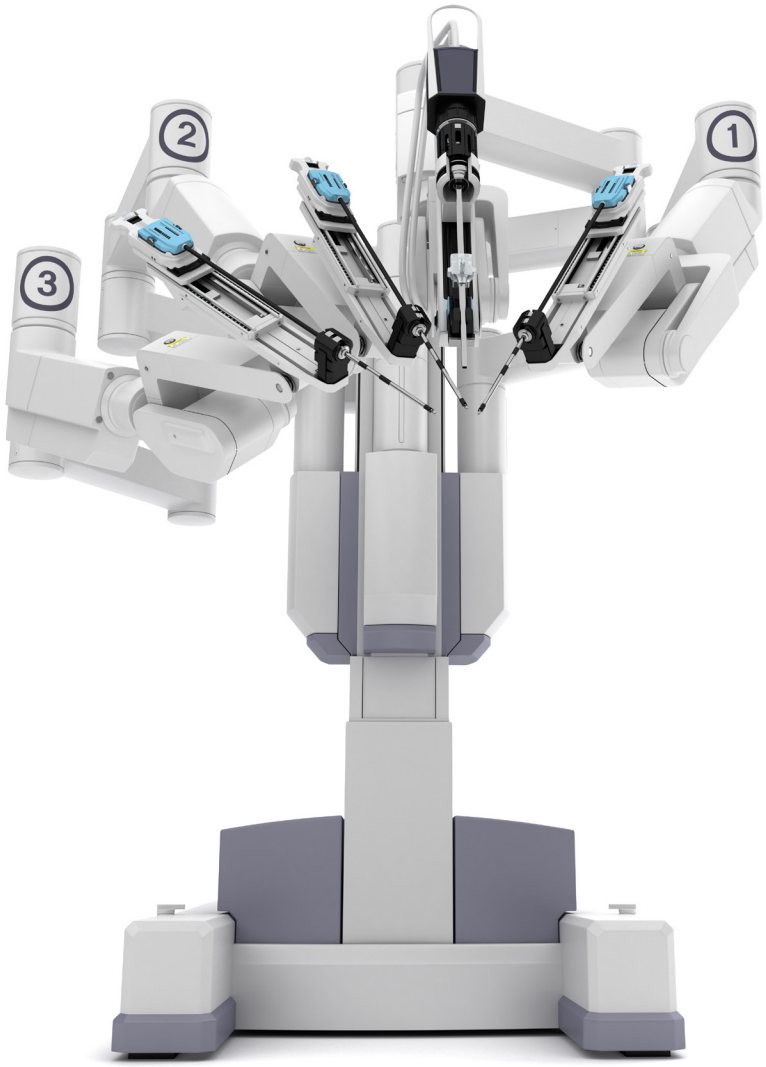
in focus

Medical devices

How to get the most out of 510(k) Pre-Submission meetings with FDA



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FDA's Pre-Submission (Pre-Sub) program is invaluable in helping companies determine a clear regulatory pathway for the successful launch of a medical device.

As a former Lead Reviewer at the FDA, TSG Consulting's Om Singh, PhD, understands what's needed to create a comprehensive Pre-Sub package to receive the most effective feedback from the FDA.

In this paper Dr Singh outlines the benefits of a Pre-Sub meeting, the information that needs to be included in the Pre-Sub package and how FDA provides feedback.

The United States regulatory landscape for approving medical devices is complex and navigating it can be a challenge. According to the US Food and Drug Administration (FDA), the regulatory agency responsible for approving medical devices, the majority of 510(k) submissions have major deficiencies or are rejected the first time. Medical device manufacturers are able to reduce the chances of rejection by obtaining feedback through the FDA's pre-submission process. By having a clear understanding of this process, companies can gain enormous benefit from the feedback given as they attempt to bring their medical device to market.

The 510(k) submission allows applicants to fast-track approval of a medical device by claiming it is "substantially equivalent" to a device that has already been cleared and marketed in the US. However, depending on the modifications made to the device, this process may begin with multiple setbacks for the applicant. A formal Pre-Submission meeting with the FDA is an opportunity for applicants to gauge the FDA's current thinking on their device's overall safety and effectiveness and help improve the likelihood of a successful 510(k) submission.

The Agency embraces and encourages applicants to participate in the pre-submission process and holds roughly 1,500 Pre-Sub meetings per year. According to the Medical Device User Fee Amendments (MDUFA) IV, FDA expects to provide feedback for at least 1,950 Pre-Subs received in 2022[1] as it strives to assure more timely access to safe and effective medical devices.

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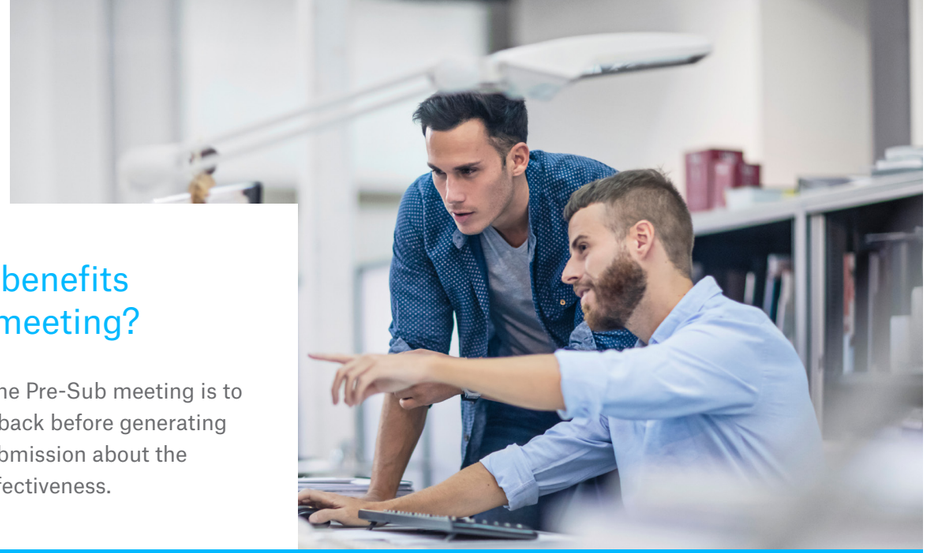
[1] MDUFA Performance goals and procedures, Fiscal years 2018 through 2022, available at https://www.fda.gov/media/102699/download



What are the benefits of a Pre-Sub meeting?

Primarily, the aim of the Pre-Sub meeting is to obtain the FDA's feedback before generating data for the 510(k) submission about the device's safety and effectiveness.

The Pre-Sub program is useful for a wide variety of regulatory strategies; however, it is particularly useful for medical device manufacturers who:

1. Are unfamiliar with the regulatory pathway
2. Are unsure how to prove their device's safety and effectiveness
3. Do not know how to generate the required data for FDA evaluation
4. Need guidance to develop methodologies for data generation
5. Are utilizing novel technology in a "first of a kind" device
6. Are unclear on indications for use that qualify a device as "first of a kind,"
7. Intend to address the FDA with upcoming technology in a "first of a kind" device
8. Intend to modify their device's design and material
9. Intend to add, remove, and/or modify intended uses for their device based on new findings
10. Are seeking guidance on the clinical and non-clinical testing requirements

Pre-Sub meetings are completely voluntary for applicants, but give you and your company an opportunity to interact with the FDA at no cost. The net outcome of a Pre-Sub meeting is to obtain the FDA's written feedback on your existing technology and the path forward for device development and clearance or approval. The FDA's feedback is highly desirable in situations where a company may need to provide more information to ensure acceptance of the submission. It is imperative that FDA's advice is sought early enough to improve the quality of the data for inclusion in the actual 510(k) submission.

When should you request a Pre-Sub meeting?

Per FDA guidance,[2] "The main purpose of the Pre-Sub program is to provide the opportunity for an applicant to obtain FDA feedback prior to an intended submission of an IDE [Investigational Device Exemption] or marketing application." This program is also helpful for applicants who are developing protocols to generate data to prove their device's safety and effectiveness during the review phase. Consequently, this program provides an efficient path to develop all types of medical devices from their basic concept and to market innovative technologies in the medical device area.

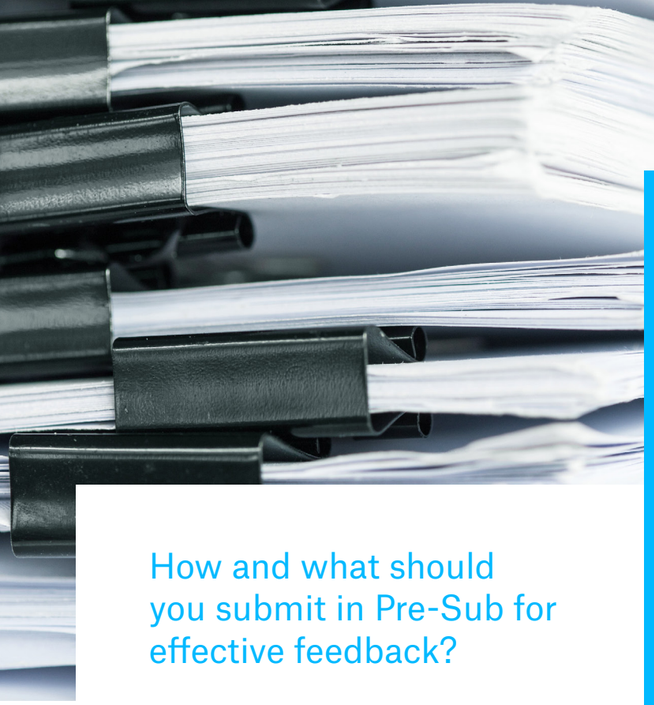
For medical device applicants, the Pre-Sub program is useful to determine a clear regulatory pathway for the successful launch of the device. As noted above, Pre-Sub meetings are not required; any simple and straightforward medical device can be submitted directly via 510(k), although you may wish to seek expert advice on the technical aspects of the submission. Nor is it necessary to proceed with a Pre-Sub for well-understood products or straightforward modifications. However, minor modifications could present challenges in labeling, which can also be addressed by seeking advice from an outside expert.

> The Pre-Sub program provides applicants with the opportunity to obtain FDA feedback prior to submitting an Investigational Device Exemption or marketing application.

It is always worth submitting a Pre-Sub request if your device is in the development phase to discuss the compatibility of the technology in the current regulatory environment and the respective testing requirements. Therefore, the Pre-Sub dossier should contain a well thought out device development strategy, mechanism of action towards intended use, related claim on draft labeling, and testing performed or tentatively planned to evaluate the safety and effectiveness of the device. The Pre-Sub dossier should be well articulated and defendable; it is not the place to disagree with FDA's prescribed testing method or to share scientific theories. It is important to note that seeking and obtaining FDA advice in a Pre-Sub meeting does not guarantee device clearance or approval. In Pre-Subs, the FDA will only review and provide feedback on protocols and the Agency does not review existing data.

Depending on the meeting type, the FDA has different time frames to provide the requested feedback. For Pre-Sub meetings, written feedback can be obtained within 70 days or five days prior to a scheduled meeting, whichever comes sooner. On-site meetings upon request are typically handled within 60-75 days. However, this time period can vary up to 21 days for urgent public health issues.

[2] Request for Feedback on Medical Device Submission: The Pre-Submission Program and Meetings with Food and Drug Administration Staff, Guidance for Industry and Food and Drug Administration Staff, 2017



How and what should you submit in Pre-Sub for effective feedback?

When making a Pre-Sub request, it is critical to understand the type of information to include in the package to receive effective feedback. The FDA recommends that the Pre-Sub package be well organized, and provide the material outlined in the box opposite.

It is important to recognize that it is FDA's mission to protect public health, and they do their job by challenging applicants to defend their product and any claims made. FDA applicants need to articulate to FDA the overview of their device, the indications for use, and the problem the company is trying to solve. The Pre-Sub program is a unique opportunity to interact with the FDA; therefore, avoid over achieving the indications for use, being argumentative or confrontational. Rather than thinking of FDA as getting in your way, it is important to engage FDA as a partner and enabler to bring to the market the safest and most effective product you can. As a former Lead Reviewer at the FDA, I understand the pressure is enormous on both parties because the wrong decision could have a huge impact on human lives.

What to submit in the Pre-Sub package

1. Cover letter, briefly introducing the device and reason for Pre-Sub request
2. Table of contents to help locate documents in the file
3. Detailed device description – key for the FDA to understand the technology
4. Identification of the predicate device and a clear and focused intended use
5. Clear explanation of the technology and product development. Remember, trade secrets and confidential commercial information (21CFR 20.61) are protected at the FDA. In addition, applicants can identify trade secrets and confidential information per 21CFR 812.38
6. Summary of performance testing and any protocols developed to evaluate the proposed technology
7. List of any previous communications with the FDA or staff
8. Questionnaire section:
   i. For efficient feedback, it is extremely important to draft questions well
   ii. If you believe any testing is incompatible with the device design, this should be supported by valid scientific evidence when you raise your concerns about the necessity of such testing for the proposed technology
   iii. It is always advisable to ask specific questions about the clinical and non-clinical evaluation requirements for the proposed technology in the subject device

How will you receive Pre-Sub feedback?

There are different avenues to obtain Pre-Sub feedback, including written feedback without a meeting, teleconferencing, or a one-on-one meeting in person. Regardless of the feedback type, the FDA responds to the Pre-Sub requests within 70 calendar days of receipt. Depending on what questions you have, written feedback could be sufficient to move forward with device development. Teleconferences or physical meetings allow you to interact personally with FDA staff and express your interest in the technology. If a teleconference or meeting is held, the meeting minutes will supplement the written feedback in the FDA's official record. The FDA reserves the right to modify their feedback based on new scientific developments. If any technical issues arise during the meeting, applicants are not obligated to address or resolve them in the final submission, but it is recommended that you do so.

Finally, the Pre-Sub program is designed to help medical device manufacturers. The FDA's feedback can help you prepare your submission package, and can also help you in the process of developing your device. It is advisable to address the feedback and file your final submission at your earliest convenience before new scientific developments occur in the field.

About the author

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Dr Singh has substantial experience working with companies looking to commercialize medical devices and antimicrobial products such as sterilants, high-level disinfectants, and antiseptics. His previous experience working at the US Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) allows him to better advise companies of anticipated regulatory hurdles when seeking approval and registration for their human health products.

How TSG can help

For almost 30 years, TSG Consulting has provided companies around the world with regulatory guidance and scientific expertise. Our consultants can help in the Pre-Sub process by:

- Working with clients to develop an overall strategy for the Pre-Sub meeting and 510(k) approval by addressing the requirements
- Assist in the preparation of the Pre-Sub documentation including the intended use statement, anticipated data/protocols, and draft product labels
- Develop specific questions for the FDA and presentation materials
- Represent and support clients at the FDA in the Pre-Sub meeting, providing consultation throughout the meeting

Interested in learning more?
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About TSG Consulting

TSG Consulting provides companies with high-quality regulatory and scientific consulting services. We help clients worldwide address the technical and regulatory issues in taking their products to market in multiple jurisdictions. Our scientific expertise, regulatory knowledge and understanding of local nuances enable our clients to navigate the complex and ever-changing regulatory landscape across the globe.

We serve a number of key markets and industry sectors including agricultural, industrial, consumer, food and beverage, animal health, and medical. Our teams comprise scientists and regulatory experts – many of whom have previously held positions at regulatory agencies, departments, and in industry. This combination of science, regulatory expertise and knowledge of how institutions and industry operate provides our clients with superior and well-rounded guidance.

TSG Consulting has offices in the USA, Canada, France, Germany, Spain and UK. TSG is a Science Group (London listed) company.

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