propharma

CASE STUDY

anchored in evidence:

how a novel, pma-track orthopedic implant received marketing approval with an RWE-led strategy

Our corporate culture fosters innovative thinking; we thrive on the complicated and complex clinical challenges that are commonly associated with the most ground-breaking technologies. This case study describes how ProPharma's team of medical device experts ideated and executed a creative regulatory and clinical strategy to get a novel Class III device to market using Real World Evidence (RWE).

Manufacturers developing high-risk medical devices are often required to conduct clinical studies to demonstrate safety and effectiveness. Depending upon region, regulatory authorities may impose different requirements for how data must be collected and presented to support a marketing application. This creates a delicate balance for manufacturers as they work to manage cost, time, and risk while designing an effective regulatory and clinical strategy. In some cases, a novel, less burdensome data collection alternative can be a viable path in place of a full-scale clinical study.

ProPharma identified an innovative approach to evaluating adverse events within a retrospective dataset for a specific orthopedic subpopulation. This validated method provided the necessary real-world data to support a PMA submission. Success was achieved through close collaboration between ProPharma's Regulatory Sciences and Clinical Services teams, enabling rapid, targeted development of the solution.

By taking a holistic and creative approach, ProPharma delivered a path forward that might otherwise have been overlooked. Without the proposed alternate solution, the client risked significant delays, financial strain, and investor uncertainty. Instead, their PMA was approved, ultimately allowing the company to achieve its goal of successful acquisition.

"By applying a novel approach, ProPharma realized the full potential of fit-for-purpose RWD to generate RWE, advancing the development of a groundbreaking device and expediting PMA marketing approval and patient access."

challenge

In the US, Class III medical devices, which are the highest-risk category, require robust clinical data to support a marketing application. These studies are often designed as prospective, randomized controlled trials (RCTs). RCTs can cost upwards of $5–10 million and extend timelines by more than three years due to subject enrollment and follow-up requirements before primary endpoint data is collected.

Our client, a start-up orthopedic medical device company developing a novel Class III device, faced significant resource constraints. They needed **a clinical strategy that would be cost-effective and avoid the burden of extended timelines that could threaten their ability to attract and retain investors.**

The device had already obtained CE Mark and had been marketed in Europe for nearly a decade, with a registry capturing data on more than 1,000 patients. Having previously partnered with the client on a regulatory due diligence project for a licensing agreement, ProPharma recognized the opportunity to leverage this unique data. By designing a regulatory strategy around the existing datasets, our team created a pathway that had the potential to save the client millions in clinical trial costs and reduce the approval timeline by orders of magnitude compared to a traditional RCT approach.

solution

ProPharma's team of medical device experts conducted a preliminary audit of the registry to determine how the data could be used to support a US regulatory strategy. At the same time, FDA had recently published their current thinking on the use of Real-World Data (RWD) to generate Real-World Evidence (RWE) for marketing applications, creating an opening for a novel approach.

It was determined that the existing registry could serve as the foundation for a PMA submission, eliminating the need for a large, costly prospective RCT**. ProPharma developed a strategy that included designing a prospective data collection protocol to define patient selection within the registry, along with processes for monitoring, auditing, and validating the data to FDA standards.**

A detailed statistical analysis plan was prepared, and the proposed approach was reviewed with FDA in a pre-submission meeting. **The Agency agreed with the strategy, allowing the client to move forward. By leveraging existing registry data. This pathway avoided the need for a multi-year RCT and saved the client millions of dollars in trial costs, while accelerating marketing approval timelines.**

This success was possible through the seamless collaboration of ProPharma's Regulatory Sciences and Clinical Research teams. By combining novel, strategic regulatory insight with clinical expertise, the team crafted a creative solution that might otherwise have been overlooked, enabling us to deliver scientific rigor and a faster, more cost-effective path to market.

outcome

Although the registry provided a robust dataset, several challenges in enrollment and study management had to be addressed. Missing data required either imputation or direct collection from geographically dispersed patients, some of whom needed to be located and re-consented up to five years post-procedure. In addition, while adverse events (AEs) had been documented in the registry, they were not categorized or grouped in the manner typically expected by FDA.

Initially, ProPharma reported the AEs as they appeared in the registry, anticipating that post-hoc regrouping without a validated framework might invite greater regulatory scrutiny. When FDA raised concerns, ProPharma leveraged its deep regulatory and clinical expertise to identify a path forward rather than allow the issue to become a barrier. Drawing on experience developing the client's Clinical Evaluation Report (CER) for CE marking under EU MDR, the team referenced published reports in the literature that validated a method for grouping and categorizing AEs specific to this type of device.

ProPharma established a Clinical Events Committee (CEC) with predefined criteria for assessing event severity and determining whether AEs were device-related or procedure-related. The CEC systematically reviewed all AEs for the enrolled subjects and categorized them according to the validated definitions. Through continued negotiation and interactive review with FDA, this approach was ultimately accepted, and additional statistical analyses were performed to mitigate remaining registry limitations.

By overcoming these obstacles, **ProPharma ensured that the registry data met FDA's standards, paving the way for PMA approval and enabling the client to achieve its ultimate goal of a successful acquisition.**

"By combining novel, strategic regulatory insight with clinical expertise, the team crafted an evidence-centric pathway that might otherwise have been overlooked, enabling us to deliver both scientific rigor and a faster, more cost-effective path to market."