Maximising the Value of a Registry Programme

Clinical trials conducted for regulatory approval of new pharmaceutical, biotech, device, and diagnostic products frequently do not provide the comprehensive market intelligence required for successful product launch, in-market brand management, and, most importantly, long-term product growth. Queries about the proper use of a new product, expectations of treatment response, key drivers of market uptake, and performance against competitors often multiply after regulatory approval. The answers to these questions require real-world data on a broad spectrum of patients and physician-prescribing patterns – data that clinical trials cannot deliver owing to rigid patient inclusion and exclusion criteria and tightly controlled study methodologies.

The information gaps that remain after a clinical trial handicap decision-makers, who must make early choices about clinical messaging based primarily on the product’s approved labelling. By comparison, real-world studies – including disease registries – can provide a sponsor’s medical affairs and marketing managers with an early warning system for possible threats, as well as insight into potential future opportunities as they map a product’s life-cycle. These managers are increasingly recognising registries as a flexible and cost-effective strategy for filling in the informational gaps left by clinical trials to obtain the intelligence needed to support clinical and marketing strategies.

In the narrowest sense, a disease registry can be defined as a prospective, observational study of patients over time that provides ongoing epidemiological data for analysis and reporting. Registries are less encumbered by many of the regulatory-imposed constraints of a clinical trial, and thus enable healthcare providers, regulators, and sponsors to observe clinical responses over time among a broader patient population from many physician settings and geographical regions. As a result, global regulatory authorities and reimbursement agencies have increased their attention towards registry-like programmes as a means to accomplish several key objectives, such as requiring drug sponsors to conduct post-marketing studies when needed to ensure the safety of drug products after approval to describe reimbursement determinations that include, as a condition of payment, the development and capture of additional patient data to supplement standard claims data. Owing to the growing awareness of the value of post-marketing data, pharmaceutical, biotechnology, device, and diagnostic companies are increasingly sponsoring registry programmes to satisfy the evolving needs of regulatory and reimbursement agencies.

This narrow definition of registry programmes, however, does not sufficiently illustrate their importance and value for sponsors seeking to optimise the clinical and commercial value of their products. Registries can be considered powerful, multifaceted tools and integrated programmes of targeted scientific and commercialisation activities and objectives that address specific challenges, both clinical and business-related. Registries, when designed effectively and integrated with a sponsor’s market research activities, can provide a steady stream of new information suitable for external communication to physicians and other healthcare providers, private and public payers, and regulatory authorities. At the same time, registries, along with market research findings, can provide early and ongoing feedback on the effectiveness of clinical messaging and brand management strategies for a sponsor’s internal audience.

Overview of Registry Design

As a starting point for a new registry programme, it is critical to “begin with the end in mind”. That is, what are the communications – i.e. the clinical messages or product positioning – that the sponsor is trying to relay? Who are the target audiences and what is/are the intended use(s) of the data. Are there any challenges linked to physicians’ perceptions about the product that may influence its uptake and adoption? For example, a new product on the market may lead to a gradual change in the current standard of care for a specific patient population. Reimbursement agencies will be interested in how the clinical outcomes (both effectiveness and safety outcomes) of patients treated with the new product compare with the outcomes of patients still receiving the current standard of care. In this case, collecting clinical response and safety data, as well perhaps as patient-reported outcomes, may provide the information needed to demonstrate the value of the new product in the target patient population. Other possible end results of a well-designed registry include establishing the company as a credible player in a new clinical domain that it seeks to enter, contributing to new disease management or treatment guidelines, establishing therapeutic goals in patient subpopulations, and defending an established franchise against new competitors. Communications from a registry can accommodate many different media, including abstracts, posters, podium presentations for scientific meetings and symposia, manuscripts for publication in clinical journals, dossiers for reimbursement authorities, and speaker bureau/physician-support activities.
Understanding the key messages, the target audiences, and the intended uses of the data will serve as a foundation for designing the operational strategy for the registry. There is a mix of registry operational elements that must be considered in order to maximise the study’s overall execution in the most cost-effective manner. Basic operational elements include, but are not limited to:

**Data Elements.** The data elements that are needed to develop a credible clinical message to the intended audiences could include clinical assessments provided by physicians, patient-reported outcomes, healthcare utilisation information, or other supporting data like market survey data. Once the data elements are defined, careful attention to the sources of the data is also key. For prospective registry programmes, data can be provided by both physicians and patients. In some registries, retrospective data collection from medical records or secondary database sources is also possible. Carefully choosing specific data elements to collect in the registry facilitates the strategy to engage the target physicians in the scientific exploration, which can ultimately provide valuable clinical information to optimise the care of patients.

**Methods for Data Collection.** Once the data elements and sources of the data are defined, the optimal technologies and workflows to collect and process the data can be selected. Similar to a clinical trial, sponsors may select either paper case report forms (CRFs) or CRFs accessed through an internet portal as the foundation of their registry programme. In addition, registries may integrate patient diaries and electronic patient-reported outcomes, mail and telephone surveys with automated communications, and centralised call centres to collect all of the requested information in a timely manner. Finally, an understanding of routine clinical practice and how data collection may vary across countries and individual sites will influence the frequency of data submission to the registry.

**Target Sites and Physicians.** Participation in a registry typically requires a lesser degree of investigator research experience than a clinical trial; therefore, physicians from an array of community practice settings may be included to provide an important window into product use within the context of prevailing treatment algorithms. This may lead to an understanding of how and why new products drive changes in current treatment patterns, or encounter resistance because of established patterns of practice.

**Target Patient Population and Recruitment Strategy.** Registries allow for more generalisable participation of patients in contrast to a clinical trial’s strict inclusion/exclusion criteria. As a result, a registry may provide a more complete demonstration of how patients respond to a sponsor’s product in a real practice, including adherence or non-adherence to the prescribed treatment regimen. It can also help create an understanding of barriers to, and facilitators of, both use and adherence, in addition to the various factors associated with clinical outcomes.

**Good Pharmacoepidemiology Practices**
Good Pharmacoepidemiology Practices (GPP) proposes minimum practices and procedures that should be considered to help ensure the quality and integrity of pharmacoepidemiologic research – like registry programmes – and to provide adequate documentation of research methods and results. The GPP do not prescribe specific research methods, nor will adherence to guidelines guarantee valid research or a successful registry. Because of the highly regulated environment in which pharmaceutical products, devices, and diagnostics are developed, approved, and studied after approval for various reasons, many sponsor companies and clinical research organisations have adopted the position that all pharmacoepidemiologic research, regardless of the purpose, should be conducted under the governance of the GPP.

**Early Phases of a Registry**
The activities surrounding the launch of a new registry, as well as descriptive statistics of early registry data, can help establish the sponsor as a credible player in a new market. Initial demographic and disease status data collected as patients enrol in a registry can better define the broader, real-world patient population beyond the narrow reach of a clinical study. This increased understanding of affected patients, with their wide range of demographic characteristics, disease severities, and comorbidities, helps to enhance the mapping of the natural course of the disease, as well as to develop evidence-based guidelines for patient diagnosis and monitoring. Through this exchange of early data from the registry, the sponsor can also begin to develop relationships with and demonstrate its support of wider (perhaps global) communication of clinical investigators and physician treatment providers. Indeed, one of the sponsor’s goals may be to enlarge the network of treatment centres at which patients can receive expert care. Finally, as the new product is introduced into a patient’s care plans, early data from the registry can help the sponsor discern whether the product is being used as expected. At first, physicians may be more comfortable staying within the bounds of approved product labelling, but over time, registry data may suggest more off-label use or experimentation with different doses or dosing regimens in an effort to optimise a product’s prescription to a specific patient’s needs. Early data from the registry can also be effectively combined with market research findings to position a new product in a new or crowded market. Effective positioning tells the physician and patient communities how a sponsor’s product is unique and the benefits it offers to the target market.

In a true disease registry, patients are enrolled without regard to the physicians’ treatment choices. As a result, data from the registry represents results from the range of products available to physicians to treat their patients from many different sponsors. In addition, some registry patients may not receive a specific product at all. In this scenario, registry data can guide the application of market research activities that help define the market in which a specific product will compete, as well as to develop and assess threats. Several market research questions can supplement the clinical data from the disease registry – for example; who are the sponsor’s competitors and their respective positioning? What are the treatment options available to physicians? What is the market’s unmet needs? What is the regulatory
Evolving the Registry to Keep Pace with Sponsor’s Needs

As the sponsor’s needs change or as the needs of the medical and patient communities adjust to new clinical advances over time, a registry can also evolve to address these new challenges. Clear strategic direction and appropriate planning can ensure that the registry will keep pace with the clinical and commercial information required for successful in-market brand management, providing early warnings for the medical affairs and marketing management teams, and monitoring effective strategy adjustments. Similar to the early phases of the registry, sponsors can begin defining why physicians are exhibiting certain prescribing behaviours based on the analysis of the registry’s clinical data, rather than tracking uptake and market share only. As a result, current (as well as future) gaps between the expected market effect of a product’s labelling and clinical messaging and actual market behaviour can be identified and addressed sooner rather than later, thereby providing opportunities for course corrections to optimise a product’s success in a complex medical marketplace. Questions to ask when addressing these gaps include: is the product meeting the needs and expectations of the patient and physician communities? Does the usage of the product, as described by registry trends, suggest any unanticipated market opportunities or threats? Why is the product generating (or not generating) expected market share? In addition to addressing these gaps, the integration of registry data analyses with market research findings can also help a sponsor defend an established franchise against new competition.

Evolving a registry to continually produce data and other important market information requires a periodic, strategic reassessment of the key registry design and operational elements previously discussed, continually building on the base of registry data and market research findings already gathered. For example: does the data suggest that a broader range of physician specialities should be recruited for registry participation? Do patient subpopulations within the overall registry population pose unique medical challenges, thereby requiring a more focused data collection effort? What data elements should be eliminated from the registry because they have yielded limited information? What data elements should be added to the registry that take into account new technologies or updated treatment guidelines? Should the assessment schedule be revised to better reflect current clinical practice? Can a physician advisory board be utilised to address emerging treatment options or to generate greater publication opportunities?

The overall goal of any registry programme is to continually produce reports and other communications that keep the registry output fresh and relevant to the participating physicians and patients, thereby encouraging their continued engagement in the registry programme. Long-term involvement in the registry may directly influence product sales at participating sites. In addition, registry findings encountered through publications, presentations, or word of mouth may sway the prescribing behaviour of clinicians or the formulary decision-making of managed care organisations or reimbursement authorities, which have never had any direct contact with the registry. These effects are not mutually exclusive, though a sponsor can emphasise some effects over others through their specific registry design choices.

A global biotechnology company expanded their long-running rare disease registry to include an even more rare subset of patients with difficult-to-treat neurological manifestations. Since well-controlled clinical trials are extremely challenging in rare disease indications, regulatory and reimbursement agencies agreed to utilise this physician-endorsed and credible registry as a source of supportive outcomes data in the development of evidence-based treatment guidelines for patients with this unique disease manifestation.

Using Registry Data to Support Communications

Many opportunities exist to disseminate information from registry programmes to fill gaps or pursue new opportunities, depending on the target audience. Typically, the primary goal of registry programmes is to publish long-term patient outcomes, including product effectiveness, safety, and patient-reported outcomes. When integrated with market research findings, however, regulatory and reimbursement trends, physician and patient satisfaction/loyalty measures, competitive analyses, physician practice patterns, behavioural drivers, and changing practice patterns can also be the topics of reports from the sponsor. Data can be presented in the form of abstracts, posters, podium presentations at scientific meetings.
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Conclusion

Pharmaceutical, biotechnology, device, and diagnostic companies’ clinical studies clear only one, crucial hurdle – gaining the government’s approval to manufacture and distribute their products to patients. The clinical trials conducted to gain regulatory approval of new pharmaceutical, biotech, and device products are not designed to provide the broader market intelligence required for successful product launch and clinical messaging, in market brand management, and long-term product growth. In addition, sponsors are under increasing pressure from different regulatory authorities and reimbursement agencies to confirm the long-term safety and effectiveness of their products, as well as to justify their product’s inclusion on as many product formularies as possible.

By designing, implementing, and maintaining a disease registry, a sponsor can illuminate the real-world use of a product. Moreover, when integrated with the sponsor’s market research activities, a registry can assist in detecting possible threats, identifying potential future opportunities, and making strategic corrections throughout the product’s life-cycle. The steady stream of new information that can be communicated to physicians and other healthcare providers, insurers, private and public payers, and regulatory authorities will establish the sponsor as a credible player in the clinical arena it has entered, position a new product in its target market, and help to defend an established product against new competitors. It may even lay the groundwork for future, well-controlled clinical trials to expand the range of indications for the product. Achieving these objectives requires a sponsor to continually evolve its registry programme to keep pace with the development of new standards of medical care, an ever-increasing clinical knowledge base, and the continually evolving needs of the many external stakeholders.

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