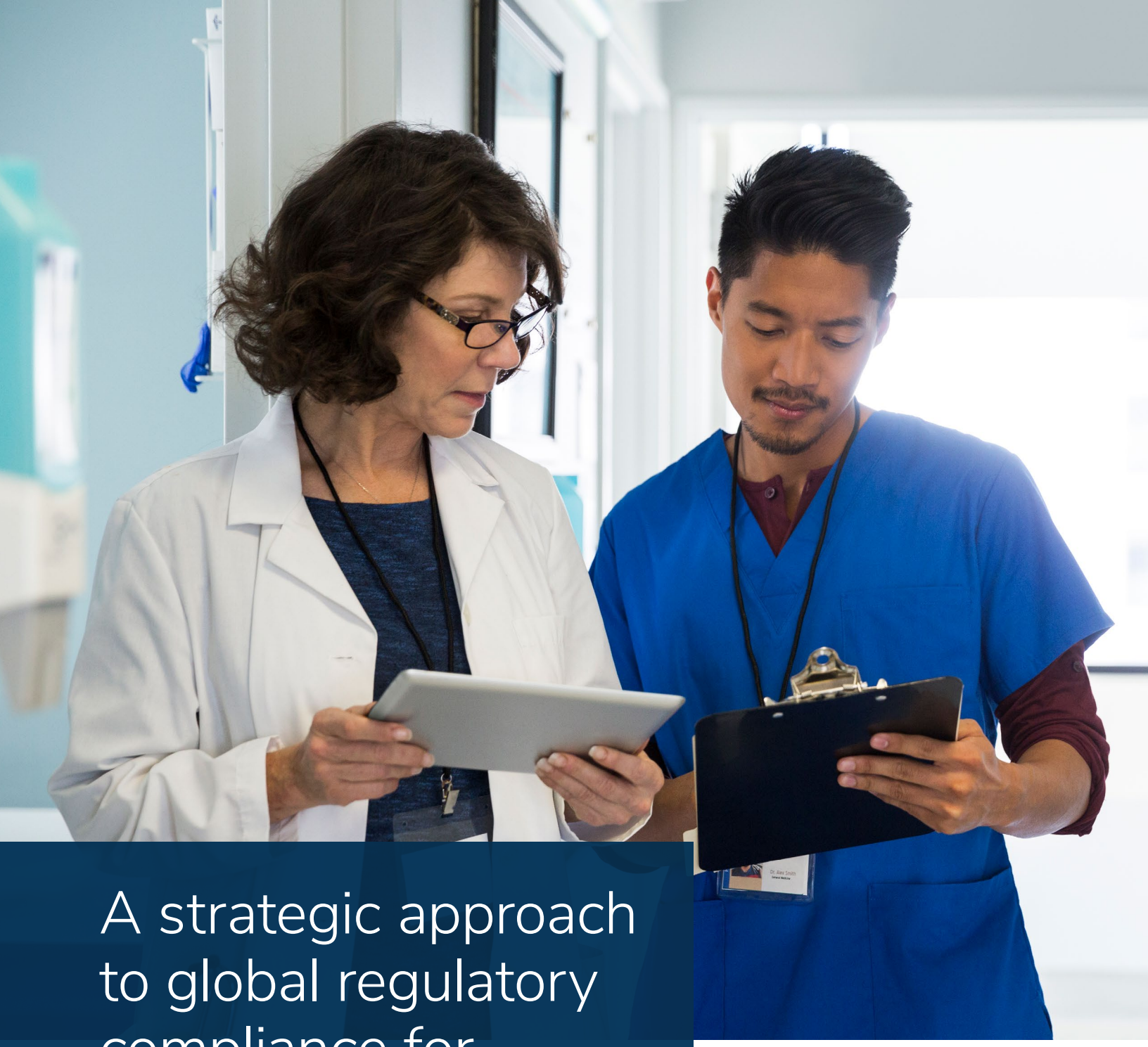

A strategic approach to global regulatory compliance for medical devices

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Executive summary

For medical device manufacturers, gaining access to multiple major markets is usually an important factor in the economic success of new and advanced medical technologies. At the same time, the checkered global landscape for the regulatory approval of new devices typically requires manufacturers to demonstrate compliance with different and often seemingly conflicting regulations and requirements. These differences and discrepancies typically result in a long and costly path to global regulatory approval.

Taking a strategic approach to achieving regulatory approval can be an effective tool in reducing the compliance burden facing medical device manufacturers. Manufacturers who first obtain approval or clearance from the US Food and Drug Administration (FDA) for access to the US market can often leverage that clearance or approval to gain a prompt and efficient review of new device applications by regulators in other markets. This can result in faster and wider deployment of new medical technologies and help to generate increased revenue more quickly from the sale of new medical devices.

This Emergo by UL white paper will discuss the importance of developing a global regulatory compliance strategy for the acceptance of medical devices in major markets. Beginning with an overview of the general regulatory frameworks found in major jurisdictions, the paper then discusses the process for obtaining medical device clearance in the US, and how device manufacturers can leverage FDA clearance to achieve acceptance in other countries. The white paper concludes with some recommended steps that manufacturers can take to help ensure the prompt and efficient review and approval of medical devices by regulators.

WITH NEARLY
45%
MARKET SHARE
the US is the
largest consumer of
MEDICAL DEVICES

The global market for medical devices

Despite continued economic uncertainty in many parts of the world, the projected growth in the global market for medical devices remains a bright opportunity for device manufacturers. According to the US Department of Commerce, the US is one of the world's largest consumers of medical devices, but markets in countries throughout Central and Eastern Europe, the Middle East, Africa and elsewhere are expected to grow more rapidly as access to quality medical care expands its reach around the world.[1] Various publicly available data reported the global medical devices market as approximately $500 billion (USD) in 2022.

The anticipated growth in medical devices can be attributed to a number of demographic factors, such as an aging population and an increased demand for smaller and more portable devices suitable for home healthcare use. Equally important in driving market growth are advances in medical devices, particularly the application of advanced technologies to legacy devices. Integration of software and wireless communications capabilities, to name just two such advances, have the potential to transform the medical device market while also dramatically improving the quality of healthcare for millions of people.

However, the expansion of the global medical device market and the application of advanced technologies are also contributing to the increased complexity of the regulatory landscape. In the EU and other jurisdictions, regulators have strengthened requirements for medical devices that include more rigorous clinical evaluation requirements and greater post-market oversight. Also, in some emerging countries with no prior regulation, officials are reportedly erecting regulatory schemes that are even more rigorous than those applicable in developed countries, either to protect domestic companies, generate revenue from regulatory review and approval fees, or both.[2]

Further adding to this complexity are national regulatory schemes utilizing frameworks that differ in fundamental ways from those applicable in other jurisdictions. For example, the US has a centralized framework in which the FDA and its field and branch operations serve as a single point of contact for device manufacturers seeking approval. The EU, on the other hand, utilizes a distributed framework in which manufacturers deal with individual regulatory agencies ("Notified Bodies") that have been authorized by accreditation organizations ("Competent Authorities" or "National Authorities") under EU directives and regulations. Although each approach offers certain advantages, the co-existence of multiple frameworks creates additional hurdles for those seeking device approvals.

The importance of a regulatory strategy

The dynamic and non-uniform landscape for the approval of medical devices directly translates into increased costs and longer lead times for medical device manufacturers, especially those who are seeking access to multiple markets versus a single market. Further, the majority of companies in the medical device industry are small and medium-sized entities, which often lack the expertise to conduct the requisite market research or to navigate the regulatory maze. This mismatch can make the task of achieving compliance even more challenging and can lead to a regulatory approval process that is more costly and time-consuming to execute.

In this context, the importance of developing a comprehensive go-to-market strategy for a new medical device cannot be understated. Such a strategy would necessarily evaluate multiple characteristics in each potential target market to determine the potential return on investment. Specific areas to examine would include anticipated market demand, current and projected competition, distribution channels, insurance reimbursement policies and legal protection of intellectual property rights, just to name a few.

In addition to these considerations, an effective strategy should also include an analysis of the regulatory framework and requirements that are applicable to medical devices in the selected target markets. Conducting such an analysis early in the product development process may help to identify markets where regulations are effectively harmonized, enabling a manufacturer to utilize the same or similar data and documentation in support of their device application. A regulatory analysis can also help to identify regulatory-specific challenges that could outweigh economic considerations in determining which markets to initially target.

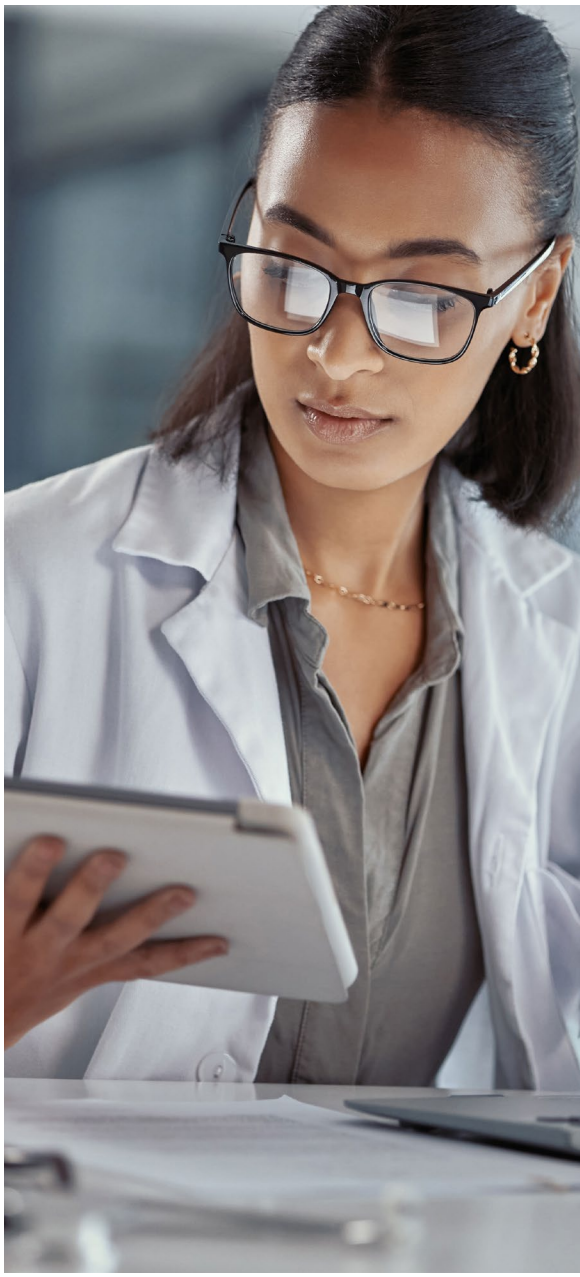
The benefits of securing US market access

As it represents the largest single market for medical devices, many device manufacturers select the US as their primary focus for initial regulatory authorization, but beyond the economic potential of the US market, first obtaining authorization from the FDA for a new medical device offers additional advantages in the effort to achieve global access.

Although FDA regulations applicable to medical devices are among the most stringent of any regulatory authority in the world, devices that have received pre-market approval (PMA) (typically Class III) or that have been cleared through the 510(k) pre-market notification (typically Class II) program are likely to gain more rapid acceptance by regulatory authorities in a number of other countries. International treaties, such as the 2020 US-Mexico-Canada Agreement (USMCA) and mutual recognition agreements between the FDA and national regulators serve to foster greater coherence in regulatory strategies and reduce regulatory barriers to trade. In addition, the FDA is also a member of the International Medical Device Regulators Form (IMDRF).[3]

Achieving compliance with FDA requirements can also be a benefit in jurisdictions where regulators conduct their own independent review of medical device applications. The scope and depth of FDA requirements means that device manufacturers that have obtained FDA approval or clearance are more likely to have assembled extensive information and data regarding the safety and performance of their devices. Having this information in hand is often sufficient to address the most rigorous requirements applicable in other jurisdictions and can facilitate the prompt review and approval of medical devices by local regulators.

For these reasons, seeking FDA authorization for access to the US market may be an effective first step for many device manufacturers as part of a larger regulatory strategy to achieve global market access. While meeting FDA requirements may require a larger initial investment of time and resources, FDA authorization provides device manufacturers with immediate access to the largest and potentially most lucrative market for medical devices in the world. Prior FDA authorization can also speed the compilation, review and acceptance of new device applications by regulators in other jurisdictions, providing a solid basis for global acceptance.



The US FDA registration process

The prospect of obtaining FDA approval or clearance for new medical devices in the US can seem overwhelming for those with little or no prior experience with regulators or the regulatory approval process. However, the essence of the process can be distilled into seven steps, as follows:

1 Classify the device

The FDA groups medical devices into different classifications (Class I, II and III) based on the degree of risk they pose to patients and their effectiveness. To determine the classification applicable to a given device, applicants can visit the FDA classification database[4] and enter a description of their device. Unless novel, the database will provide a product code and regulation number that matches this description, enabling applicants to identify the appropriate classification.

Devices based on a predicate device are usually categorized as Class I or Class II. Higher-risk devices, such as implants or automated external defibrillators (AEDs), are usually categorized as Class III. New or innovative technologies for which a current regulation cannot be found are automatically categorized as Class III devices.

2 Establish a US agent

Applicants located outside of the US are required to designate a US Agent who can serve as a point of contact with the FDA and can represent the applicant in connection with the FDA's ongoing oversight of approved devices.

3 Implement a quality management system

The FDA requires all applicants to have in place a quality management system (QMS) compliant with 21 CFR 820 (QSR) and the requirements of ISO 13485 *Medical devices - Quality management systems - Requirements for regulatory purposes*. In addition, if a manufacturer obtains an ISO 13485 certificate under the Medical Device Single Audit Program (MDSAP),[4] this can be used as a substitute for FDA's routine inspections.

4 Pre-market approval vs. 510(K) pre-market notification clearance

The determination of whether a device must obtain pre-market approval (PMA) or 510(k) pre-market notification typically depends on the device classification. Applicants of some Class I devices may only need to register their device, while other Class I and most Class II devices will need to file a 510(k) application. The FDA has indicated that the use of the eSTAR online automated submission compilation tool will be mandatory for all 510(k) applications as of October 2023. A De Novo request can be submitted for a Class I or Class II device for which there are no predicate devices or in response to an FDA 510(k) review of not substantially equivalent (NSE). Class III devices and most new and/or innovative high-risk technologies usually require a PMA application.

5 FDA reviews application

Once an application is complete and submitted, applicants can monitor the FDA website for updates on the application review. During the review process, the FDA may take several actions, including issuing a request for additional information. For a 510(k), a manufacturer has 180 days to respond to the request.

6 FDA conducts QMS facility inspection

FDA will perform pre- and post-approval inspections on manufacturers with a PMA. Once an application has been approved or cleared, the FDA can conduct facility inspections to verify compliance with its QMS requirements. For Class III devices, the FDA will also conduct facility inspections for all major suppliers involved in all aspects of the product's design and manufacture. Random inspections may also be conducted.

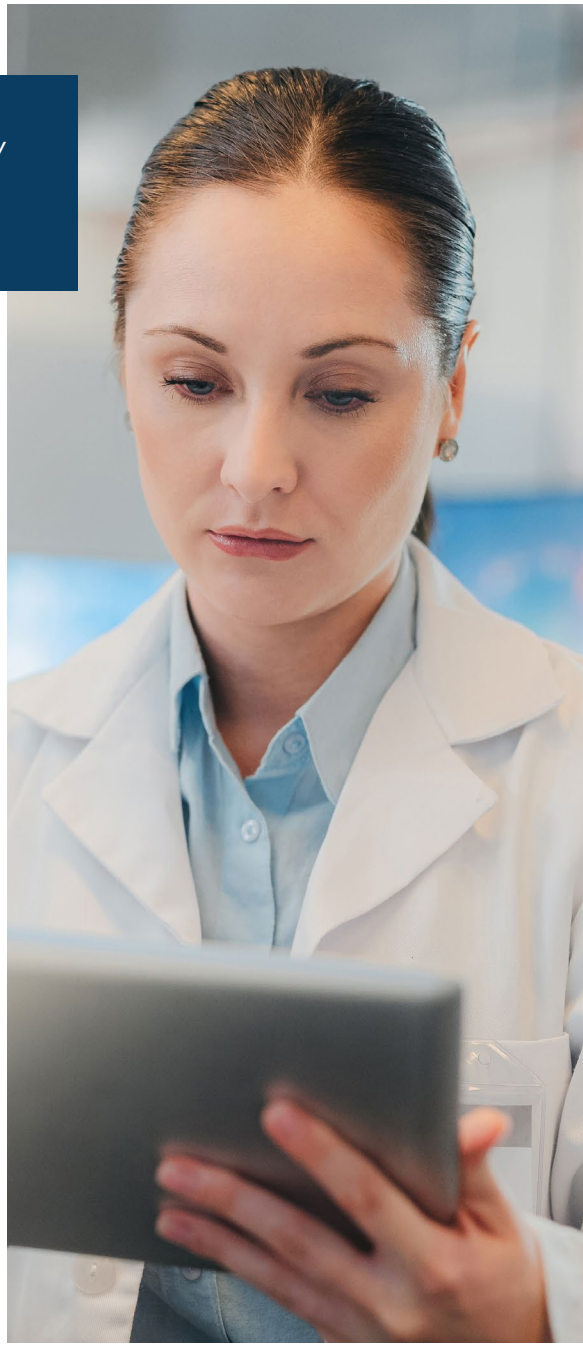
7 List and register approved devices

Finally, applicants can list and register their FDA-approved or cleared devices on the FDA's Unified Registration and Listing System (FURLS).

Leveraging FDA authorizations outside the US

Medical device manufacturers who have obtained US approval or clearance for their medical devices should then consider seeking access to countries and jurisdictions where local laws or regulations provide for an abbreviated review and registration procedure for devices previously authorized by the FDA. In many cases, the regulatory approach in these jurisdictions shares the centralized framework embodied in the FDA, and specific regulations share a common structure with equivalent FDA regulations. Further, underlying regulations applicable to medical devices typically reference internationally accepted standards such as ISO 13485 or ISO 13485 (MDSAP) for QMS, or standards addressing product safety, labeling and other issues that have been harmonized across multiple countries. While several countries currently provide for an abbreviated review process, Canada and Mexico should be obvious target markets for manufacturers that have obtained FDA approval or clearance. In Canada, a Canadian medical device license (MDL) and ISO 13485 (MDSAP) is required for companies selling medical devices above Class I. The MDL process is comparable to the FDA's 510(k) pre-market notification process, except that small differences in device classification may ease the process for manufacturers of some high-risk devices. In addition, Health Canada is piloting the FDA eSTAR program.

Canadian safety standards applicable to medical devices are generally harmonized with US consensus standards, and Canadian medical device regulations also require ISO 13485 under MDSAP.



In Mexico, devices that have been previously authorized in the US, Canada or Japan may qualify for an equivalency review which requires fewer documents as part of the application submission process. Mexico also requires compliance with its NOM standards, which are generally harmonized with comparable US standards, as well as the QMS requirements in ISO 13485. It is important to note, however, that COFEPRIS (the regulatory authority in Mexico) requires that all applications and supporting documentation be submitted in Spanish, along with all product documentation and labeling.

Outside of Canada and Mexico, Australia's Therapeutic Goods Administration (TGA) and Israel's Ministry of Health can also offer an expedited review of medical devices that have previously been approved or cleared by the FDA. In the EU, although the regulatory framework is different from that in place in the US, the underlying regulations are generally comparable, including requirements regarding the pre- and post-marketing auditing of QMS. However, similar to Mexico, regulators in most jurisdictions require that applications and all other documentation supporting a request for approval of a medical device, as well as required product documentation and labeling, be submitted in the local language.

Finally, it should be noted that many authorities outside of the US may mandate authorization in the US or other regions as a prerequisite for market entry. For example, regulatory agencies in several countries in South America, Africa and the Middle East require either FDA certification, CE marking certification, or both to gain entry. Although regulations and requirements in individual countries are subject to change, identifying such countries as part of the effort to develop an overall regulatory strategy can reduce the time and investment required to achieve global market access.

Global access recommendations for medical device manufacturers

As this paper illustrates, successfully achieving global access for new medical devices is a long and complex process. However, there are several actions that device manufacturers can take to make the process of obtaining regulatory approvals as smooth and as efficient as possible. Those actions include:

1 Develop an early go-to-market strategy

The dynamic global market for medical devices presents an abundance of opportunities for device manufacturers but an equal number of ways to fail. Developing a detailed strategy early in the product development process can identify the options offering the best return on investment while providing a road map for success.

2 Study the regulatory compliance landscape

While there are many commonalities in the regulatory requirements applicable to medical devices in major jurisdictions, there are also important differences. Developing an in-depth understanding of the processes and requirements applicable to medical devices in selected target markets can help manufacturers avoid delays and setbacks that can derail the go-to-market strategy. In addition, review the activities of the IMDRF related to global harmonization.

3 Strengthen the focus on quality

The implementation and maintenance of a robust quality management system is an essential requirement under nearly all regulatory approval schemes for medical devices. Meeting the provisions of ISO 13485 or ISO 13485 (MDSAP) generally serves as evidence of compliance with QMS requirements in most jurisdictions around the world.

4 Implement formal documentation collection and retention systems

The volume and breadth of documentation and other data required by regulators in support of applications for device approvals, as well as post-market activities, can be significant. An effective document management system can eliminate duplication of effort and can facilitate timely responses to inquiries from regulatory authorities.

5 Engage a knowledgeable advisor

There is no substitute for experience. A knowledgeable advisor or consultant with extensive medical device expertise and first-hand experience in dealing with regulatory authorities can quickly determine the requirements applicable to specific medical devices in key target markets and anticipate most of the challenges encountered by manufacturers who choose to navigate the process alone.

Summary and conclusion

For medical device manufacturers, the global acceptance of new and advanced medical devices requires a focused effort to obtain regulatory approval for their products in key target markets. Such an effort requires a detailed understanding of the regulatory requirements and the device approval process applicable in those markets, as well as a strategy that helps leverage the work of each regulatory approval achieved in support of future device approval applications. An effective regulatory strategy can help device manufacturers achieve global acceptance more efficiently, bringing potentially life-saving devices to people around the world.

Emergo by UL has extensive experience working with medical device manufacturers to obtain FDA approval or clearance for new medical devices. As a global constancy, Emergo also has expertise in securing medical device authorizations in major regulatory jurisdictions. Emergo by UL can provide manufacturers with customized market access reports that detail up-to-date regulatory considerations in specified targeted markets. These and other capabilities make Emergo by UL a valuable long-term partner for medical device manufacturers seeking to implement an effective global market access strategy for their products.

For additional information about Emergo by UL global access services for medical devices, visit EmergobyUL.com.

End Notes

1. An Overview of the U.S. Medical Devices and Biopharmaceutical Industries February 2022. https://www.trade.gov/sites/default/files/2022-03/Medical%20Devices%20and%20Biopharmaceuticals%20Research%20Report%20(Final)(1).pdf
2. https://www.imdrf.org/about
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About the authors

Ken Pilgrim has over 20 years of industry experience at the Manager/Director level, overseeing corporate quality systems and providing input on business decisions and strategy, regulatory oversight, and risk management strategies for existing and new products. Ken specializes in regulatory submissions, including those for IVDs, implantable devices, and tissue products. His expertise includes international regulatory compliance such as MDR/IVDR support and strategy; 510(k) clearances and other FDA activities, such as Pre-Sub meetings and 513(g)s; Class II–IV Medical Device Licenses for Health Canada; EU Technical Files (MD / IVD); Risk Management files; and global regulatory strategy. Ken's quality system background includes: implementing quality management systems (QMS) and supplier audits to FDA QSR, J-GMP, ISO 13485, and MDSAP. Additionally, Ken oversees Emergo by UL's RA/QA Consulting activity in Canada. In this role, he has peer reviewed 100+ regulatory filings and reports.

Evangeline Loh, Ph.D., RAC (US, EU) holds one of the most senior positions in the Emergo by UL consulting group and has over 15 years of global regulatory experience. Her background includes compiling European Technical Files and Design Dossiers; European Technical File reviews and gap assessments; borderline classifications; and 100+ peer reviews of Technical Files, including Clinical Evaluation Report reviews and responding to Notified Body findings. She specializes in borderline classification assessments, global vigilance, and global regulatory strategy. As the Global Regulatory Manager, Evangeline manages Emergo by UL's in-country representation services, including EU Authorized Representative, US Agent, and Australian Sponsor, and oversees global vigilance activities for these clients. She also supervises a team of international consultants and reviews dozens of device submissions and clinical evaluation reports each year. Prior to Emergo by UL, she held positions at Cook Incorporated and The Association of American Medical Colleges. Evangeline holds a PhD in pharmacology from The University of Texas Health Science Center at San Antonio and studied microbiology at Cornell University. She joined Emergo by UL in 2007.

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