Improve Your Pre-Market Review,
Know What's New!

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# MDUFA IV Performance Goals Overview

<table>
<thead>
<tr>
<th>Submission Type</th>
<th>Action</th>
<th>FDA Review Days</th>
<th>Percent of Submissions to Meet FDA Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>510(k)</td>
<td>Substantive Interaction</td>
<td>60</td>
<td>FY18: 95%</td>
</tr>
<tr>
<td></td>
<td>Decision</td>
<td>90</td>
<td>FY18: 95%</td>
</tr>
<tr>
<td>De Novo</td>
<td>Decision</td>
<td>150</td>
<td>FY18: 50%</td>
</tr>
<tr>
<td>Original PMAs &amp; Panel Track Supplements</td>
<td>Substantive Interaction</td>
<td>90</td>
<td>FY18: 95%</td>
</tr>
<tr>
<td></td>
<td>Decision if No Panel</td>
<td>180</td>
<td>FY18: 90%</td>
</tr>
<tr>
<td></td>
<td>Decision With Panel</td>
<td>320</td>
<td>FY18: 90%</td>
</tr>
<tr>
<td>180 Day PMA Supplements</td>
<td>Substantive Interaction</td>
<td>90</td>
<td>FY18: 95%</td>
</tr>
<tr>
<td></td>
<td>Decision</td>
<td>180</td>
<td>FY18: 95%</td>
</tr>
<tr>
<td>Real Time Supplements</td>
<td>Decision</td>
<td>90</td>
<td>FY18: 95%</td>
</tr>
<tr>
<td>Pre-Submissions</td>
<td>Written Feedback</td>
<td>70 or 5d prior to mtg</td>
<td>FY18: 1,530 (65%)</td>
</tr>
<tr>
<td>CLIA Waiver by Applications</td>
<td>Substantive Interaction</td>
<td>90</td>
<td>FY18: 90%</td>
</tr>
<tr>
<td></td>
<td>Dual CLIA/ 510(k)</td>
<td>180</td>
<td>FY18: 90%</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
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</tr>
</tbody>
</table>
General Overview

510(k) Submission Core Process

1. Submission Receipt
2. RTA Review
3. Substantive Review
4. SI Decision (PI or AI hold)*
5. Final Review & Rec.

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

1. Submission Receipt
2. RTA Review
3. Substantive Review
4. SI Decision (PI or AI hold)*
5. Final Review & Rec.

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

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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

START
Submission Receipt

Applicant submits a 510(k) submission to FDA

DCC date stamps submission upon receipt

DCC adds submission to tracking system

Issue resolved by Day 180?

Yes

DCC puts submission on hold

No

User Fee and/or eCopy issue?

Yes

Clock is set to zero. DCC assigns submission to an OHT/DHT

No

END
Submission Deleted

END
Industry Perspective

**eCopy Review Experience**
- eCopy holds
  - File name too long
  - FDA form format not accepted
  - Exceeded maximum file size of 50 MB
- User Fee holds
  - User Fee not paid
  - Back up during government shutdown

**Tips**
- Run submission through eSubmitter to package and check through eCopies software
- Submit user fee request and pay at least 2 weeks prior to submission and check website to see that it has been credited
Industry Perspective

Additional Thoughts???
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.

- **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

### 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
STEP 2: Refuse to Accept (RTA) Review

**START RTA Review**

- Submission is re-routed to right OHT/DHT in CTS
  - **OHT/DHT**
    - Does the 510(k) belong in another OHT/DHT or Center?
      - No
        - **Another Center**
      - Yes
        - **HOLD RTA1**
  - **HOLD RTA1**

- **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)

- **STEP 2. RTA Review**
  - Submission is assigned to LR. Review conducted using RTA checklist.
    - Conversion to another 510(k) type required?
      - Yes
        - Is it a General Wellness product?
          - Yes
            - **YES**
          - No
            - **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)
          - **HOLD RTA1**
        - **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)
    - **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)
  - **HOLD RTA1**

- **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)

- **CLASS III/PMA or pending PMA for the same device?**
  - Yes
    - **Consult Orange book Liaison and/or CDRH jurisdictional Officer**
  - No
    - **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)

- **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)

- **High-level NSE issues confirmed?**
  - Yes
    - **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)
  - No
    - **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)

- **Day ≤ 10 for Traditional & Abbrev. Day ≤ 5 for Specials**

- **Review completed by Day 15?**
  - Yes
    - **END REVIEW**
  - No
    - **Response received as Supplement by Day 180?**
      - Yes
        - **END RTAN**
      - No
        - **HOLD RTA1 (w/concurrence from DHT AD/Designee)**

- **Administratively acceptable?**
  - Yes
    - **END RTAA (w/concurrence from DHT AD/Designee)**
  - No
    - **STOP RTA REVIEW** Consult DHT AD to determine how to proceed. (RTAS* possible)

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*RTAS (RTA Skip) in CTS is rare. Please consult 510(k) Staff before RTAS recommendation.

**RTAN recommendation is an automatic acceptance of the 510(k) submission."**
Industry Perspective

RTA Review Experience
• Received only 1 RTA in the last year (20+ submissions)
  • Due to labelling issue
    • not included in submission (it was a Special with no change to labeling)

• RTA review process has become very consistent

• Reviewers may contact firms to avoid RTA

Tips
• Use Checklists

• Specify on checklist and in your table of contents where the required information is within the submission

• Use current FDA forms wherever possible
Industry Perspective

Additional Thoughts???
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

1. Submission Receipt
   - LR receives submission

2. RTA Review
   - LR reviews for basic completeness

3. Substantive Review
   - LR reviews for technical completeness

4. SI Decision (PI or AI hold)*
   - LR decides whether to Proceed Interactively (PI) or Issue an Additional Information (AI) Letter

5. Final Review & Rec.
   - LR completes final review

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**

**STEP 3. Substantive Review**
- **Input needed from FDA SME(s)?**
  - **Yes**: Interact with SME(s) within first week after RTA review
  - **No**: LR reviews submission and may interact with Applicant

- **LR provides review and SI recommendation in CTS**

  - **LR works interactively to address remaining deficiencies and provides a final recommendation.**

  - **SI Decision occurs by Day 60 for Traditional & Abbrev and target by Day 20 for Specials.**

**STEP 4. PI or AI**
- **SI Decision PI or Hold?**
  - **PI**: LR provides review and SI recommendation in CTS
  - **AI Hold**: Issue deficiencies in AI Letter

  - **Applicant requests Day-10 Call and/or SIM?**
    - **Yes**: Hold Day-10 Call and/or Submission Issue Meeting (SIM)
    - **No**: Applicant provides response by Day 180?
      - **Yes**: Submission is deleted. See 04220.510(k) Incomplete Responses and Deletions
      - **No**:
Industry Perspective

Substantive Review Experience
• Consistent, timely decisions from reviewers
• Common Submission AI Requests
  • Human Factors Testing or Rationale not to test
  • Cybersecurity Risks and Resolutions
  • Sample Size Rationale
  • Engineering Drawings
  • CAS numbers for chemical components including colorants

Tips
• Prior to submitting
  • Review Guidance Documents for Requirements
  • For any connected device include proper Cybersecurity information
  • Follow Recognized Consensus Standards whenever possible
  • Review the Submission – multiple individuals and times
• Following RAI receipt
  • Call the reviewer to get clarification (10 day call) – it may look like they are requesting testing when they just need a rationale
• When in doubt – Q-sub!!!!
Industry Perspective

Additional Thoughts???
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**

- **START**
  - Did Applicant address all the deficiencies?
    - No
      - If identified within the first 5 d, inform Applicant of INCR*
      - See 04220. Incomplete Response and Deletions SOP. Contact 510(k) Staff if identified after first 5 d
    - Yes
      - Complete response provided within remaining days on clock?
        - No
          - LR reviews response and works with SME(s) when appropriate
        - Yes
          - New info/response raises new deficiencies?
            - No
              - LR identifies major deficiencies not sent in original AI letter?
            - Yes
              - LR works interactively w/Applicant to resolve clarification questions and deficiencies when necessary
      - Applicant responds by Day 180?
        - No
          - See Missed MDUFA SOP
        - Yes
          - LR confirms that there are no patent exclusivity issues
          - LR provides review and final recommendation in CTS
            - By Day 80 for Traditional & Abbrev
            - By Day 28 for Specials
          - Review anticipated to exceed 90 Days?
            - No
              - See SE WI
            - Yes
              - See NSE WI
          - Is the submission heading towards NSE?
            - No
              - Designated authority/designee works with LR to make revisions when appropriate.
            - Yes
              - Designated authority/designee issues letter after Final concurrence.
      - If there is disagreement with review/recommendation see Section 6.5.8
- **END REVIEW**

**Notes:**
- *INCR = Incomplete Response
- See Section 6.5.8 for final concurrence procedure.
- By Day 90 for Traditional & Abbrev
- By Day 30 for Specials
Industry Perspective

Interactive Review Experiences
• 510(k) Summary revisions
  • Table format
  • Conclusion Statement
  • Other formatting and language requests
• FDA minimizes Industry work in many instances!!!
• No experience with new substantive questions during interactive review
• Most difficulty regarding clarification questions.

Tips
• Respond quickly (within hours as FDA wants to move as quickly as industry does)
• Review recent submissions for formatting and Conclusion wording
Industry Perspective

Additional Thoughts???
“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
New policies based on suggestions provided by review staff.

1. ODE Divisions provided ideas.

2. Ideas were collected and narrowed down by ODE Front Office.

3. Volunteers piloted selected ideas.

4. Office + Pilot Divisions/Branches discussed pilot implementation approach and general guidelines.

5. Pilot was initiated and tracked for four (4) months.*

6. Office evaluated pilot outcome and feedback.

7. Implementation of new policies w/ consideration of feedback.

*Data cut-off December 04, 2017
New 510(k) Policies

510(k) Submission Core Process

1. Submission Receipt
2. RTA Review
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RTA Addendum Policy

Day 10 Call Policy

Branch-level SE Policy**
First Round NSE (FR-NSE) Policy

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

New Policies
- Day-10 Call: Provides clarification prior to final review
- RTA Addendum: Notifies Applicant of issues earlier in review cycle
- DHT-level SE sign-off: Reduces time waiting for Division level sign off and review
- First Round NSE: Addresses NSE issues earlier in review cycle

Goal: Decrease TTD
Improve Efficiency

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

Submitter requests Day-10 Call.

Lead Reviewer or project manager schedules call around Day 10 after AI letter is issued.

Applicant provides clarification questions 48 h before the teleconference.

Call is Held

- The call is not expected to exceed 30 minutes

*LR ensures appropriate participants are included

*Day 10 window is flexible

*AI = Additional Information
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
Industry Perspective

Day-10 Call Experiences
• Highly recommended since it is very helpful in getting clarification from FDA on any AI item
• Typically just between the reviewer and company liaison
  • May include additional individuals from both parties depending on nature of the item(s)
• Helps to understand reviewers’ concerns
• Can indirectly give information on how to approach your response
• Reviewer may suggest a Submission Issue Q-sub
• Timing hasn’t always been within 10 days but has been less than 15
• Has saved unnecessary testing to support a response

Tips
• Use this process whenever possible to get insight around reviewer’s concerns
• Do not attempt to provide a full response on the call and receive FDA opinion or acceptance of planned response
• Be reasonable!!!
Industry Perspective

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

George Bernard Shaw, Irish writer
Industry Perspective

Agreed!!!
**SE Final Concurrence at the Branch Level**

**Description:** Straightforward 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
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

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responsive Applicant but cannot meet timeframe</td>
<td>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 <strong>NSE letter is issued within 30 calendar days from email issuance.</strong></td>
</tr>
<tr>
<td>Responsive Applicant and meets timeframe</td>
<td>LR reviews response and addresses minor clarification questions when appropriate.</td>
</tr>
<tr>
<td>Non-responsive Applicant</td>
<td>If the Applicant does not provide any response to the original email or voicemail, an NSE letter is issued <strong>no sooner than one day after the response was due.</strong> 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.</td>
</tr>
<tr>
<td>Late Responder</td>
<td>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 <strong>NSE letter is issued within 30 calendar days after email issuance.</strong> The LR is not obligated to review a late response if there is not sufficient time for an adequate review.</td>
</tr>
</tbody>
</table>
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.
Industry Perspective

Thoughts???
Least Burdensome (LB) Flag: What it is

• The LB flag is an approach to allow 510(k) submitters the opportunity for the informal review by or on behalf of Division management of an issue raised in an FDA request for additional information.

• **The goal** is to quickly address FDA requests that submitters do not believe are least burdensome or when submitters believe they are being held to a different standard
LB Flag: Criteria

• Discuss with Branch management first (e.g. day 10 call, email, Q-Sub)
• Limit to two topic areas (e.g. biocompatibility, sterility, reprocessing, software, etc.)
• More than two topic areas contact 510k_Program@fda.hhs.gov
• Should throw the flag within 60 calendar days of the deficiency letter
LB Flag: What to include in your Email

• Upon meeting the criteria, send a short email (e.g., 1 -2 page) that includes
  1. Summary of the deficiencies under disagreement
  2. Summary of relevant communications with Branch Management
  3. A proposed path forward
LB Flag: How to Submit

• Send email to the lead reviewer and their Branch Chief. Also copy 510(k) mailbox
• Within 2 business days of your email you should receive an acknowledgment
• If you do not meet the criteria you will be notified
LB Flag: Additional Interactions

- FDA may request a phone call to discuss your concern further
- Intend to communicate feedback from Division Management no later than 21 calendar days of the receipt
- The LB Flag does not change the deadline for response (180 days)
- Started on March 4, 2019
Industry Perspective

Thoughts???
Safety and Performance Based Pathway

• Expansion of the concept of the Abbreviated 510(k) for certain, well understood device types

• FDA expects to begin implementation of this pathway once the first device types and applicable performance criteria have been identified

• Once the FDA begins to implement this pathway, a medical device manufacturer will be able to meet FDA-identified performance criteria to demonstrate the device is as safe and effective as a predicate device
Safety and Performance Based Pathway: Eligibility

• Appropriate when the new device has indications for use and technological characteristics that do not raise different questions of S & E than the identified predicate

• The predicate is within the scope of the eligible device types

• The performance criteria align with the performance of one or more legally marketed devices of the same type as the new device; and

• The new device meets all the FDA-identified performance criteria
Safety and Performance Based Pathway: Future Plans

• FDA will issue future guidance

• Industry may suggest device types for consideration

• FDA intends to maintain a list of device types as well as the testing methods recommended in the guidances where feasible and any other relevant information
Industry Perspective

Thoughts???
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
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.

<table>
<thead>
<tr>
<th>INCREASE IN RISK</th>
<th>DECREASE /EQUIVALENT RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CONDUCTING A BENEFIT-RISK ASSESSMENT IS RECOMMENDED.</strong></td>
<td><strong>Conducting a benefit-risk assessment is likely not recommended to determine whether the new device is “as safe and effective” as the predicate device.</strong></td>
</tr>
<tr>
<td>FDA evaluates the nature of the increased risk and considers whether additional measures may help to mitigate the increased risk. <strong>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.</strong></td>
<td>FDA will generally determine the new device <strong>SE</strong> to the predicate device when there is increase/equivalent benefit and decreased/equivalent risk.</td>
</tr>
<tr>
<td><strong>Conducting a benefit-risk assessment is likely not recommended to determine whether the new device is “as safe and effective” as the predicate device.</strong></td>
<td><strong>Conducting a benefit-risk assessment is recommended.</strong></td>
</tr>
<tr>
<td>FDA will generally determine the new device <strong>NSE</strong> to the predicate device when there is a decrease in benefit and an increase in risk.</td>
<td>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”. <strong>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.</strong></td>
</tr>
</tbody>
</table>
Industry Perspective

Thoughts???
Pilots

Pilot Webpage
Quality in 510(k) Review Pilot

**Description:** The purpose of the Quality in 510(k) Review Program pilot is to determine 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
Industry Perspective

Thoughts???
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

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Industry Perspective

Special 510(k) Pilot Experience
- Utilized Pilot with 4 submissions
- Reliance on consensus standards or same test methods as used to validate the original design
- HUGE benefit due to several submissions each year to expand Indications for Use Statements — now can be submitted as Specials and save two months of review time per submission

Tips
- Use the New Checklist that has been posted on FDA website
- Be reasonable with submissions
- When in doubt – Q-sub!
Industry Perspective

Additional Thoughts???
IVD Smart Template

- 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
Industry Additional Thoughts

• Decreased time to final decision!
  • Submission-to-clearance time has decreased!
• Increased interactive review
• RAI Trends
  • Human Factors (Usability) Engineering
  • Cybersecurity – every device with any kind of connectivity
  • More detailed Indications for Use Statements
• Overall more collaborative approach to review and clearance
  • FDA working with industry on novel approaches to reduce the submission-to-clearance time
  • Least Burdensome means something
  • Transparency is very clear
“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!