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Medical Devices - Pitfalls and safeguards in robust evidence of safety and performance for regulatory submissions

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Introduction

The journey of bringing a new medical device to market is littered with potential pitfalls and obstacles that need to be overcome.

A common challenge facing innovators is how to navigate regulatory pathways. Typically, this is a topic that is low on people's to-do lists.

Irrespective of the regulatory pathway that is applicable to your product, you will have to demonstrate that your product has valid scientific evidence of adequate safety, performance and efficacy throughout the lifecycle of the product. Failure to provide this information is a common reason for delays and rejection of regulatory documentation by FDA and EU Notified Bodies. This frequently leads to increasing costs and failure to obtain market access of a device that may have a positive health outcome and better safety profile.

Therefore, taking time to evaluate regulatory pathways early in the development of a product will mean that you better understand evidence requirements and minimise the likelihood of material issues arising during regulatory approval processes. It will also mean that you have a better understanding of regulatory costs and timelines

Once a positive regulatory decision has been made and your device is on the market, that is not the end of the journey. No medical device is infallible so plan to expect issues to arise. Each year, regulators such as the FDA (US) and MHRA (UK) receive thousands of adverse incident reports regarding medical devices.

The harm or potential to cause harm to patients and users caused by device or manufacturing failure, use error or new unidentified hazard can result in recalls, changes in design, further validation and verification and reputational risk.

A product life cycle approach underpinned by a proactive and reactive regulatory and compliance strategy ensures that you are able to consider key steps from first having your idea, to placing a medical device on the market.

This approach requires the involvement of a range of subject matter experts such as technical, quality, and commercial to analyze a broad scope of requirements, standards and guidance. It is critical to know what applies and when, know how to keep abreast of changes and plan how to obtain the evidence necessary to fulfil requirements.

For start-ups and small businesses, it isn't always feasible to have all these in-house capabilities.

The evidence

The first step is to identify whether your product is a medical device. To do this, you need to be clear about what your product does (intended purpose) and its functional characteristics (is it powered, what materials are used in its construction etc.). You can then review the legal definition of a 'medical device' in your target country to check whether it meets the definition.

If your product is a medical device then the next step is to confirm its risk classification (Class I = low risk, Class III = high risk) as this will narrow down the conformity assessment/submission route options.

Depending on classification, you will then start to gain an understanding of pre-clinical evidence you will need to collect, analyze and report on. This may include cases demonstrating how your new device is equivalent to a legally marketed device. It represents a large proportion of your application and technical documentation

Device manufacturers with market acceptance in other markets may not realize the evidence requirements differ from the market they want to access.

The most common regulatory route to market in the US is the FDA 510(k) for Class I and II products. If your application doesn't meet the minimum threshold of acceptability this could result in an FDA 'Refuse to Accept' decision.

Products that are classified as the highest risk undergo the most intense scrutiny through the FDAs premarket approval application (PMA) process. Applications that are incomplete, inaccurate, inconsistent, omit critical information, and poorly organized have resulted in delays in approval, requests for new clinical and/or pre-clinical data, or refusal or denial of these applications.

Product safety is a core focus of regulatory bodies. Safety is primarily evaluated through pre-clinical testing, and it is essential to have considered potential risks and undertaken appropriate testing to gather evidence.

Avoidable delays create uncertainty and add both time and cost.

75%

Rejection rate*

Percentage of 510(k) applications that are rejected first time

180

Days†

Review period for an FDA PMA

18

Months‡

Time required for an EU MDR QMS+Product certificate to be issued

**Greenlight Guru. Common mistakes that can tank your FDA 510(k). 16 Nov 2017.*

† FDA Post Market Approval (PMA) Review Process 13 Sep 2021. ‡ European Commission Notified bodies survey on certifications and applications 13 Mar 2024.

Identification of test requirements is carried out by considering essential principles of safety and performance in the context of your product's functional characteristics and intended purpose. These safeguarding principles are generally adopted in legislation and apply to pre-market and post-market responsibilities to ensure a lifecycle approach to product safety & performance.

There are many methods to generate evidence to verify and validate your device against relevant principles and requirements in the legislation. This includes bench performance testing methods such as in vitro, ex vivo and in silico based on recognised standards or validated methods. The voluntary use of recognized product and process standards can give a presumption of conformity to relevant requirements. They generally satisfy only a portion of an application but play a significant contribution to evidence of compliance to relevant principles. You also have the option to provide alternative data or information along with a scientific rationale for why the alternative addresses the principle.

Standards also give confidence that you are applying 'state-of-the-art' requirements. They help you understand that a high level of protection has been achieved, giving increased predictability and facilitates the premarket process. With a large number of recognized standards in each country (about 1500 FDA consensus standards and about 2000 industry and national Chinese standards), identifying relevant standards applicable to your device to meet requirements can be a challenge. Keeping up to date with changes to standards adds to that challenge.

Once you have identified the relevant standard you will want to achieve a level of confidence in the test results. One rationale for refusal of a PMA application by FDA is when the pre-clinical data is not conducted in compliance with good laboratory practices and so does not support the validity of the data generated. Selecting third-party testing providers early in your journey enables you to adapt your design verification and validation plans. You have greater confidence that what you are doing is correct and the result more certain, gaining an increased assurance your device is safe and performs as intended.

Before deciding on which test provider to use, it is prudent to review a national accreditation body website based in the country you want testing to take place in (such as UKAS, ANAB or CNAS) to ensure that the test provider is accredited and has the competency to undertake the testing you require. Accreditation certificates for every testing provider are freely available to download and list the standards that they are certified to provide. Test providers may be able to undertake testing that they are not certified for. You also need to consider the impact of any deviations that could impact the results and overall conclusions

Testing undertaken to recognized standards is strongly encouraged by regulatory bodies and will make the regulatory conformity assessment process much smoother. Testing to recognized standards is also valuable when entering into commercial discussions as end users gain confidence that standards of quality, safety and performance have been met.

The need

In an environment where change is the only constant, there is a need to have a system that is able to evaluate the legal requirements against the product characteristics, and intended purpose/use in real time. Through advanced algorithm and data analytics identifying the key requirements defined within relevant standards, legislation, applications and guidance gives assurance that legal requirements are not missed.

Conclusion

Ultimately regardless of how medical technologies are brought to market and the legislation addressing conformity, we all need to work smarter rather than harder using digital tools to augment evidence gathering for conformity assessment activities, giving faster yet reliable data/results to bring safer medical devices to market that improve patient outcomes.

Three key takeaways

getting it right first time

1

Invest in developing a regulatory and compliance strategy and keep it up to date

2

Use digital tools to identify relevant requirements and solutions for safety and performance

3

Ensure you hold robust scientific data to demonstrate requirements are fulfilled, ideally from a third party testing provider.

Authors

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