The content on this webpage is developed by NIH SEED based on its collective experience working with the NIH innovator community. This information has been developed, for informational purposes, to address questions frequently asked by NIH awardees, and represents the experiences of the subject matter experts who contributed to its development.

De Novo Pre-Submission Meetings

Context

Most Class II (moderate risk) devices are "cleared" through review of a 510(k) submission—you provide data that demonstrates the new device is substantially equivalent to another device (i.e., a predicate device) already cleared by FDA. However, a new device may be novel enough that it may not be comparable to existing legally marketed devices because of differences in intended use, technological characteristics, or both. In that case, novel low-to-moderate risk devices may instead receive marketing authorization through the De Novo regulatory pathway. Unlike a 510(k) submission, where the new device must demonstrate substantial equivalence to the predicate device, review of the De Novo request is a standalone determination of whether general controls[1] (for a Class I device) or general and special controls[2] (for a Class II device) can provide reasonable assurance of safety and effectiveness, taking into account the probable benefits and probable risks of the device. It is also likely that granting of your De Novo request will define the special controls (if class II) that will set the standard for similar devices in the future.

As soon as you think your new low to moderate-risk device may not have an acceptable predicate, you may have questions about FDA's thoughts regarding your intended use/indications for use (IFU), and pre-clinical testing plan (e.g., biocompatibility, sterility, electromagnetic compatibility). You may also have questions about the proposed special controls or the expectations of clinical data needed to support your request. These and other types of questions may be addressed prior to the submission of your De Novo Classification Request, within a pre-submission meeting. FDA may also provide feedback on whether a device is eligible for the De Novo classification process, including whether a potential predicate device exists, and/or to advise you on the documentation needed in a subsequent De Novo request.

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[1] General controls mean the controls discussed under sections of FDA regulations concerning adulteration, misbranding, registration, listing, and premarket notification, banned devices, notification and other remedies, records, reports, and unique device identification, and general provisions.

[2] *Special controls* mean the controls needed to provide reasonable assurance of safety and effectiveness for a generic type of device that is Class II. Special controls include performance standards, performance testing, post-market surveillance, patient registries, development and dissemination of guidelines.

How to Prepare

Become Familiar with the Content of a De Novo Request

The De Novo request review process focuses on two important elements that include the benefit-risk analysis and general/special controls.[1, 2]

Benefit-Risk Analysis

A De Novo request should include a discussion of the probable benefits from use of the device and any probable risks from such use. As you start to develop the benefit-risk analysis, reviewing existing De Novo decision summaries of similar devices may help you develop the appropriate scope and content.

General/Special Controls

A De Novo request should identify the device as Class I or Class II. If it's Class I, the De Novo request should include a description of why general controls provide reasonable assurance of safety and effectiveness. If it's Class II, the De Novo request should identify proposed special controls and describe how general controls and special controls provide a reasonable assurance of safety and effectiveness.

Reviewing existing De Novo decision summaries will provide examples of special controls and the level/language/content of information likely to be needed to support your proposed De Novo request.

Technical Data and Information

For pre-submissions to discuss a potential De Novo, it is often helpful to include:

- A description of your device, including its function
- A description of the technological characteristics of the device
- The proposed indications for use of the device
- Identification of similar/related medical devices with a comparison of how they are similar/different compared to your device, as applicable
- A detailed plan of how the safety and effectiveness of the device will be demonstrated, as applicable
- Proposed special controls for the device, as applicable, if proposed device is Class II.

It is important to include specific questions in your pre-submission package addressing your proposed validation plan and proposed special controls for the device, as applicable. FDA's role is to respond to your pre-submission. FDA will not plan your product development strategy.

Regulatory Resources

- De Novo Classification Request public webpage
- Regulations
    - Medical Device De Novo Classification Process Final Rule – this final rule establishes procedures and criteria related to requests for De Novo classification
- Guidance documents

    - Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program – overview of mechanisms for requesting FDA feedback
    - De Novo Classification Process (Evaluation of Automatic Class III Designation)– guidance on the process for the submission and review of a De Novo classification request
    - Acceptance Review for De Novo Classification Requests – describes procedures and criteria FDA uses in assessing whether a De Novo request contains the information necessary to permit a substantive review
    - Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications – overview of benefit-risk considerations
- Public FDA databases
    - Product Classification – access to regulatory information such as product descriptions, codes, and Center for Devices and Radiological Health (CDRH) review panels
        - Tip: Include information on related product codes and regulations in the background information section to support that the De Novo pathway is appropriate for the proposed device
    - PMA, De Novo, 510(k) – access to decision summaries for related devices
        - Tip: Read and review decision summaries for clinical and non-clinical testing overviews, IFU statements, and any relevant general/special controls for similar devices
- NIH network
    - Work with program officers and obtain regulatory feedback within NIH
    - NIH awardees can request a meeting with the NIH Small Business Education and Entrepreneurial Development (SEED) Innovator Support Team to ask questions about this process and request they review the draft cover letter and overall approach. However, the SEED office does not review or comment upon the scientific validity or data elements of the submission.
- Direct links to NIH resources on related topics
    - Written communication (add hyperlink when posted)
- Submission procedures
    - CDRH information page on medical device submissions (eCopy, eSTAR). This is a recently updated process so obtain the most up to date information from FDA.
    - User Fees and Refunds For De Novo Classification Requests – outlines policy and procedure for De Novo request user fees and refunds
    - FDA and Industry Actions on De Novo Classification Requests: Effect on FDA Review Clock and Goals – outlines actions that FDA and industry can take on a De Novo request and how that affects the submission review clock

What to Expect

Timeline

The timeframe for FDA to provide feedback on your pre-submission requests is within 70 days of receipt of the accepted pre-submission or five days prior to the scheduled meeting, whichever is sooner.

Along with the pre-submission, you should provide FDA with three or more proposed dates, generally between 60 and 75 days after submission, to hold the pre-submission meeting. FDA may reach out to find a mutually agreeable date if none of the three proposed dates are possible.
It is your responsibility to take notes and submit meeting minutes, along with any presentation materials, to FDA for review within 15 days of the meeting. These minutes will be added as an amendment to the submission.

For the De Novo submission itself, FDA intends to complete its review within 150 total review days. During the review process, FDA may send a Request for Additional Information letter, which pauses the review clock. You will have 180 days to fully respond to any deficiencies outlined in the letter. After you respond to the request for additional information, the review clock resumes. Once FDA has received your complete response, they intend to engage in an interactive review process (e.g., via email) until a decision is communicated.

Plan for Meeting Outcomes and Next Steps

Before your pre-submission, the Product Classification Database can help you determine which classification your device might fall into. If FDA's feedback suggests that a De Novo may be appropriate, you may reference the meeting and FDA feedback in the De Novo request itself.
If, prior to sending in your De Novo, you believe additional feedback from FDA is needed, then a supplement to the pre-submission may be submitted. A pre-submission supplement is a new request for feedback and/or a meeting about the same device and indications for use and has the same review timelines as the pre-submission. If FDA provides feedback that the device is not appropriate for a De Novo submission, your device may be a higher risk Class III device requiring a full Premarket Approval (PMA) application. If there is precedent for products like yours to be approved via PMA or cleared via 510(k), then that precedent will typically be upheld.

FDA intends the feedback they include in response to a pre-submission will not change for any future submission related to the same device provided that the information submitted does not raise any important new issues materially affecting safety or effectiveness.

General Tips

- Carefully consider the progress of the device development when determining when to initiate a De Novo pre-submission meeting request with FDA. A good time to request a De Novo pre-submission meeting with FDA is when the device is near its final design. You should have a well-

documented design plan, general and/or special controls, and details of the validation data (as applicable) supporting the De Novo submission.
    - Initiating a pre-submission meeting early might mean that you still have several unanswered questions related to the design of your device, special controls, or plan of study. Under these circumstances, FDA may not be able to provide as valuable feedback as when finalized designs and plans are provided.
    - Submitting a pre-submission meeting request too late may mean you have spent time and money collecting data that FDA views as insufficient to support a marketing application.
- It is your responsibility to develop the controls, design a study, and write an IFU statement. As part of the De Novo pre-submission meeting process, FDA reviewers provide feedback to the information submitted in the meeting request. All written questions should refer to content provided in the pre-submission package accompanying the pre-submission meeting request.
- Use the pre-submission meeting to address any confusion or lingering questions based on the FDA's written feedback. Re-presenting information already provided in the pre-submission is not advisable. Also, FDA will not provide feedback on any new data presented during the meeting.

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