U.S. FOOD & DRUG ADMINISTRATION

Pre-Market Notification [510(k)] New Policies and Pilots

FDA-Industry IVD Roundtable Meeting

November 9, 2018

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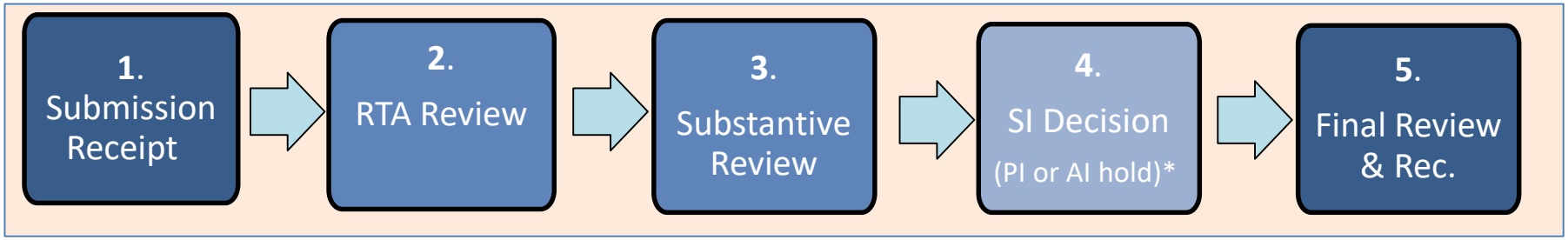
Director, 510(k) and 513(g) Staff
Program Operations Staff
Center for Devices and Radiological Health

MDUFA IV Performance Goals Overview

Submission Type	Action	FDA Review Days	Percent of Submissions to Meet FDA Days				
			FY18	FY19	FY20	FY21	FY22
510(k)	Substantive Interaction	60	95%	95%	95%	95%	95%
	Decision	90	95%	95%	95%	95%	95%
	Shared Outcome Goal	Avg. TTD	124	120	116	112	108
De Novo	Decision	150	50%	55%	60%	65%	70%
Original PMAs & Panel Track Supplements	Substantive Interaction	90	95%	95%	95%	95%	95%
	Decision if No Panel	180	90%	90%	90%	90%	90%
	Decision With Panel	320	90%	90%	90%	90%	90%
	Shared Outcome Goal	3yr. Avg. TTD	320	315	310	300	290
180 Day PMA Supplements	Substantive Interaction	90	95%	95%	95%	95%	95%
	Decision	180	95%	95%	95%	95%	95%
Real Time Supplements	Decision	90	95%	95%	95%	95%	95%
Pre-Submissions	Written Feedback	70 or 5d prior to mtg	1,530 (65%)	1,645 (70%)	1,765 (75%)	1,880 (80%)	1,950 (83%)
CLIA Waiver by Applications	Substantive Interaction	90	90%	90%	90%	90%	90%
	Dual CLIA/ 510(k)	180	90%	90%	90%	90%	90%
	Decision if No Panel	150	90%	90%	90%	90%	90%
	Decision With Panel	320	90%	90%	90%	90%	90%

General Overview

510(k) Submission Core Process

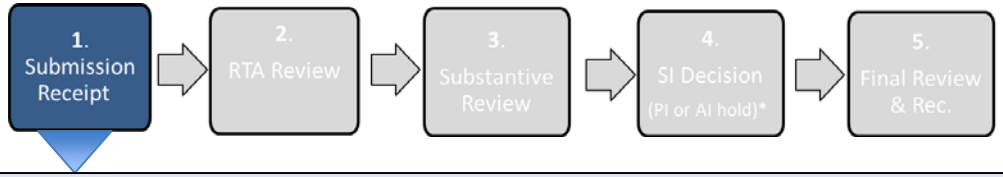


Sub-Processes

- Bundling
- Withdrawal
- Missed MDUFA
- Deletion
- Appeal
- Corrected SE
- New Product code creation
- Compliance Action 510(k)
- 510(k) Amendments (nine types)

*PI = Proceed interactively, AI = Additional Information

Submission Receipt

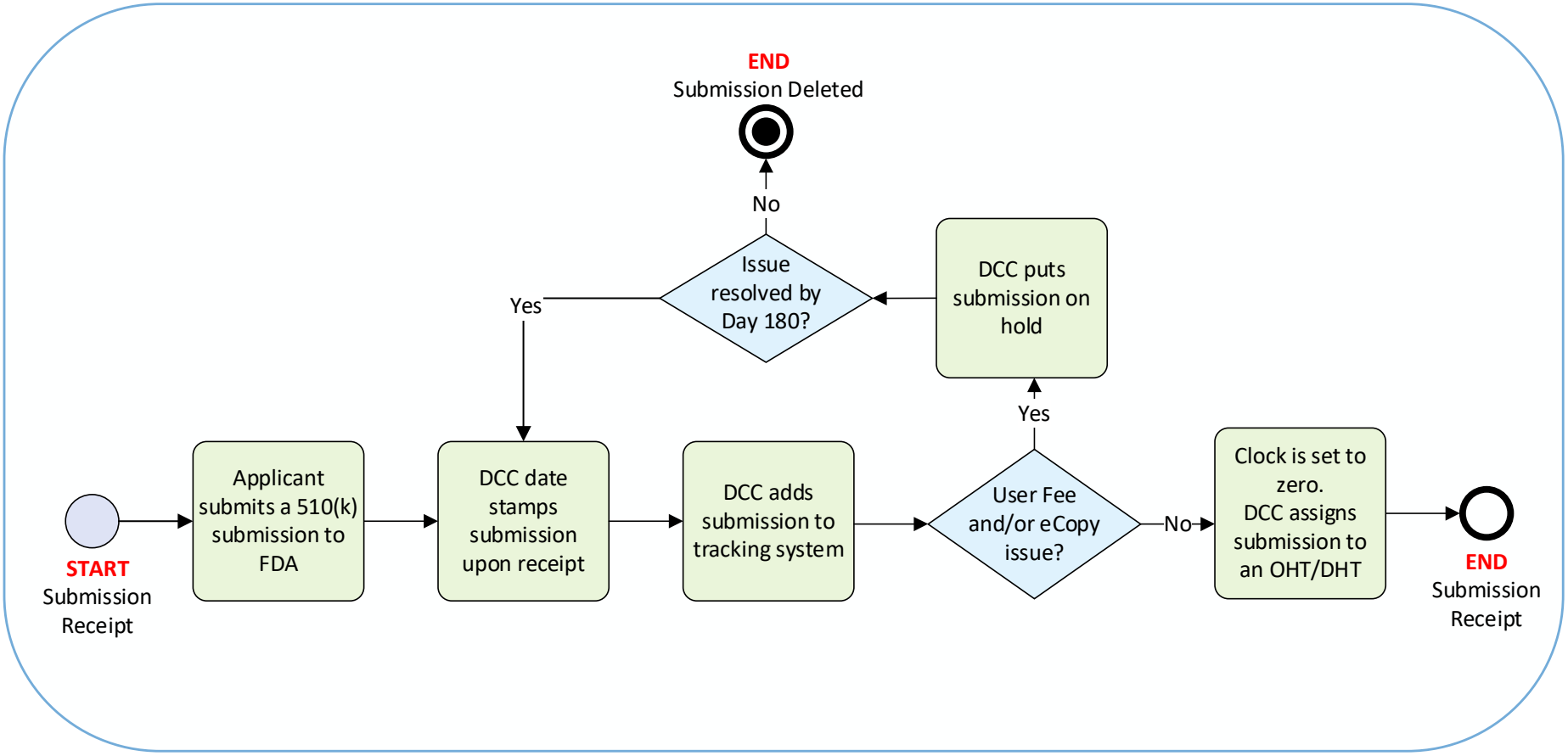


Document Control Center (DCC) receives and processes all 510(k) submissions, supplements and amendments.

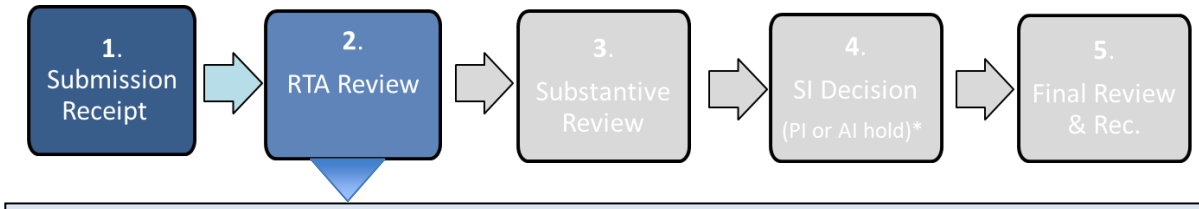
- 510(k) submissions are given a submission ID upon receipt.
- Submission ID starts with the letter 'K' and contains six numbers. example, K18####
- DCC checks for appropriate eCopy and user fee
- If there are issues, submission is put on hold
- If there are no issues, submission is assigned to a Division of Health Technology

eCopy: eCopy Program for Medical Device Submissions, 2015
510(k) User Fees: User Fees and Refunds for Premarket Notification Submissions (510(k))s

STEP 1: Submission Receipt



Refuse to Accept (RTA) Review

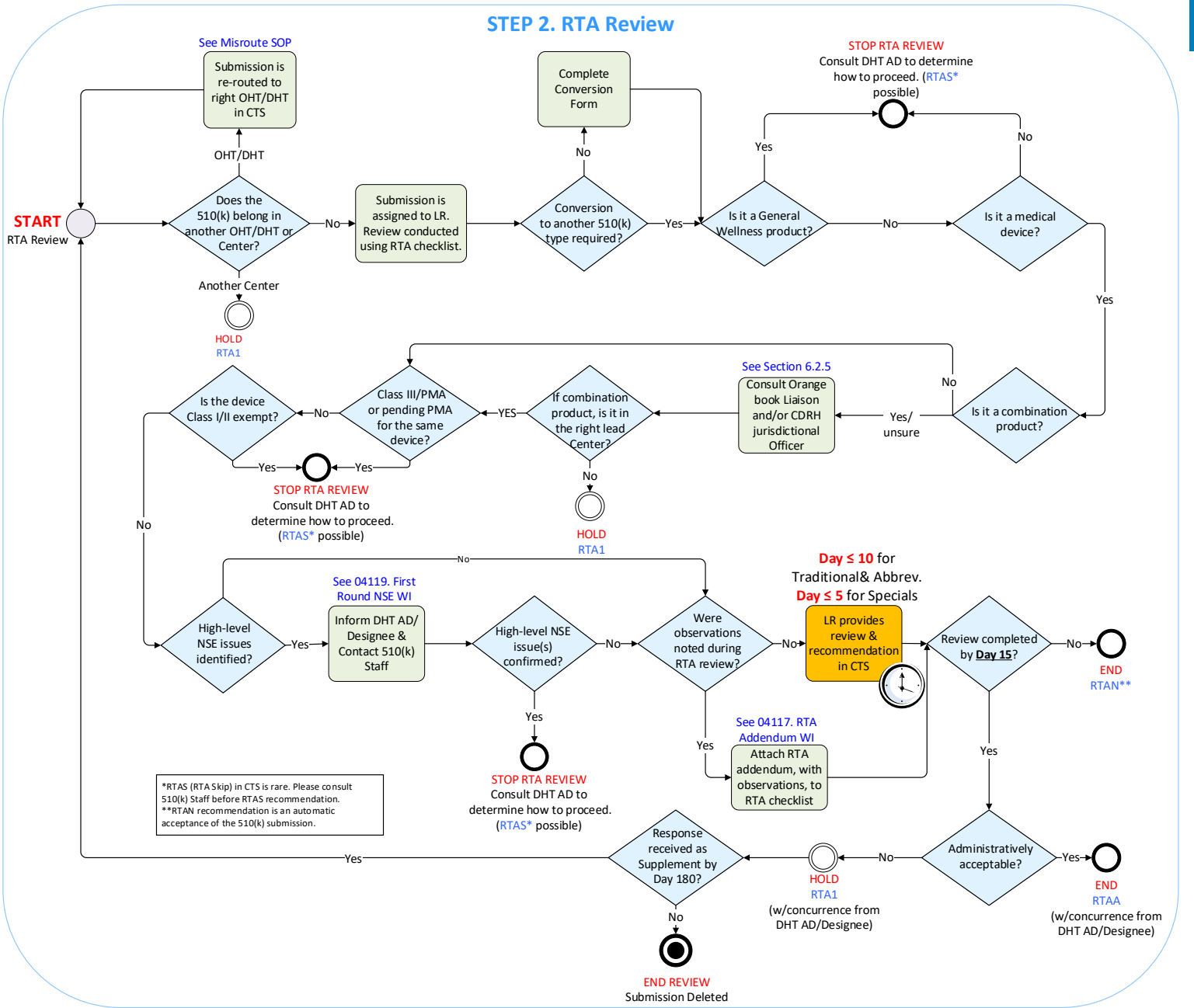


Administrative quality check that occurs within the first fifteen (15) days of a 510(k) submission review. This phase is used to assess the administrative completeness or acceptability of a submission prior to the substantive review.

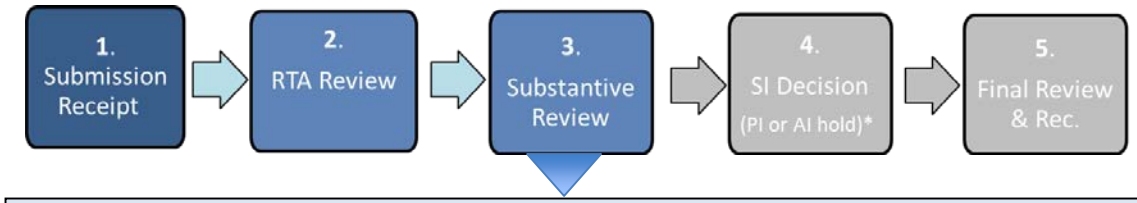
Links to RTA Checklists
04205. Acceptance Checklist for Traditional 510(k)s
04204. Acceptance Checklist for Special 510(k)s
04200. Acceptance Checklist for Abbreviated 510(k)s

- Completed **within fifteen (15) calendar days**.
- Lead Reviewer (LR) assess appropriateness of review track. Converts when appropriate.
- LR can work interactively with the Applicant to obtain additional information
- RTA addendum can be used to address issues ("observations") that does not determine acceptability
- If a high-level NSE is identified RTA review (**RTAS**) is skipped & proceeds to Substantive Review
- LR provides recommendation by **Day 10 for Traditional & Abbreviated** and by **Day 5 for Specials**
- When **unacceptable** LR recommends **RTA1** & submission is put on hold
- When **acceptable** LR recommends **RTAA** & proceeds to Substantive Review

STEP 2: Refuse to Accept (RTA) Review



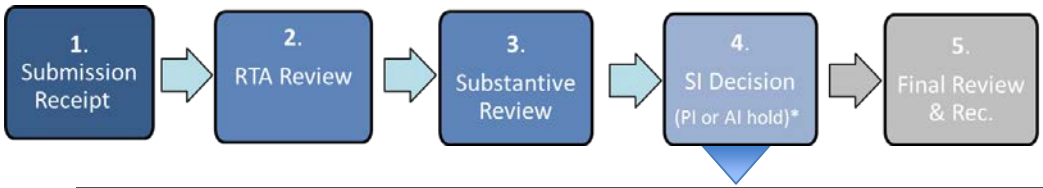
Substantive Review



LR reviews the submission in detail and may interact with the Applicant to determine whether the information provided is acceptable for determination of SE.

- LR downloads the SMART Template Memo (SMART memo) and documents review
- LR decides whether consultation with SME(s) is needed. If so, LR seeks input within the first three (3) weeks of substantive review.
- LR may work interactively with the Applicant to address clarification questions.
- LR provides a reasonable timeframe for the Applicant to respond depending on the information being requested. (1-2 days for minor questions, 7-10 days for significant question.)
- LR provides SI decision by **Day 50 for Traditional & Abbreviated** and by **Day 25 for Specials**
- Substantive Interaction (SI) decision or final decision by **Day 60 for Traditional & Abbreviated** and by **Day 20 for Specials**.

Substantive Interaction (SI) Decision



By Day 60, LR decides whether to Proceed Interactively (PI) or Issue an Additional Information (AI) Letter.

PI

(*via email and/or phone call***)**

- Address questions that can be resolved quickly
- Response timeframe ranges from two to seven (2-7) calendar days
- Applicant can negotiate response timeframe w/Lead Reviewer

- Applicant's response sent directly to Lead Reviewer.
- See 04004.Interactive Review During Review of 510(k) Submissions Work Instruction.

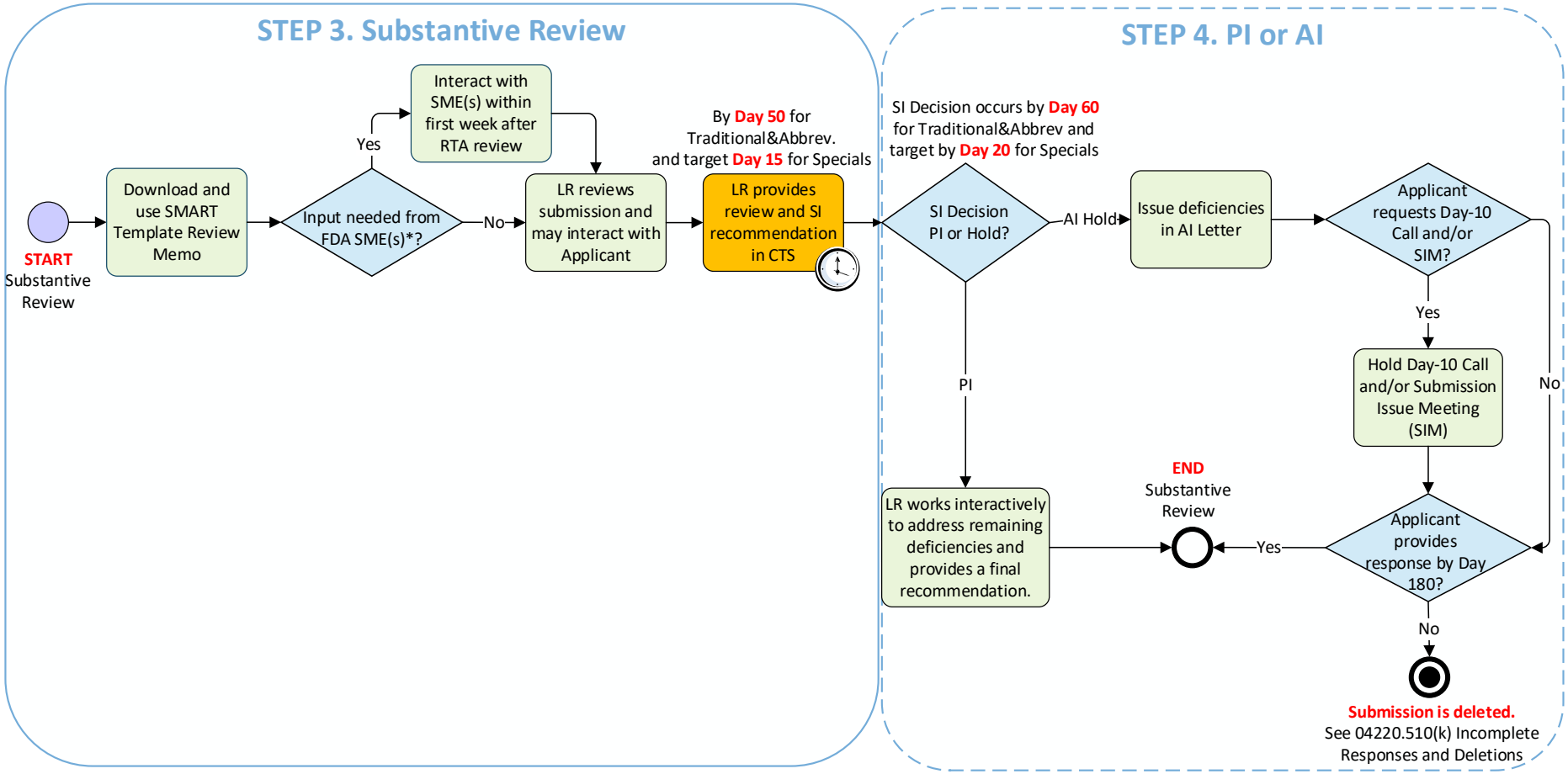
OR

AI Letter

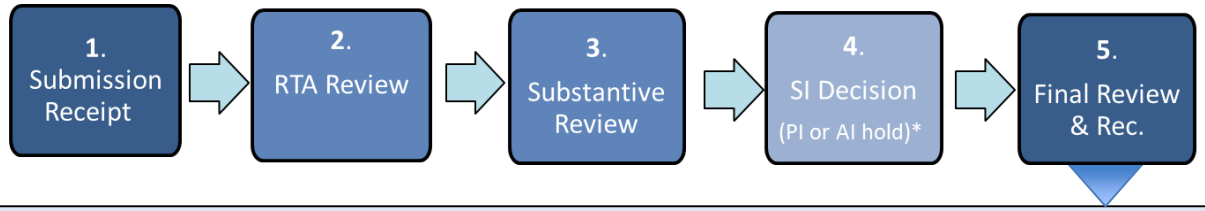
- To address questions that can not be adequately resolved interactively
- To address complex questions that cannot be resolved quickly
- Applicant is granted 180 days to respond (late submissions are deleted.)

- Applicant's response sent as supplement to original 510(k) via DCC.
- See 04356. Premarket Deficiency Letters for Marketing Applications - Policy and Process SOP

STEPS 3 &4: Substantive Review & SI Decision



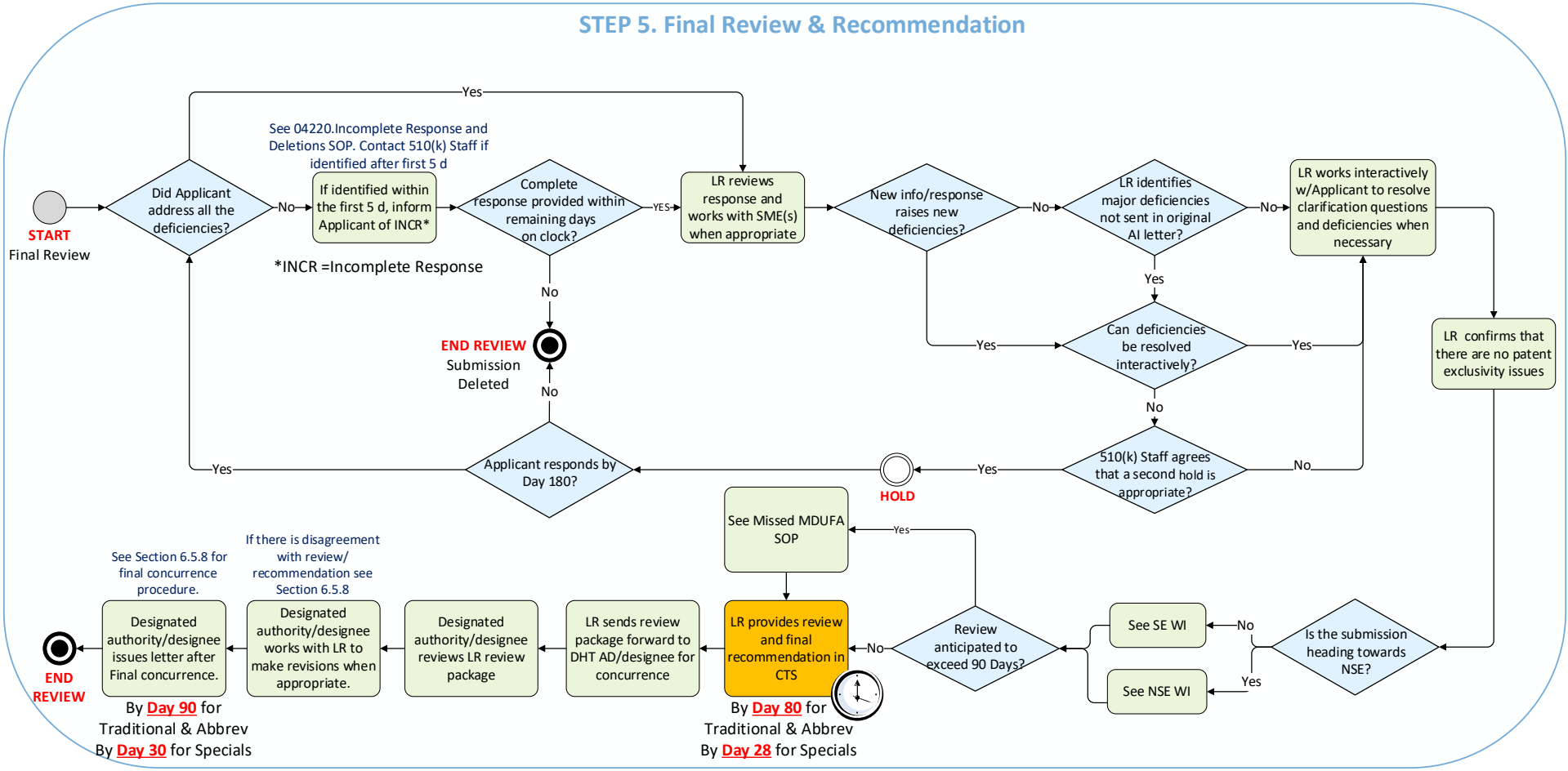
Final Review & Recommendation



Final review occurs after the SI decision and is a continuation or completion of the substantive review until a final decision is reached. If the submission was placed on hold, FDA clock resumes upon receipt of response to an AI letter.

- LR checks whether the Applicant provided a complete response to all the deficiencies within the first five (5) days of supplement
- If the response is complete, the LR reviews the Applicant's response and works with SME(s) to when appropriate
- When necessary, LR resolves remaining questions and deficiencies interactively.
- Follow 04226.Missed MDUFA Decision Procedures SOP if LR anticipates that a final recommendation will not be provided within the expected 90 FDA days
- LR provides a final recommendation for Traditional 510(k) and Abbreviated 510(k) submissions by **Day 90** and **Day 30** for Specials.
- Recommendation and review package are reviewed by DHT and OHT designated authorities for concurrence before letter is issued.

STEP 5: Final Review & Recommendation

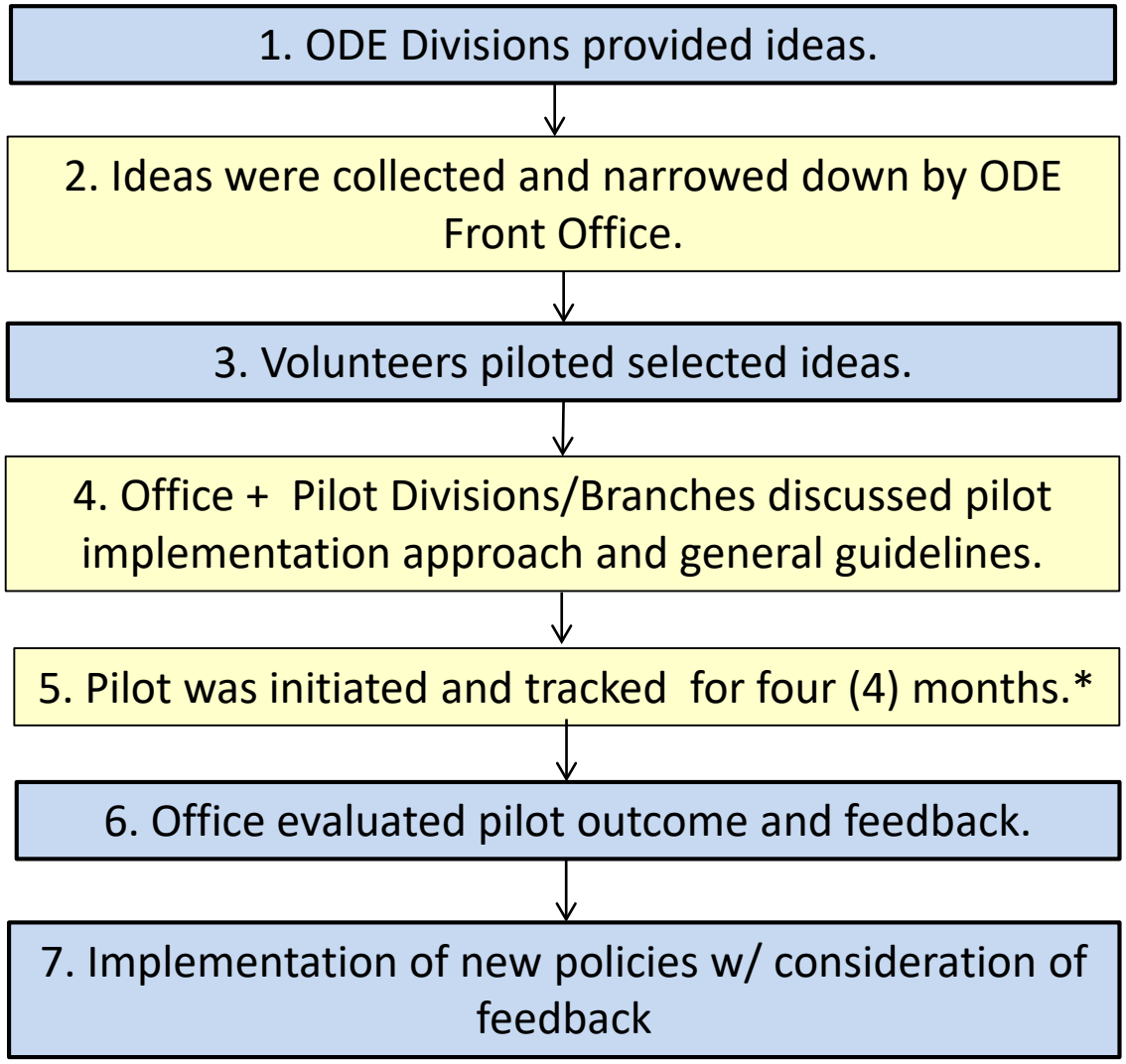


“Coming up with an idea is the least important part of creating something great. ... The execution and delivery are what's key.”

Sergey Brin,
computer scientist and entrepreneur

Background

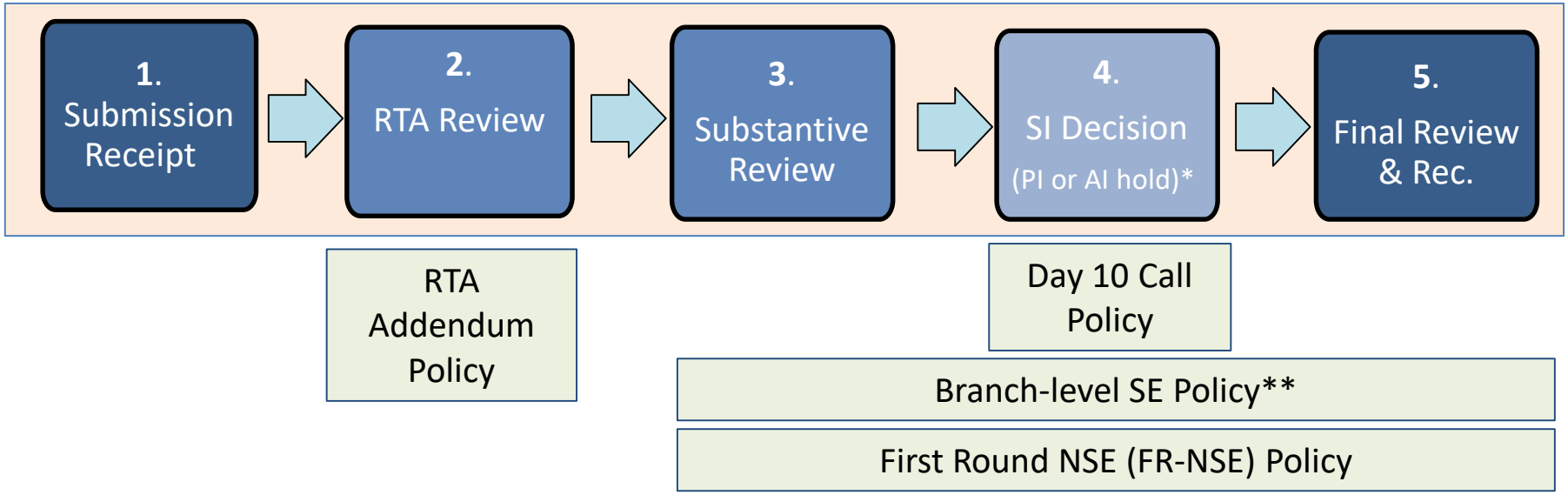
New policies based on suggestions provided by review staff.



*Data cut-off December 04, 2017

New 510(k) Policies

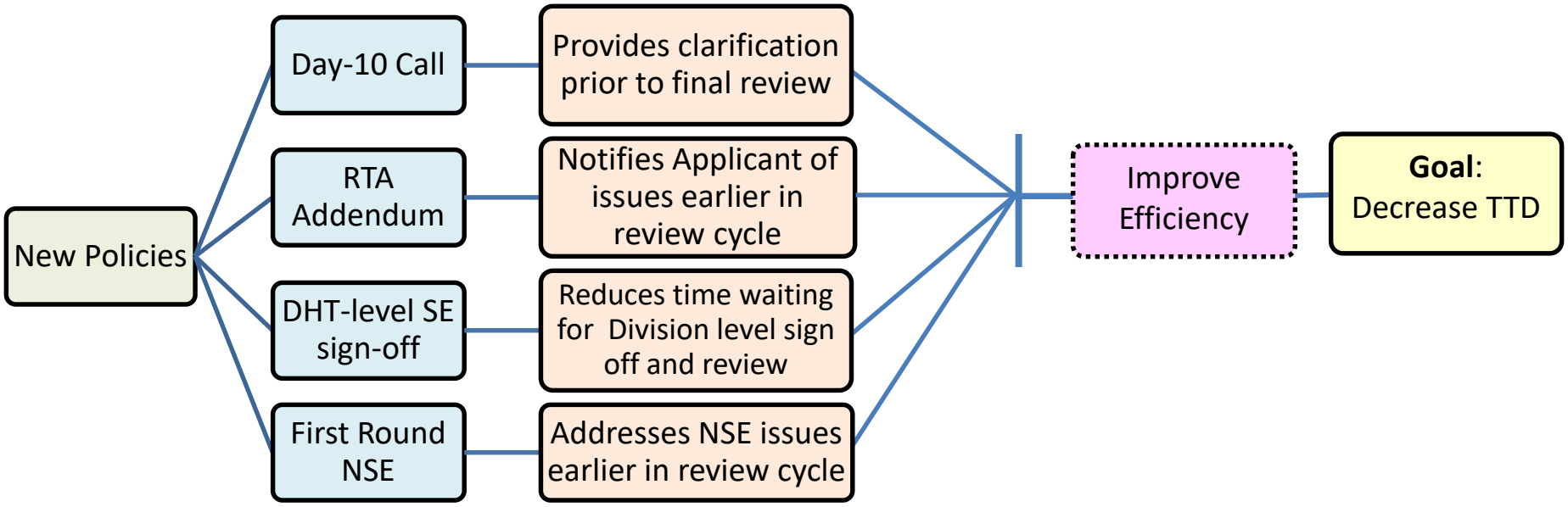
510(k) Submission Core Process



TPLC Key:
Branch = Division of Health Technology (DHT)
Division level = Office of Health Technology (OHT)

*PI = Proceed interactively, AI = Additional Information
** Previously Branch-level SE pilot

Goal of New Policies



TPLC Key:
Branch = Division of Health Technology (DHT)
Division level = Office of Health Technology (OHT)

RTA Addendum Policy

What it Is

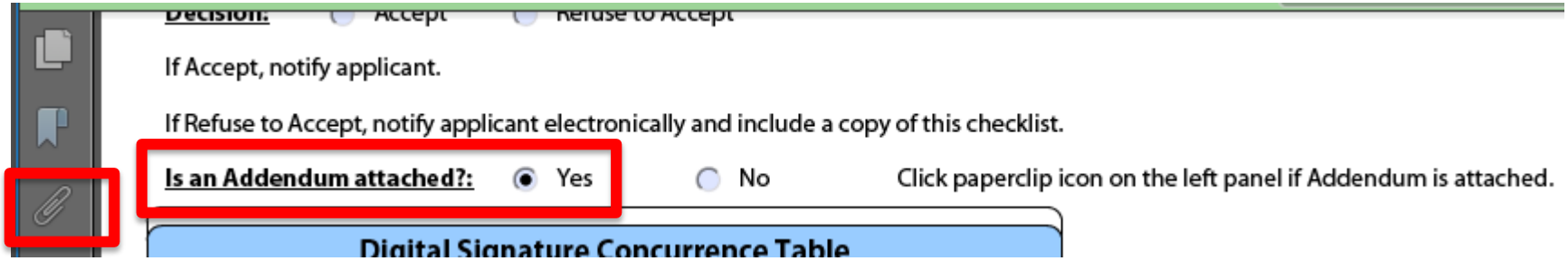
- An attachment to the RTA checklist embedded into the PDF
- Early notification of "observations" made during the initial RTA review
- An opportunity to address issues interactively during substantive review

What it Is Not

- Substantive review of the submission
- In place of an additional information hold
- An official "ask" for additional information
- A delay in the RTA review or decision

WHAT IS AN OBSERVATION?

Issue noted during the administrative review that does not determine the acceptability of a submission but would result in a deficiency during substantive review. (Example: Missing a required animal or engineering test.)



Day-10 Call Policy

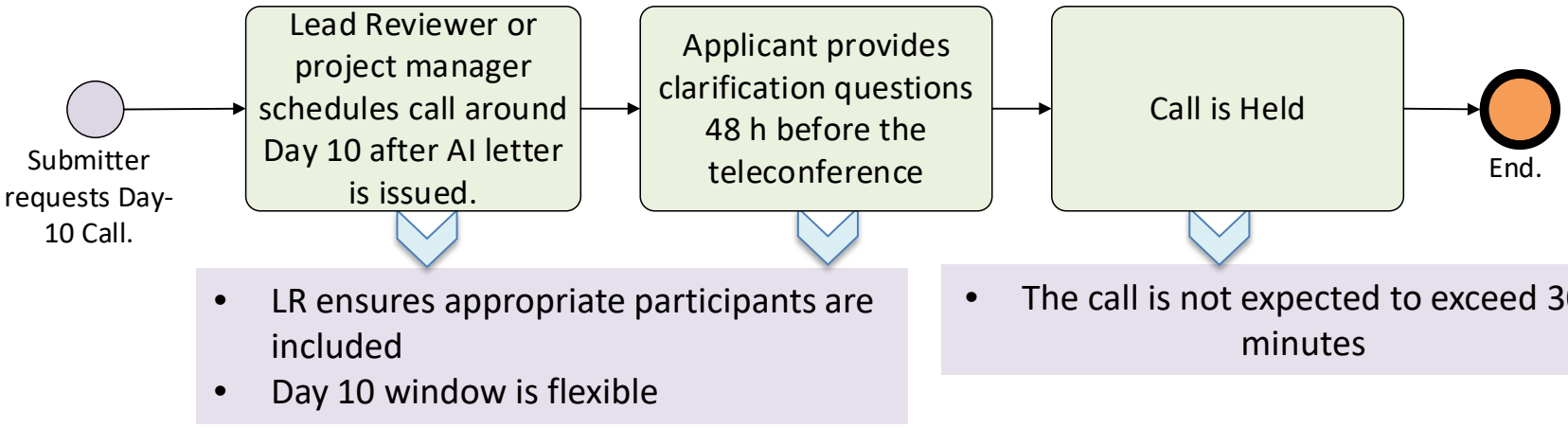
Description: Voluntary call offered by FDA that occurs within ten (10) days after issuance of an AI* letter. The purpose of the call is to address clarification questions pertaining to the deficiencies in the letter.

WHAT IT IS

- Teleconference
- Confirmation that Applicant understands deficiencies in the letter
- Can be used to determine whether a Q-Submission is needed.

WHAT IT IS NOT

- Review of additional information provided by Applicant
- Discussion of issues unrelated to deficiencies in the AI letter
- A Q-Submission meeting



*AI = Additional Information

Day-10 Call Policy Continued…

- **Day-10 Call Language in 510(k) AINN letter**

FDA is offering a teleconference within 10 days from the date on this letter to address any clarification questions you may have pertaining to the deficiencies. If you are interested in a teleconference, please send the following information to the contact specified in this email: (1) proposed dates and (2) a list of your clarification questions at least 48 hours before the teleconference. We would like to emphasize that the purpose of the teleconference is to address specific clarification questions. This teleconference is not intended for review of new information or your approach to address the deficiencies. If you would like a meeting or teleconference to discuss your planned approach for responding to the deficiencies, please submit your request for feedback as a Submission Issue Q-Submission (Q-Sub). For additional information regarding Q-Subs, please refer to the Guidance for Industry and FDA Staff on Medical Devices: The Pre-Submission Program and Meetings with FDA Staff at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

“The single biggest problem in communication is the illusion that it has taken place.”

George Bernard Shaw, Irish writer

SE Final Concurrence at the Branch Level

Description: Straight forward SE letters are signed out at by the branch chief. This approach reduces time spent waiting for Division Director's review and concurrence.

When Can a Branch Chief provide final concurrence on an SE recommendation?

- Branch has extensive knowledge of the product area
- The device or submission is not complex from a regulatory or performance data standpoint (Example: Clinical data needed for a change in indication and/or technology might not be appropriate for Branch-level SE concurrence.)
- SE recommendation is not controversial and/or does not have potential to be controversial. (Example: A 510(k) claiming equivalence to a recalled device might not be appropriate.)
- The review team has reviewed similar devices with similar regulatory requirements

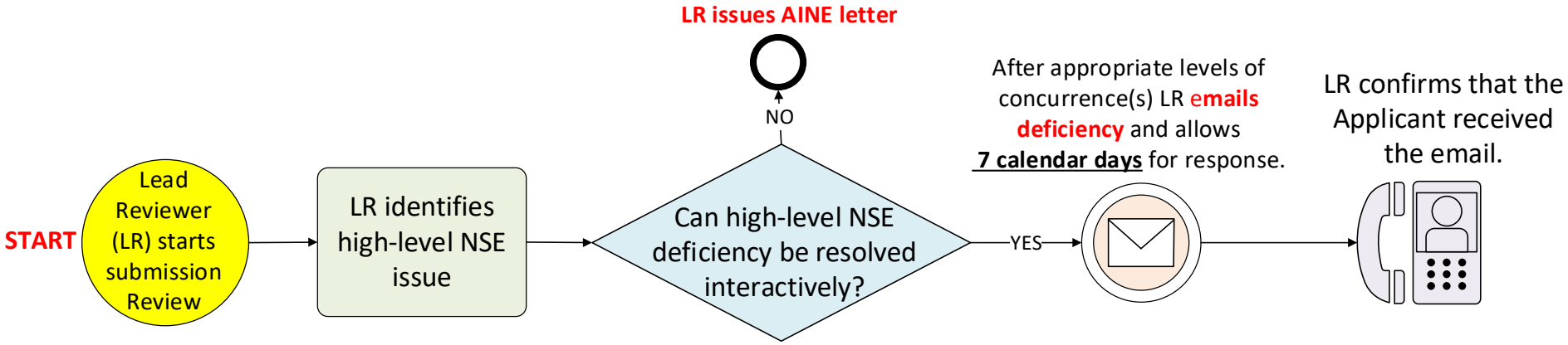
TPLC Key: Branch Chief = Division of Health Technology Assistant Director (DHT AD) OHT = Office of Health Technology

First-Round (FR-NSE) Policy

Description: A submission does not have to go on hold before a high level NSE recommendation is issued as long as the Applicant has an opportunity to resolve the NSE issue interactively.

High-level NSE reasons:

- No valid predicate
- New intended use
- Different technological characteristics that raise different questions of safety and effectiveness when compared to the predicate.



NOTE: Potential NSE letter (AINE) can still be issued if FR-NSE was attempted and the deficiency cannot be adequately resolved interactively.

First-Round (FR-NSE) Policy

Approach for FR-NSE based on Applicant's Responsiveness with concurrence from Branch Chief

Table 1: Approach on FR-NSE based on Applicant's Responsiveness	
Responsive Applicant but cannot meet timeframe	If the Applicant responds, they must confirm whether a complete response can be provided within the timeframe specified in the email. If a complete response cannot be provided, and Applicant and LR do not agree upon an alternative date, an **NSE letter is issued within 30 calendar days from email issuance.**
Responsive Applicant and meets timeframe	LR reviews response and addresses minor clarification questions when appropriate.
Non-responsive Applicant	If the Applicant does not provide any response to the original email or voicemail, an NSE letter is issued **no sooner than one day after the response was due.** 510(k) Staff does not need to review the NSE letter if the deficiency is unchanged from what was evaluated prior to issuing email, and the boilerplate text in the NSE letter is not modified.
Late Responder	It is at the review team's discretion to determine whether there is sufficient time remaining to address a late response. If there is not sufficient time, **an NSE letter is issued within 30 calendar days after email issuance.** The LR is not obligated to review a late response if there is not sufficient time for an adequate review.

TPLC Key: Branch Chief = DHT AD

First-Round NSE (FR-NSE) Policy

Reviewing Response to FR-NSE Email:

- **Adequate response.** If the interactive response is adequate, the LR continues with substantive review.
- **Interactive review.** The LR works interactively to address minor clarification questions to the response when needed**.**
- **Inadequate response.** If the response is not adequate, the LR, with appropriate levels of concurrences issues an NSE letter within 30 calendar days.
- **Additional information letter (AINN).** An AINN letter can still be issued for non-NSE issues that cannot be adequately resolved interactively.

Benefit-Risk Assessment Policy

510(k) Benefit Risk Guidance outlines the policy for evaluating substantial equivalence in a 510(k) when the benefit-risk profile of a new device is different from that of the predicate device based on performance data.

510(k) B-R Guidance:

- Serves as **an aid** for evaluating benefit-risk factors to determine SE in a 510(k)
- This guidance **does not change the 510(k) premarket review standard** or create extra burden on a submitter to provide additional performance data from what has traditionally been expected for 510(k)s.
- Provide guidance **specifically for situations when the benefit-risk profile of a new device is different from that of the predicate device**
- Provides **additional clarification** on factors that FDA takes into consideration when evaluating the benefit-risk profile of a new device when compared to a predicate device
- Improves the **predictability, consistency, and transparency** of the 510(k) premarket review process

Benefit-Risk Assessment Policy Continued

Table serves as a guide for when benefit-risk assessment is recommended in a 510(k). This table should be used with the guiding principles provided in the rest of the guidance.

	INCREASE IN RISK	DECREASE /EQUIVALENT RISK
INCREASE/ EQUIVALENT BENEFIT	**Conducting a benefit-risk assessment is recommended.** FDA evaluates the nature of the increased risk and considers whether additional measures may help to mitigate the increased risk**. FDA will generally not deem a new device SE to a predicate when the increased risk cannot be mitigated and is not accompanied by an increase in benefit**. **1**	**Conducting a benefit-risk assessment is likely not recommended to determine whether the new device is "as safe and effective" as the predicate device.** FDA will generally determine the new device **SE** to the predicate device when there is increase/equivalent benefit and decreased/equivalent risk. **2**
DECREASE IN BENEFIT	**Conducting a benefit-risk assessment is likely not recommended to determine whether the new device is "as safe and effective" as the predicate device.** FDA will generally determine the new device **NSE** to the predicate device when there is a decrease in benefit and an increase in risk. **4**	**Conducting a benefit-risk assessment is recommended.** If the aggregate benefit of a new device is decreased in and the risk level is decreased, FDA may determine the new device to be SE if the differences do not impact whether the new device is at least "as safe and effective". **However, if there is a decrease in benefit without a decrease in risk, FDA would likely find a device NSE to the predicate especially if the B-R assessment confirms that the new device is not "as safe and effective" as the predicate device**. **3**

Pilots

Pilot Webpage

Quik Review Pilot

Description: The purpose of the Quik Review Program pilot is to whether use of the FDA's free eSubmitter software will produce well-organized submissions that can be reviewed more efficiently to help promote timely access to safe, effective, and high-quality medical devices.

- **Eligibility:**
  - Specific product codes
  - Required use of eSubmitter to construct 510(k) submission
  - Not a combination product
  - Traditional and Abbreviated 510(k)s (no Specials)
- **No RTA review**
- **Interactive review**
- **Final decision expected by FDA Day 60**
- **If ineligible, submission is converted to 90 FDA Day timeframe**
- **Complex issues could render the file ineligible for the pilot**

Link to Pilot Webpage:
https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm618561.htm#quik

Special 510(k) Program Pilot

Description: The purpose of the Special 510(k) Program pilot is to expand on the types of changes eligible for the program to improve the efficiency of 510(k) review.

Eligibility factors:

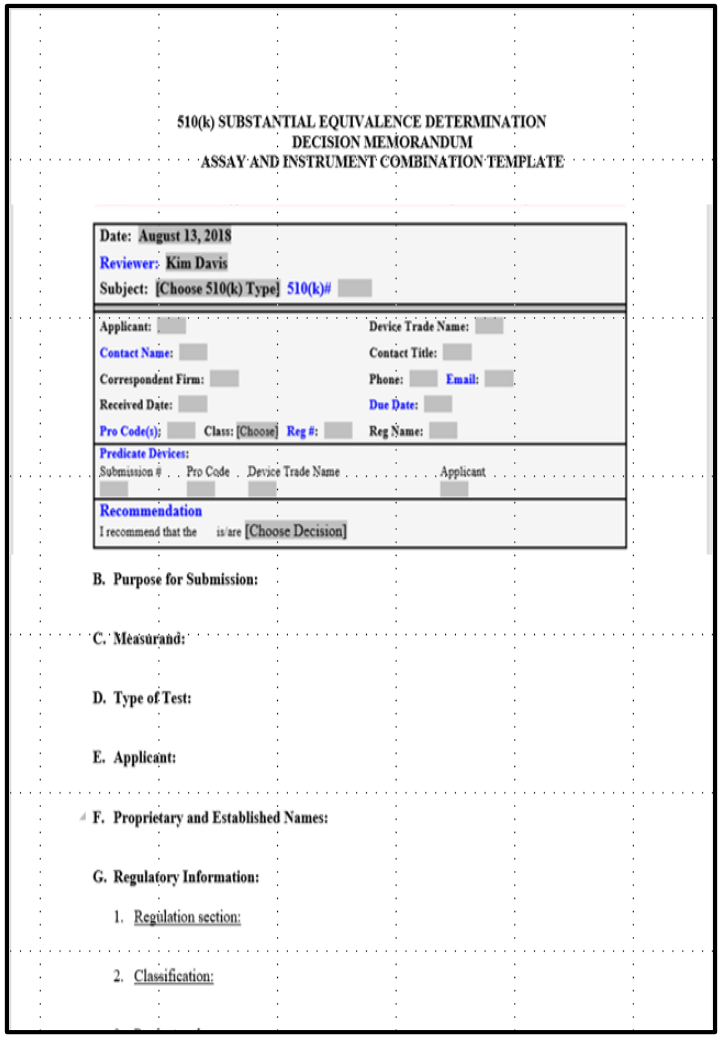
1. The proposed change is made and submitted by the manufacturer authorized to market the existing device
2. Change can be due to labeling (IFU) or technology
3. Performance data are unnecessary
4. If performance data is necessary, **well-established methods** are available to evaluate the change. Example of well-established methods includes , recognized consensus standard, previously cleared test methods and widely available/accepted methods
5. All performance data necessary to support substantial equivalence can be reviewed in a summary or risk analysis format.

If there is not a well-established method, FDA intends to convert the submission to a Traditional

Link to Pilot Webpage:

https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm618561.htm#pilot

IVD Smart Template



510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

Date: August 13, 2018
Reviewer: Kim Davis
Subject: [Choose 510(k) Type] 510(k)#

Applicant: Device Trade Name:
Contact Name: Contact Title:
Correspondent Firm: Phone: Email:
Received Date: Due Date:
Pro Code(s): Class: [Choose] Reg #: Reg Name:

Predicate Devices:
Submission # Pro Code Device Trade Name Applicant

Recommendation
I recommend that the is/are [Choose Decision]

B. Purpose for Submission:

C. Measurand:

D. Type of Test:

E. Applicant:

F. Proprietary and Established Names:

G. Regulatory Information:

1. Regulation section:

2. Classification:

- OIR is piloting an IVD-specific Smart template
- Smart templates help ensure consistency and simplify reviews for staff
- Includes standardized deficiencies for common situations
- Supports IVD decision summaries

“If all else fails, immortality can always be assured by spectacular error."

-- John Kenneth Galbraith,
Canadian-American economist

Current Resources

Guidance Documents

- Deciding When to Submit a 510(k) for a Change to an Existing Device, Draft Guidance - August 8, 2016
- Guidance for Industry and Food and Drug Administration Staff - User Fees and Refunds for Premarket Notification Submissions (510(k)s)
- Refuse to Accept Policy for 510(k)s, August 4, 2015
- The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], July 28, 2014
- The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications, May 20, 1998
- FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Goals, October 15, 2012
- Suggested Format for Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions of FDAMA
- Procedures for Class II Device Exemptions from Premarket Notification, February 19, 1998
- Bundling Multiple Devices or Multiple Indications in a Single Submission, November 26, 2013
- The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles, October 4, 2002
- Medical Device Classification Product Codes Guidance, April 11, 2013

Questions? Contact 510k_Program@fda.hhs.gov

Thank-you!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