Six steps to obtaining 510(k) premarket clearance for medical devices

TSG Consulting’s Laurie Clarke, VP and Principal of Medical Device Regulatory, says it’s a good idea to devise a regulatory strategy at an early stage of medical device development. In this article she outlines six major steps that underpin an effective approach.
What’s the best way to go about obtaining FDA authorization to market a medical device? This is the key question frequently put to us at TSG. Naturally, every situation is different, but the single most important factor is a regulatory strategy. And the earlier this can be developed, the better.

A regulatory strategy brings focus and purpose

Put simply, a regulatory strategy aims to achieve FDA authorization in the most efficient way possible for the device in question. It clearly lays out steps that need to be taken to reach the desired goal, which for many medical device companies is obtaining FDA clearance for the proposed indication via a 510(k) premarket notification. For that reason, we focus on 510(k) notices in this discussion, although the general principles also apply to other types of premarket submissions.

How to develop and implement a successful 510(k) regulatory strategy: six key steps

1. Do the groundwork
   Assess the product concept, look at the technologies involved and consider how well known and widely used they are. If there’s an established regulatory path for devices of this type, there’s a good chance that the new product will follow a similar route. With 510(k)s, it’s important to think about how ‘substantial equivalence’ might be demonstrated. Getting this right results in a more streamlined route to authorization.
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Take advantage of FDA’s pre-sub option when appropriate

A pre-submission (pre-sub) is a voluntary step whereby companies submit a formal written request for FDA feedback ahead of a premarket submission. The goal is to convince FDA to accept the company’s proposed approach.

This step should be considered when it is not clear whether FDA would agree with proposed predicate device(s) and/or the type and amount of performance data needed to demonstrate substantial equivalence to the predicate(s). In addition, pre-subs are commonly used to obtain FDA’s feedback on proposed protocols for clinical (human studies). In such cases, the pre-sub typically describes the device, identifies the most significant similarities and differences between that device and its predicate(s), summarizes any testing already conducted and provides protocols for proposed testing. The pre-sub explains how the company intends to demonstrate substantial equivalence based on the proposed comparison and the results of testing. It also includes specific questions for FDA about the key regulatory issues.

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Meet with the FDA

If the pre-sub is accepted, FDA will schedule a meeting with the company, and provide written responses to the company’s questions before this takes place. Such meetings are a valuable opportunity to work through any remaining issues regarding the proposed regulatory pathway and to take on board any suggestions regarding predicates, if applicable, or testing that might be conducted.

It’s important to be well prepared for these meetings, and to understand the type of guidance that can be given. FDA representatives cannot answer overt questions about whether a certain approach will lead to clearance. However, the meeting should provide a good understanding of the type and amount of data required to evaluate the safety and efficacy of the device. In addition, the company can obtain clarification regarding FDA’s responses to its questions or explain how it proposes to address Agency recommendations.
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4 Obtain the required data
Armed with FDA feedback, companies can take a decisive and well-informed approach to the generation of data surrounding device performance and capabilities. This might involve bench, animal, and/or clinical data. FDA’s approval of an IDE is required to conduct a significant risk device clinical study. If the company obtained FDA’s feedback on a test protocol and agrees with the Agency’s suggested changes, the company should revise the protocol accordingly. If the company wants to reject or modify FDA’s suggested changes, it should obtain additional Agency concurrence to reduce the risk of FDA rejecting study data. If the company did not submit a pre-IDE, it should base the study protocol, to the maximum extent possible, on FDA’s testing recommendations in a guidance document about that specific type of device, if any, and/or the testing conducted on its predicate device(s).

5 Prepare premarket notification
Following completion of testing, the 510(k) submission can be compiled, drawing on supporting data and outlining substantial equivalence to the primary as well as any secondary predicates. Care must be taken to ensure the submission is clear, concise and free from mistakes to reduce the risk of FDA misunderstanding the device, requesting unnecessary additional testing, and/or questioning the validity or relevancy of the data. At this stage, it’s always a good idea to pass the documentation to a trusted third party for an impartial review. They may notice inconsistencies or ambiguities that the core team has overlooked due to close involvement with the project.
**What are the benefits of a 510(k) regulatory strategy?**

Taking a proactive and premeditated approach from the outset puts the company in the driving seat. It can satisfy any existing FDA requirements for demonstrating that the type of device is substantially equivalent, or define those requirements and apply them to its device.

If the company files a pre-sub, it will obtain substantive feedback from FDA. If the company then modifies its regulatory plan based on FDA feedback prior to submitting the 510(k) notice, it minimizes the risk of a delayed or negative decision. For instance, the agency is less likely to request a major change or additional performance data during its review of the device. Ultimately, a well-conceived regulatory strategy increases the likelihood of FDA clearing the device and accelerates time to market.

**FDA’s 510(k) review and decision whether to clear the device**

If the 510(k) is physically submitted to FDA, an Agency communication naming the lead reviewer and Acceptance Review status will be sent within 15 days. If the submission is not accepted for review, it’s placed on Refused to Accept (RTA) Hold and the submitting company has 180 calendar days to address any deficiencies cited. Upon submission of the missing information, FDA will conduct another RTA review. The ideal outcome at this stage is for FDA to accept the 510(k) and progress to Substantive Review where a comprehensive analysis of the submission takes place. If the company uses FDA’s voluntary electronic 510(k) form, the Agency does not conduct an RTA review regarding the submission.

FDA’s goal is to provide substantive feedback within 60 days of receipt of the 510(k) that resulted in FDA’s acceptance of the submission.

In many cases, the substantive feedback is a request for additional information (RAI). The company has 180 days to respond to an RAI, or the 510(k) is automatically withdrawn. FDA usually stops the review clock until an RAI response is submitted unless it believes that the requested information could be provided in a short period of time (often a week or less). In this case, it may decide to let the review clock run and work interactively with the company to address any remaining issues by a certain date. FDA’s goal is for its total review time for the initial 510(k) plus the company’s responses to be 90 days or less.

Based on information and data provided in the 510(k) notice and responses to RAIs, FDA determines whether the device is substantially equivalent. If FDA determines that the device is Not Substantially Equivalent (NSE), it will identify the grounds for that determination in its decision letter. The company would have to address those deficiencies in any subsequent premarket submission to market the device. The type of subsequent premarket submission required (another 510(k) notice, a de novo request, or a premarket approval application) would depend on the grounds for NSE.

If FDA finds that the device is substantially equivalent, it will issue a letter granting premarket clearance. An attachment to that letter will identify the indications for use for which FDA cleared the device and its designation as a prescription and/or over-the-counter (“OTC”) device. The company can then market the device for those indications if the manufacturer complies with FDA’s device establishment registration and listing requirements and the applicable quality systems regulations.

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Laurie Clarke has previously worked as FDA partner for several US law firms. Her more than 30-years of FDA regulatory experience regarding medical devices means she brings valuable insights to support companies developing new device concepts.
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 France, Germany, Spain, UK, USA and Canada. TSG is a Science Group (London listed) company.

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