance with Best Practices
Pre-Submission Program	**4.6 Pre-Submission Program**
By October 1, 2018, the Agency will update the Guidance on "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff" to include: • Additional information to assist applicants in determining the need for a Pre-Submission • An enhanced Pre-Submission acceptance checklist • Examples of frequently asked Pre-Submission questions that lend themselves to productive Pre-Submission interactions • Edits to reflect the revised process outlined above FDA will provide an opportunity for the public to comment on the updated guidance. No later than 12 months after the close of the public comment period, the Agency will issue a final guidance. FDA will implement this guidance once final.	4.6.1 Appropriate Use of Pre-Submissions
Assess whether (a) CDRH is providing guidance specific to the questions being asked; (b) CDRH is using Pre-Submissions appropriately; and (c) CDRH and Industry are adhering to the procedural aspects as set forth in this agreement).	4.6.1 Appropriate Use of Pre-Submissions
Assess whether (a) CDRH is providing guidance specific to the questions being asked; (b) CDRH is using Pre-Submissions appropriately; and (c) CDRH and Industry are adhering to the procedural aspects as set forth in this agreement).	4.6.2 Responsiveness to Pre-Submission Questions
Assess whether CDRH and Industry are adhering to the procedural aspects as set forth in this agreement: • Within 15 calendar days of receipt of a Pre-Submission, FDA will communicate with the applicant regarding whether the application has been accepted and, if applicable, regarding scheduling of the meeting or teleconference • FDA intends to reach agreement with the applicant regarding a meeting date within 30 days from receipt of accepted submission • For all requests for meetings or teleconferences that do not have such a meeting or teleconference scheduled by 30 days from receipt of an accepted submission, an FDA manager will contact the applicant to resolve scheduling issues by the 40th day • FDA will provide written feedback that addresses the issues raised in the pre-submission request within 70 calendar days of receipt date or five calendar days prior to a scheduled meeting, whichever comes sooner, for at least 1,530 Pre-Submissions received in FY 2018, at least 1,645 Pre-Submissions received in FY 2019, at least 1,765 Pre-Submissions received in FY 2020, at least 1,880 Pre-Submissions received in FY 2021, and at least 1,950 Pre-Submissions received in FY 2022 • Applicants will be responsible for developing draft minutes for a Pre-Submission meeting or teleconference, and provide the draft minutes to FDA within 15 calendar days of the meeting.	4.6.3 Adherence to MDUFA IV Procedures
Third Party Review Program	**4.7 Third Party Review Program**
Strengthen the process for accreditation of Third Parties. • Provide training for Third Parties seeking accreditation by FDA. This training shall include the opportunity for Third Parties to have access to redacted review memos and other information as appropriate. • When FDA's expectations for a particular device type change, FDA will have in place a process to convey this information to the Third Parties and to industry.	4.7.1 Strengthen the Process for Recognition of Third Parties
By the end of FY 2018, establish a plan for eliminating routine re-review by FDA of Third Party reviews and implement the plan within 12 months.	4.7.2 Efforts to Eliminate Routine Re-Review
Implement a program to audit reviews conducted by recognized Third Parties and provide tailored re-training to recognized Third Parties based on the results of audits.	4.7.2 Efforts to Eliminate Routine Re-Review
By the end of FY 2018, issue draft guidance outlining criteria for rerecognition, suspension, or withdrawal of recognition of a Third Party. Issue final guidance within 12 months of the conclusion of the public comment period.	4.7.1 Strengthen the Process for Recognition of Third Parties
Publish performance of individual recognized Third Parties with at least five completed submissions on the web.	4.7.2 Efforts to Eliminate Routine Re-Review

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Require the independent assessment of the Third Party Review Program to evaluate efficiency including the circumstances when FDA re-reviews were conducted; and suggest process improvements.	4.7.2 Efforts to Eliminate Routine Re-Review
The Agency will seek greater authority to tailor the program. Specifically, FDA intends to expand the scope of the program to some product codes that require clinical data and to remove product codes from eligibility when appropriate, such as if/when safety signals arise.	4.7.1 Strengthen the Process for Recognition of Third Parties
Digital Health	**4.8 Digital Health**
Establish a central digital health unit within CDRH's Office of the Center Director to ensure proper coordination and consistency across the Agency. The Agency will not reorganize staff such that existing review staff would be reassigned to the central digital health unit, while retaining and not disrupting the existing digital health talent within the reviewing divisions who have established, long-term therapeutic and device expertise.	4.8.1 Enhance Digital Health Review Capacity
Develop software and digital health technical expertise ("Technical Experts") to provide assistance for premarket submissions that include SaMD, SiMD, interoperable devices, or otherwise incorporate novel digital health technologies.	4.8.1 Enhance Digital Health Review Capacity
Utilize Technical Experts as appropriate or when requested by the manufacturer for submissions that include SaMD, SiMD, interoperable devices, or otherwise incorporate novel digital health technologies.	4.8.1 Enhance Digital Health Review Capacity
Incorporate appropriate metrics for digital health improvements to monitor, track, analyze and report the results of digital health premarket review timelines.	4.8.1 Enhance Digital Health Review Capacity
Explore opportunities to establish premarket approval/clearance pathways tailored to SaMD, SiMD, and novel digital health technologies that take into account real world evidence while incorporating principles established through international harmonization.	4.8.2 Explore Innovative Regulatory Pathways
Revise existing and/or publish new relevant guidance documents, including publishing a draft revised version of the "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" (issued in 2005) by the end of FY 2019, and within 12 months of the close of the comment period, publish the final revised version. The Agency will incorporate applicable concepts from its Guidance for "Off-The-Shelf Software Used in Medical Devices."	4.8.2 Explore Innovative Regulatory Pathways
Publish final guidance addressing when to submit a 510(k) for a software modification to an existing device within 18 months of the close of the comment period.	4.8.2 Explore Innovative Regulatory Pathways
Engage through roundtables, meetings, and teleconferences.	4.8.3 Harmonize and Engage with Stakeholders
Hold a public workshop.	4.8.3 Harmonize and Engage with Stakeholders
Participate in international harmonization efforts related to digital health, including work on developing SaMD and other digital health convergence efforts through the IMDRF.	4.8.3 Harmonize and Engage with Stakeholders
Patient Science and Engagement (PSE)	**4.9 Patient Science and Engagement**
Develop clinical, statistical, and other scientific expertise and staff capacity to respond to submissions containing applicant-proposed use of publicly available and validated, voluntary PPI or voluntary PROs.	4.9.1 Develop Expertise and Capacity
These staff will provide submission review and early consultation/advice to industry during study planning.	4.9.1 Develop Expertise and Capacity
By the end of FY 2020, hold one or more public meetings to discuss the topics below and publish the findings and next steps. Discuss approaches for incorporating PPI and PRO as evidence in device submissions, as well as other ways of advancing patient engagement;	4.9.2 Hold Public Meetings to Advance PPI, PROs, and Patient Engagement
Discuss ways to use patient input to inform clinical study design and conduct, with a goal of reducing barriers to patient participation and facilitating recruitment and retention;	4.9.2 Hold Public Meetings to Advance PPI, PROs, and Patient Engagement
Public meetings should include specific examples and case histories for PPIs and PROs to ensure clarity and understanding by workshop attendees; and	4.9.2 Hold Public Meetings to Advance PPI, PROs, and Patient Engagement
Identify priority areas where decisions are preference-sensitive and PPI data can inform regulatory decision-making, in order to advance design and conduct of patient preference studies in high impact areas. Publish the priority areas in the Federal Register for public comment following the public meeting.	4.9.2 Hold Public Meetings to Advance PPI, PROs, and Patient Engagement

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FDA will undertake several activities to improve the regulatory predictability and impact of PROs, including: Clarify to device review divisions that use of PROs is voluntary and may be one potential way of demonstrating safety or effectiveness (or elements of either or both, such as in a composite endpoint). Consistent with least burdensome principles, applicants may use alternative approaches.	4.9.3 Improve Regulatory Predictability and Impact of PROs
Modify the guidance to outline a flexible framework for PRO validation thresholds. These thresholds may vary depending on the particular regulatory use of the PRO.	4.9.3 Improve Regulatory Predictability and Impact of PROs
Work on developing a model for "bridging studies" to make efficient use of existing validated PROs which may be improved or adapted to other subpopulations or other regulatory uses in a more streamlined and expeditious manner than creating novel PROs.	4.9.3 Improve Regulatory Predictability and Impact of PROs
The existing dispute resolution process should be used in the event of disagreement between the applicant and the Agency on the need for PPI or PRO.	4.9.3 Improve Regulatory Predictability and Impact of PROs
Real World Evidence (RWE)	4.10 Real-World Evidence
The Agency will use user fee revenue to support the NEST by providing funding for NESTcc and hiring FDA staff with expertise in the use of RWE.	4.10.1 Establish NESTcc
FDA will contract with an organization to serve as NESTcc to facilitate use of real world evidence to support premarket activities.	4.10.1 Establish NESTcc
The Agency will use user fee revenue to support NEST by providing funding for the NESTcc and hiring FDA staff with expertise in the use of RWE.	4.10.2 Build RWE Expertise
The Agency will establish criteria for streamlining MDR requirements.	4.10.3 Streamline Medical Device Reporting
FDA will not require postmarket surveillance studies (i.e., 522 Studies) for devices for which registries and/or other RWD sources exist if FDA has access to the information/data in the RWD source and has determined that the information/data in the RWD source is sufficient to take the place of a postmarket surveillance study.	4.10.4 Use RWD in Place of Postmarket Surveillance Studies, as Appropriate
Special 510(k) Conversions	4.11 Special 510(k) Conversions
Analyze conversions of Special 510(k)s to Traditional 510(k)s.	4.11.1 Assess the Conversion of Special 510(k)s to Traditional 510(k)s

APPENDIX B. GLOSSARY

Abbreviation or Acronym	Definition
4PH	Four-Part Harmony
510(k)	Premarket Notification
ACLA	American Clinical Laboratory Association
ACP	Algorithm Change Protocol
ADA	Agency Directed Assignments
AdvaMed	Advanced Medical Technology Association
AI	Artificial Intelligence
APS	Alternative Pay Structure
CA	Corrective Action
CAPA	Corrective and Preventive Action
CBER	Center for Biologics Evaluation and Research
CCP	Customer Collaboration Portal
CDRH	Center for Devices and Radiological Health
CERSI	Center of Excellence in Regulatory Science and Innovation
COA	Clinical Outcome Assessment
COI	Concept of Interest
CorGen	Correspondence Generator
COU	Context of Use
COVID-19	Coronavirus Disease of 2019
CTS	Center Tracking System
Cures Act	21st Century Cures Act
DCI	Data Collection Instrument
DCR	Document Change Request
DCS	Document Control System
DDH	Division of Digital Health
DDVV	Design, Development, Verification and Validation
DETD	Division of Employee Training and Development
DHA	Direct Hire Authority
DHCoE	Digital Health Center of Excellence
DHSC	Digital Health Steering Committee
DWM	Division of Workforce Management
EHR	Electronic Health Records
EI	Early Interaction
EIR	Entrepreneurs in Residence
ELP	Experiential Learning Program
eSTAR	Electronic Submission Template and Resource
FD&C	Federal Food, Drug, and Cosmetic Act
FDA	Food and Drug Administration
FDARA	FDA Reauthorization Act of 2017
FG	Final Guidance
FPP	Focal Point Program
FR	Final Rule
FS	Final Standard
FTE	Full-Time Equivalent
FY	Fiscal Year
HDE	Humanitarian Device Exemption
HR	Human Resources
IAA	Inter-Agency Agreement
IDE	Investigational Device Exemption
IFU	Indications for Use
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization
IT	Information Technology

Abbreviation or Acronym	Definition
ITR	Insight Time Reporting
IVD	In Vitro Diagnostic
LB	Least Burdensome
LR	Lead Reviewer
MAUDE	Manufacturer and User Facility Device Experience
MDIC	Medical Device Innovation Consortium
MDMA	Medical Device Manufacturers Association
MDR	Medical Device Reporting
MDUFA	Medical Device User Fee Amendments
MDUFA III	Medical Device User Fee Amendments of 2012
MDUFA IV	Medical Device User Fee Amendments of 2017
MDUFMA	Medical Device User Fee and Modernization Act of 2002
MITA	Medical Imaging and Technology Alliance
ML	Machine Learning
MMA	Mobile Medical Application
NC	Nonconformance
NESTcc	National Evaluation System for Health Technology Coordinating Center
NoDEx	Network of Digital Health Experts
NoE	Network of Experts
NSE	Not Substantially Equivalent
OCD	Office of the Center Director
OCEA	Office of Clinical Evaluation and Analysis
ODE	Office of Device Evaluation
OFI	Opportunity for Improvement
OHT	Office of Health Technology
OIR	Office of In Vitro Diagnostics and Radiological Health
OM	Office of Management
OPEQ	Office of Product Evaluation and Quality
OPM	Office of Personnel Management
ORP	Office of Regulatory Programs
OSEL	Office of Science and Engineering Laboratories
OST	Office of Strategic Partnerships and Technology Innovation
OTS	Office of Talent Solutions
PBM	Position-Based Management
PDP	Professional Development Program
PEAC	Patient Engagement Advisory Committee
PFDD	Patient-Focused Drug Development
PGHD	Patient-Generated Health Data
PHE	Public Health Emergency
PIF	Presidential Innovation Fellows
PIP	Process Improvement Program
PMA	Premarket Approval
PPI	Patient Preference Information
PRO	Patient-Reported Outcome
PSE	Patient Science and Engagement
PTS	Panel-Track Supplement
QM	Quality Management
QMOE	Quality Management and Organizational Excellence
QMR	Quality Management Review
QMS	Quality Management System
RCP	Reviewer Certification Program
RTA	Refuse to Accept
RWD	Real-World Data
RWE	Real-World Evidence
RWP	Real-World Performance
SaMD	Software as a Medical Device
SE	Substantial Equivalence
SGE	Special Government Employees

Abbreviation or Acronym	Definition
SI	Specific Issue (i.e., specific scientific, clinical, or regulatory issue)
SiMD	Software in a Medical Device
SIR	Submission Issue Request
SMART	Submission Memo and Review Template
SME	Subject Matter Expert
SOP	Standard Operating Procedure
SPS	SaMD Pre-Specifications
SWIFT	SOPs, WIs, Forms, and Templates
TA	Topic Area
Third Party	Third Party Review Organization
TN	Transmittal Notice
TPLC	Total Product Life Cycle
TSR	Tools and Services Request
TTD	Total Time to Decision
UCSF	University of California San Francisco
VMSR	Voluntary Malfunction Summary Reporting
VOC	Voice of Customer
WI	Work Instruction