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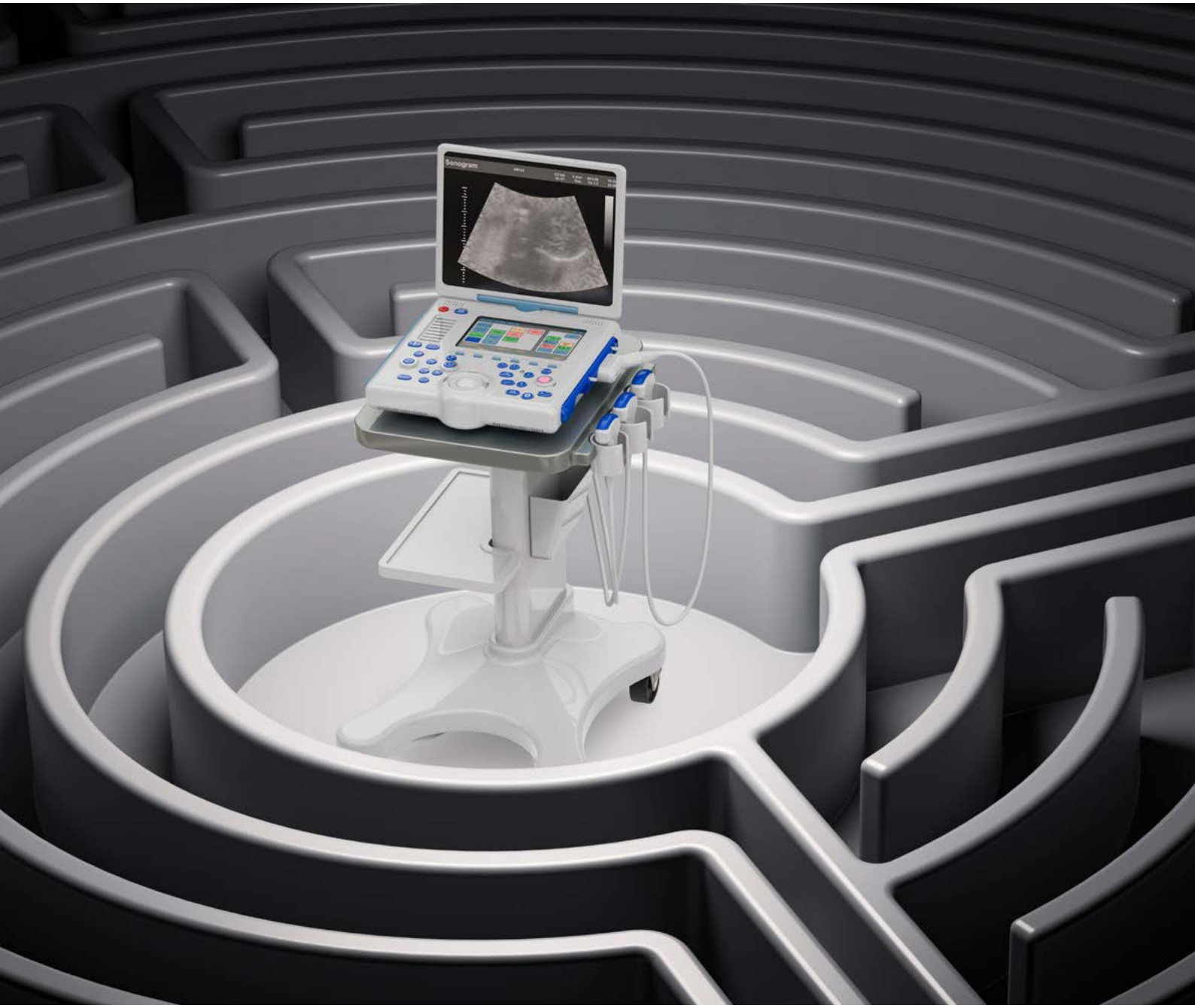
INSIGHT PIECE

Determining the best regulatory path for your medical device

TSG's Laurie Clarke (VP of Medical Device Regulatory) and Sagentia Innovation's Rob Morgan (VP Medical) pool their expertise to help manufacturers find the most effective route to market.



What's the best route to market for your medical device? Read our insights on how to balance regulatory and commercial requirements.

When it comes to regulatory matters, manufacturers of medical devices often hold conflicting objectives. On the one hand, they want to market their product as being novel or unique. At the same time, they need to market their devices as soon as possible to generate revenue and capture market shares. The 510(k) premarket notification path is generally the quickest and least expensive route for obtaining FDA's authorisation to market a device. However, the 510(k) route is only for devices that are substantially equivalent to legally marketed devices. Accordingly, 510(k) devices cannot claim to be novel or unique. FDA reviews novel devices through the De Novo review route, if they are low to moderate risk, or the Premarket Approval (PMA) route, if they are high risk. Thus, it often takes longer to obtain premarket authorisation for a novel/unique device.

So, what are the pros and cons of PMA versus 510(k)? What are the alternatives such as De Novo down classification? And how can manufacturers of medical devices exert more influence over their regulatory destiny?

Premarket Approval vs. Premarket Notification 510(k)

The 510(k) clearance route offers significant advantages over PMA in terms of time to market. FDA's goal is for the Agency's total review time for a 510(k) notice to be 90 days or less. In 2021, the average total time from submission of a 510(k) notice accepted for review until FDA reached a final decision was 124 days, of which 76 days were FDA's total review time and 47 days were the submitter's total response time to FDA's requests for additional information. Naturally, the preparation of 510(k) submissions still requires care and expertise to evidence safety and effectiveness. Relevant performance data will be needed unless the new device is identical to its predicate. Furthermore, FDA might request additional data during the Agency's review of the submission, which will delay FDA's decision on the submission. If the company cannot provide the study within 180 days of its receipt of FDA's request, e.g. FDA asked for clinical data with the primary endpoint being measured at one year, or the company decides not to do so, then the 510(k) notice will automatically be withdrawn at the expiration of the response period. The same response time frame applies to PMAs. However, the review process overall is far less burdensome than that for PMA.

Progressing a new device from concept to market via the PMA route is longer and more complex. PMA applicants must conduct in-depth scientific studies to provide reasonable assurance of the device's safety and effectiveness for its intended use. Most PMAs include data from at least one clinical (human) study. FDA usually conducts a pre-approval Quality System Regulation (QSR) inspection of the manufacturing facility or facilities and Bioresearch Monitoring (BiMo) audits of the study sponsor and one or more of the clinical study sites, both of which can reveal issues that the company needs to resolve before FDA can approve the device. The average total time for FDA to reach a decision on a PMA in Fiscal Year (FY) 2020, which is the most recent period for which data is publicly available, was 524 days of which 319 days were FDA's total review time and 205 days were the applicant's total response time. In comparison, the average total time for FDA to reach a decision on a 510(k) during that same period was 142 days.

The fee FDA charges to review a PMA, which is called a user fee, is also significantly higher than the Agency's standard user fee for 510(k) notices ($374, 858 vs. $12,745 in FY 2022). A company that FDA has designated as a small business because its gross sales or revenue were/was $100 million or less the previous year qualifies for reduced user fees of $93,714 for PMAs and $3,186 for 510(k)s, which is still a big difference. However, FDA will waive the user fee for the first PMA for a designated small business with $30 million or less in gross sales or revenue the prior year. The company must obtain small business designation each year to continue to qualify to the reduced user fees.

In addition, PMA devices are subject to numerous postapproval requirements. FDA conditions approval of many PMAs on their conducting postmarket studies or postmarket registries, which the Agency rarely requires for 510(k)-cleared devices. PMA-approved devices, unlike 510(k)-cleared devices, must submit annual reports, which include summary information about adverse events and recalls, to FDA. The user fee for an annual report is $13,130 or $3,280 for small businesses in FY 2022.

Almost all modifications to PMA-approved devices require FDA approval, while only modifications that could significantly affect the safety or effectiveness of a 510(k)-cleared device would require a new 510(k) clearance. The user fee for 180-day PMA supplement is $56,229 ($14,057 for small businesses). Moreover, major changes, such as a new indication, require approval of a new PMA. Thus, FDA's more rigorous regulation of Class III PMA devices, as well as higher user fees, continue after their approval.

A PMA is a significant and costly undertaking, and it is only feasible for smaller or start-up device manufacturers if they have raised substantial funding. However, in some circumstances, the benefits of being first to market with an entirely new medical device outweigh the costs, timescales and risks involved. For some devices, the PMA route is the only regulatory path available. From a commercial perspective, achieving PMA demonstrates sophistication, differentiation and market leadership.

A commercially minded regulatory strategy

In the later stages of the product development lifecycle, it can be really difficult to make changes that will alter a device's classification. That's why we advocate integrating regulatory and product development strategies from the outset. In this way, technical decisions that will impact the regulatory path can be shaped by the desired commercial outcome.

When you're armed with the right knowledge, it is sometimes possible to influence devices' regulatory path for closer alignment with business goals. The following points illustrate how regulatory insight can be used strategically to shape technical and commercial decision making.

Think carefully about device claims and intended use

It's extremely important to establish and interrogate the desired claims and target uses at the front-end of medical device development. Pin down the core proposition you're aiming for, then figure out the regulatory repercussions of this. If the likely FDA route for your initial proposition doesn't sit well with commercial objectives, consider any adjustments that might resolve the situation.

For instance, the company may be able to make a device 510(k)able by modifying its indications so that it has a predicate. Even if FDA requires that the 510(k) include clinical data to demonstrate that the device is substantially equivalent because of technological differences between the new device and its predicate, the review process is still likely to be significantly shorter than if the device required PMA approval. If there is no indication for which there is a predicate, it might be possible to develop an indication for which the device presents a lower risk than the PMA indication and thus, De Novo review might be an option. For example, a device that decreases a parameter that is an indicator of a condition might have a predicate for that indication and thus be 510(k)able while the same device might require De Novo review for treating the symptoms of that condition if there are no predicates for that indication or PMA approval for curing that condition.

FDA almost always requires clinical data in De Novo requests. However, the clinical study needed to generate the safety and efficacy data for a low/moderate risk De Novo indication may be smaller, shorter, and/or less complex, than the study needed to demonstrate that the device is safe and effective for higher risk PMA indication. In other words, the clinical study needed to support a De Novo request may cost less to conduct and/or present less risk of not being successful than the study needed to support PMA approval. Those factors may help make De Novo route an attractive option.

While the De Novo requests review times and user fees are higher than for 510(k), they are lower than for PMAs. In FY2020, which is the most recent period for which data is publicly available, the average total time from submission of a De Novo request to FDA's final decision was 344 days of which 169 days were FDA's total review time and 175 days were the submitter's total response time.

A De Novo downclassifed device can serve as a predicate in a 510(k) notice to expand the device's indications and possible to add or modify its technological characteristics. This stepwise approach may get the company close to the device it ultimately wants to market and thus, generate revenue and brand recognition for it before it seeks PMA approval for that version of the device. However, it also provides a predicate device for competitors to reference in their own 510(k) submissions, so the removal of this competitive barrier to entry must also be considered.

Ultimately it comes down to making a cost-benefit assessment that considers the commercial benefit of a given claim or use versus the costs of obtain FDA authorisation to market the device with that claim. Conducting this at an early stage informs high-level planning, so device development becomes more purposeful and focused from the get-go.

Take a pragmatic approach to the inclusion of features

When you're working with a new medical device it's tempting to integrate any features and capabilities that might enhance or extend its use. But it's important to understand the impact this has from a regulatory perspective.

In some cases, a certain feature might raise safety or efficacy questions, especially if there's no history of its use in a similar medical context. This may lead to FDA reviewers requesting additional data – and potentially new studies. A device which would have received 510(k) clearance for its core function might escalate to the De Novo or PMA route because of a feature that's nice to have but not essential.

On the other hand, integrating a new feature might enable the device to be commercially successful due to its enhanced performance and claims. In addition, if the device is intended to be used for an unmet medical need in the treatment of a serious or life-threatening condition, it may qualify for an expedited regulatory pathway, reducing time to market and conferring significant commercial benefits.

As with device claims and intended use, expert regulatory insights allow decisions surrounding features to be handled more objectively. It is important to understand what is likely to be considered safe and effective and what might raise questions. A key issue is whether a feature is truly novel or whether there is a potential predicate for it.

Applying this depth and breadth of regulatory knowledge to the front-end phase of product design pays dividends further down the line.

Working with confidence and assurance

There's always an element of risk in the development of new devices for medical applications; gaining FDA approval or clearance is often perceived as the biggest hurdle. However, grasping the regulatory nettle at an earlier stage makes that final hurdle more manageable. It can even inform strategic changes to product design that alter the regulatory path. Most importantly, key decisions can be taken with confidence, and stakeholders can be assured that appropriate steps have been taken to reduce the risk of innovation.

This is not about avoiding the need for PMA. The medical industry needs manufacturers who are prepared to break new ground with innovative devices that offer simpler, quicker or more accurate treatment or diagnosis. It's about understanding the best regulatory path for a specific device when there are options, and then ensuring design phase decisions support this.

When product development and regulatory strategies are integrated, the path to FDA approval or clearance becomes easier to navigate. This leads to better outcomes for everyone: healthcare professionals, device manufacturers and, of course, patients.

Contact info@sagentiainnovation.com to speak with Laurie Clarke or Rob Morgan and find out how we can support your company.

About Sagentia Innovation

Sagentia Innovation is a global science, product, and technology development company. Our mission is to help companies maximize the value of their investments in R&D. We partner with clients in the medical, consumer, industrial and food & beverage sectors to help them understand the technology and market landscape, decide their future strategy, solve the complex science and technology challenges, and deliver commercially successful products. Sagentia Innovation employs over 180 scientists, engineers and market experts and is a Science Group company. Science Group provides independent advisory and leading-edge product development services focused on science and technology initiatives. It has ten offices globally, two UK-based dedicated R&D innovation centres and more than 400 employees. Other Science Group companies include Leatherhead Food Research, TSG Consulting and Frontier Smart Technologies.

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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 France, Germany, Spain, UK, USA and Canada. TSG is a Science Group (London listed) company.

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