Achieve Success with European Medical Device Commercialization

By Russ King

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Given the complexity of the FDA's regulatory pathway, many medical device companies are asking whether a Europe-first strategy for bringing their medical devices to market makes sense. The regulatory path in Europe has a reputation for being a quicker, less expensive path when compared to US FDA clearance projects. Whether you are a US company bringing your medical device to market in the European Union, or an EU company commercializing a new product, the regulatory route for medical device approval in the European Union is very manageable – given the right knowledge and tools. Our goal here is to outline the EU regulatory path and get you thinking about how your device might be successfully commercialized in the European medical device market.

Beginning the EU Commercialization Process

The EU compliance path begins with the Medical Device Directive (MDD), which consists of a framework of three Directives (Directive 90/385/EEC, Directive 93/42/EEC, and Directive 98/79/EC) and rules for manufacturers, called Annexes (Annex I through XII). A detailed discussion about this regulatory framework is a topic for a different article. The important point for now is that the rules and regulations for medical device manufacturers are available in these Directives, just as US medical device regulations can be found in 21 CFR Part 820, GxPs and other FDA regulations. A company implementing this regulatory framework would greatly benefit from contributions of experienced regulatory professionals who can properly interpret the requirements, ensuring the expectations of EU regulators are met.

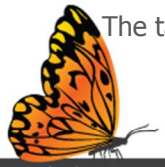
Meeting the requirements of the MDD in the broadest sense has two parts: a company part and a product part. Usually, each part is respectively satisfied with an ISO 13485 certification (the ISO quality standard for medical device companies) and CE mark (a mandatory medical device product conformance). The EU approval process typically sees your company audited by a Notified Body to qualify your company for ISO 13485 certification, and which subsequently audits your company annually to maintain your certification. Depending on the classification of your product, your Notified Body may audit your product Technical File to qualify your product for CE mark.

Types of Medical Device Classification

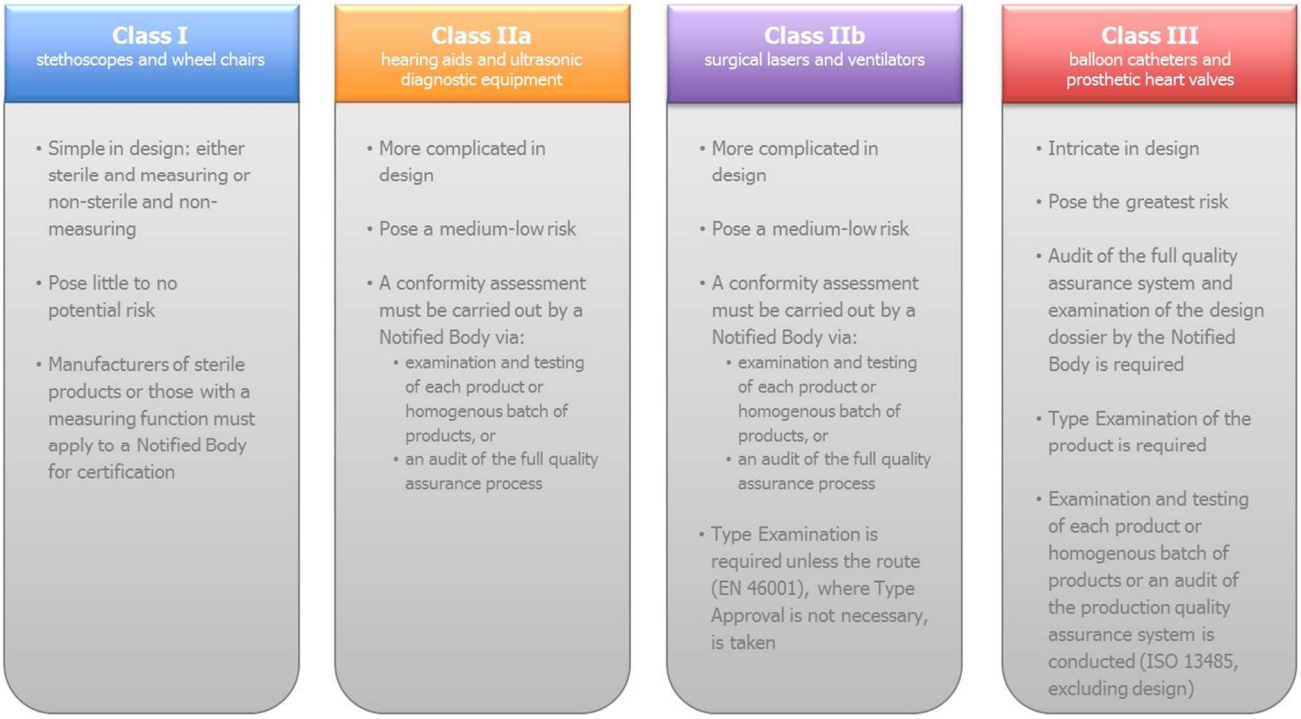
To ensure conformity under the MDD, manufacturers should determine their product's classification as soon as possible. Early product classification sets the stage for the correct compliance path by enabling the opportunity for early implementation of corporate quality requirements for EU product commercialization as well as product conformity requirements for CE Mark.

We should note that EU medical device classification, like US FDA device classification, is risk-based, where Class I products pose the least risk with their use, and Class III products the greatest risk. The EU and US medical device classification structure differs regarding how they treat medium risk products. While the EU designates medium-low risk products as Class IIa and medium-high risk products as Class IIb, the FDA does not make this classification distinction, designating all medium risk products as Class II products.

The table below offers a more detailed summary of EU Medical Device Classifications.



Medical Device Classification in the European Union



Regardless of your device classification, most routes to compliance require the involvement of a Notified Body, which is an organization appointed by the national accreditation authorities and "notified" to the European Commission to approve products covered by the Medical Device Directive. An exception to the general rule are Class I products that are "non-measuring" or "non-sterile."

There are many different Notified Bodies, including Underwriters Laboratories, BSI, Intertek, TUV Sud, and TUV Rheinland to name a few. All Notified Bodies are accredited and required to follow the same regulatory standards. There may be reasons, however, to choose one Notified Body rather than another:

- *some understand certain medical devices better than others*
- *some have different approaches to satisfying areas of compliance that might subtly impact the cost of compliance*
- *some have varying reputations for the quality of their work*
- *others may have a backlog of commitments that may impact your commercialization timeline.*

Also, a medical device company's relationship with a Notified Body tends to be different than the relationship they might have with the FDA. A relationship with a Notified Body can last years and may be characterized as more of a "business relationship" than you will experience with the FDA. Your choice of Notified Body should be reasoned and deliberate. If you are having difficulty making your selection, a regulatory professional experienced with EU product approval processes should be able to help you make your selection.

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Quality Management Systems are Mandatory

EU Quality Management Systems regulations, outlined in Annex II, V or VI of the MDD, are mandatory and establish the "company" part of meeting EU device regulations. The most common means for meeting EU Quality Management System regulations is through ISO 13485 certification. While this route is not necessary, alternative routes tend to be more difficult and more expensive. Consequently, the ISO 13485 certification path for demonstrating that a company complies with EU quality regulations has more or less become the *de facto* standard. Again, though some Class I product manufacturers can escape the necessity of ISO 13485 certification (see above), all medical device manufacturers selling products in the EU must comply with EU quality regulations.

ISO 13485 sets the requirements for a comprehensive Quality Management System for the design and manufacture of your medical device. Compliance with ISO 13485 will:

- *Establish a risk based approach to product development and realization*
- *Complete the validation of processes*
- *Ensure compliance with regulatory requirements*
- *Implement effective product traceability and recall systems*

One final note for those unfamiliar with ISO certifications: they are renewed annually with an audit. Not only does this create a line item in your annual budget, but it also creates an interesting impetus for maintaining your Quality Management System throughout the year. If an annual audit by a Notified Body results in major observations, then the Notified Body could force a stop to your EU sales until the observations are resolved. In contrast, unless special reasons exist for regular inspections, it is very difficult to predict when – or even if – the FDA will inspect your company.

Preparing the Necessary Documentation

Technical Files, also known as technical dossiers, are required for all medical devices sold in the EU. A Technical File is a comprehensive collection of information and documents detailing everything about your medical device and is used to justify the Declaration of Conformity and CE mark. That is, the product Technical File is a core component of the "product" part of EU medical device commercialization. The Technical File must demonstrate compliance of the device with the MDD's essential requirements and must be maintained for five years after the last product placement.

The Technical File is similar to the Design History File required by the FDA. The high level common elements of a Technical File include:

- *Cover page*
- *Index*
- *Declaration of conformity and classification*
- *Name and address of the Manufacturer/European Representative and Manufacturing Plants*
- *Detailed Product description*
- *Product specifications*
- *Product verification*

The Technical File is key for CE marking because it contains the most important information about the device, how it works, how it is manufactured, etc., thereby demonstrating how the device conforms to the requirements of the MDD. An incomplete, inconsistent or improperly completed CE Technical File may result in unexpected delays or even prevent market entry.

Risk Management

Like the FDA, the EU has embraced a risk-based approach to medical device design and approval and risk management is an essential component to successful medical device commercialization. Not only is risk management required by ISO 13485 and for product approval in the EU, but the best risk management systems proactively cultivate extensive benefits, including the mitigation of liability, a deep understanding and knowledge of the product, and information that can drive product improvements.

The EU risk management standard for medical devices is ISO 14971. This standard specifies a process for identifying hazards associated with medical devices including:

- *Risk analysis*
- *Risk evaluation*
- *Risk control*
- *Residual risk acceptability*
- *Report and documentation*

Safety Testing is Critical

Medical devices incorporating electrical components require testing to establish the safety of the device. The IEC 60601-1 standard is globally recognized for electro-medical equipment safety, and a parent standard to 60 particular device standards (also known as collateral standards).

Until recently, the standard was designed to ensure the safety of medical electrical devices exclusively through testing by a test lab, such as Underwriters Laboratories, Medical Equipment Compliance Associates (MECA), and TUV. With the transition of 60601-1 2nd Edition to *3rd Edition* (in effect in the EU as of June 30, 2012, soon to be in effect in the US), several changes occurred that have forced electrical medical device manufacturers to rethink how they manage safety testing. For example, 3rd Edition has adopted compliance with ISO 14971 as a key component. Now in addition to product testing, the manufacturer is responsible for demonstrating with documented evidence that their medical device is free from unacceptable risk during its entire product life cycle. From the practical planning perspective, medical device manufacturers must not only plan for safety testing by a test lab, but they also must plan for the development of a lot more risk-based and product lifecycle documentation as part of a safety program.

IEC 60601-1, 3rd Edition has several other changes, including updates regarding device identification, marking and providing accompanying documents, hazards (electrical, mechanical, radiation, temperature and fire, accuracy, software etc.), and the assessment of hazardous situations and fault conditions.

Meeting the documentation requirements of 60601-1 can be complex and, without planning, difficult. In our experience, the difficulties of meeting its rigorous requirements have caught the largest best-resourced manufacturers, as well as small manufacturers, off guard. Making IEC 60601-1 3rd Edition compliance part of your regulatory planning can trump this kind of disruption to your business. If you have questions about how to shepherd your product through IEC 60601-1, your test lab or a regulatory professional with 60601-1 experience can help you.

Working with a European Authorized Representative

Non-European manufacturers are required to have a European Authorized Representative (EAR), a neutral party who acts as a liaison with the national Competent Authorities. The EAR:

- *is the primary contact with the EU on behalf of the manufacturer*
- *maintains technical files available to EU authorities, while they maintain the manufacturer's product confidentiality*
- *has their contact information on all products*
- *must notify EU authorities of all major product incidents*
- *ensures Class I registration requirements are met*
- *observes manufacturer's compliance with the conformity assessment procedure of applicable EU directives*

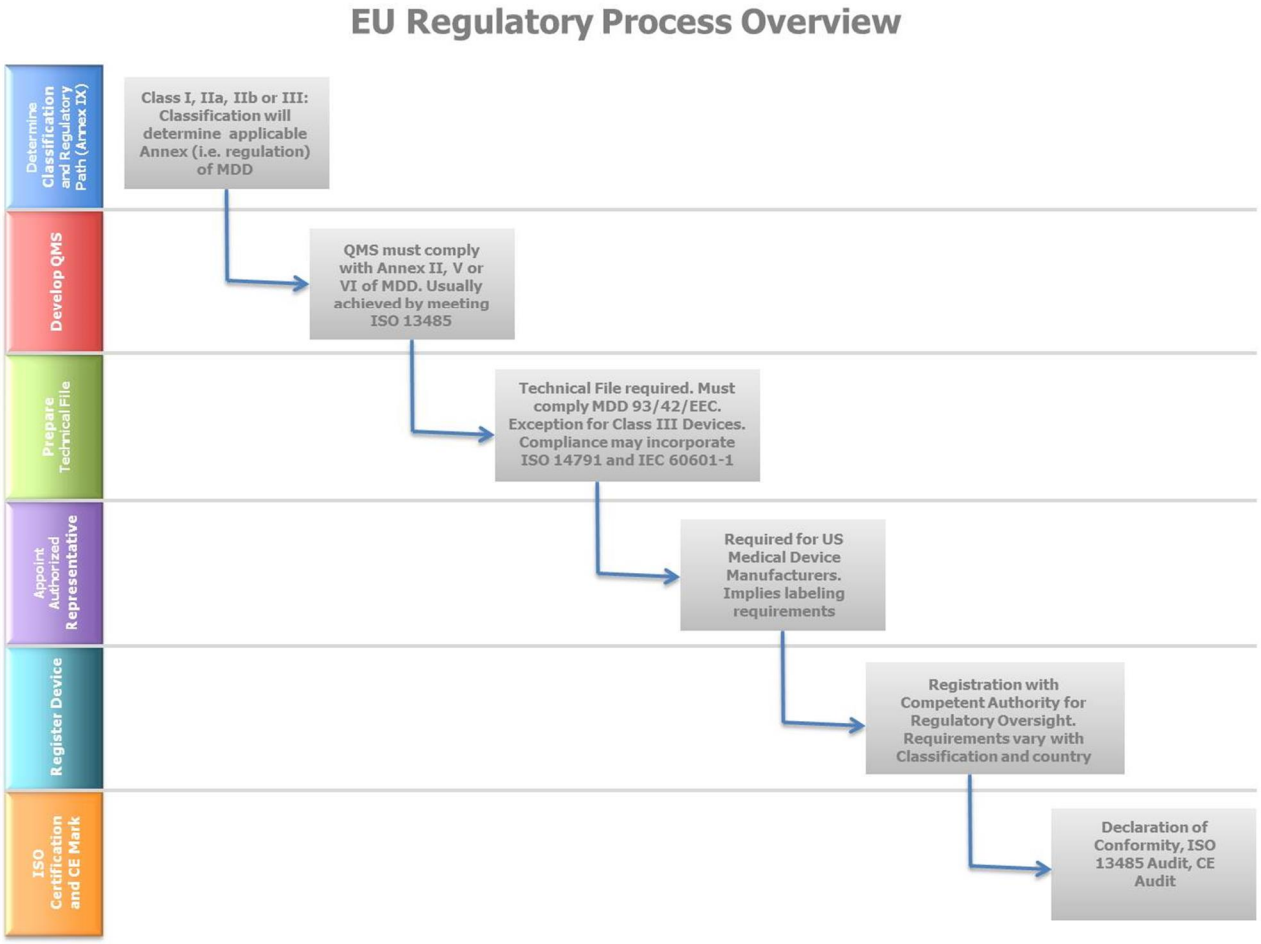
Class I devices must be registered with the Competent Authority where the EAR is based. The Competent Authority is the national Ministries of Health, which are responsible for ensuring compliance with the directive in their national market.

Registration of Class IIa, IIb and III devices are not required by most EU countries, however, some countries require registration of all devices, regardless of classification. Alternatively, there are some countries that require registration of high risk devices only. Answering such registration questions can be addressed by contacting the Competent Authority in the region you are targeting in your commercialization effort or with the assistance of a regulatory professional.

The Final Step: ISO Certification and CE Mark

Once you have developed the quality systems for satisfying the quality requirements of ISO 13485 and completed your product documentation, you should be prepared for an audit by your Notified Body. The Notified Body will audit your quality system for compliance with ISO 13485 to certify that you operate to specific medical device quality standards. They, or an alternatively chosen Notified Body, will also review (though not necessarily at the same time) your technical file for conformity with the MDD (some Class I devices are exempt from this process as identified above).

In the event either audit results in major observations or deficiencies, ISO 13485 certification and CE Certificate can be withheld until the observations or deficiencies are addressed. But once awarded, you can issue a product Declaration of Conformity (a legally binding declaration that the product complies with the essential requirements of the relevant European health, safety and environmental protection legislation) and the CE mark may be affixed to the product.



Summary

Many US companies are turning to the European Union for the initial launch of their medical devices. Recognizing the subtle differences between US and European markets, learning the requirements of European commercialization and implementing a successful launch strategy are necessary considerations. Working with a team who knows the intricacies of how to plan and manage a business from thousands of miles away will help you launch and grow your business overseas.

About MethodSense

MethodSense is a life science consulting firm with offices in the US and Europe. We guide medical device, biotech and pharmaceutical companies with quality, regulatory and technology solutions. Our services enable clients to operate more effectively during the commercialization process and beyond.

MethodSense is the developer of InfoStrength Smart Enterprise Suite (SES), an enterprise document and business management software. InfoStrength SES is a 21 CFR Part 11 compliant Software as a Service (SaaS) application designed specifically for regulated businesses. Rita King, CEO of MethodSense, created InfoStrength SES to make FDA compliance, business process management and business communication efficient for life science companies.

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MethodSense was founded to deliver two key pieces to a very important puzzle: the development and implementation of FDA compliant commercialization processes combined with the means to maintain compliance and effective business collaboration with a proven technology solution

You can learn more about MethodSense at www.methodsense.com and about InfoStrength Smart Enterprise Suite at www.infostrength.com.

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