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case study

sponsor successfully completes acquisition after efficient PMA submission

This case study describes how we ideated and executed a creative regulatory and clinical strategy to get a novel Class III device to market using Real World Evidence (RWE).

A major Top 10 Medical Device Sponsor engaged M2, a ProPharma company, to collaborate and support innovation to reduce complexity associated with a successful PMA submission.

M2's team took a novel approach to the review of Adverse Events (AE) in a retrospective dataset for a particular orthopaedic subpopulation.

> "Specializing in devices, biologics and combination products for a wide range of therapeutic areas and disease spaces, M2, a ProPharma company, is an established partner of med tech companies ranging from start-ups to multinational device manufacturers.

The regulatory team worked closely with clinical personnel to develop a creative solution to a clinical study challenge that could have cost the client significant time, financial resources and investor turbulence. Applying this novel approach, the client's PMA was approved and the company met its goal of successful acquisition.

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challenge

In the US, the highest-risk device category – Class III – requires clinical data to support a marketing application. Frequently, the clinical study to support a Class III device will be designed as a randomized controlled trial (RCT).

RCTs can have their drawbacks, including their high cost in terms of time and money, problems with generalizability (participants who volunteer to participate might not be representative of the population being studied) and loss to follow-up.

Our client, a start-up orthopaedic device company with a novel Class III implant, had significant resource constraints and challenged us to help devise a clinical strategy that would be both cost effective and avoid the burden of an extended timeline.

The device was previously CE Marked, had been marketed in Europe for almost a decade, and a university-based registry was maintained that, at the time of project initiation, included data for more than 1,000 patients. Having already worked closely with the client on a regulatory assessment as part of the due diligence activities for a licensing agreement for the device, we developed a regulatory strategy based on the unique availability of registry data that could potentially support a premarked approval (PMA).

solution

Our clinical team conducted a preliminary audit of the registry data to evaluate whether the regulatory strategy could be supported.

From policy and regulatory changes to COVID-19 and driving customer engagement, the healthcare environment continues to require healthcare stakeholders to adapt their strategies.

In order to stay ahead of trends impacting our client's business, we developed a pathway forward using the registry data (i.e., RWE) to support a Class III marketing application in the US, without the need to collect prospective data. This approach was based on the development of a prospective data collection protocol, including subject (patient) selection for the dataset that would support the PMA, and the monitoring, auditing, and validation of the registry data.

A detailed statistical analysis plan was also prepared, and the proposed strategy was reviewed with FDA during a pre-submission meeting.

After a successful meeting with the Agency, the prospective protocol for collection of data was finalized and the study was initiated.

results

While the data existed in a robust registry, there were enrollment and study challenges that had to be considered, including missing data that needed to be either imputed or collected from geographically dispersed subjects. This involved locating and re-consenting of patients up to 5 years post-procedure.

Importantly, adverse events had been documented in the registry: however they were not categorized and grouped in a way that FDA commonly required. We originally reported the AEs exactly as they were documented in the registry, under the assumption that FDA would create more criticism if the groupings were changed post-hoc without established parameters.

Due to our regulatory work with the client, including developing the Clinical Evaluation Report (CER) to maintain CE marking, the team identified a published report in the literature that validated a method for grouping and categorizing AEs for the indication for use for this type of implant.

A Clinical Events Committee (CEC) was established, with pre-defined criteria for assigning event severity and whether AEs were device-related or procedure-related. The CEC reviewed all AEs for the enrolled subjects and categorized them according to the published literature definitions.

After continued negotiation and interactive review with FDA, the approach was accepted and additional statistical analyses mitigated outstanding registry issues.

Contact us to learn how our experienced team can help ensure successful outcomes throughout the product lifecycle.

www.ProPharmaGroup.com
Info@ProPharmaGroup.com