

EVIDENCE GENERATION IN DRUG DEVELOPMENT

IDENTIFYING CHALLENGES AND OPPORTUNITIES

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Making sound choices about health care requires the best possible evidence. The use and scope of research activities within the pharmaceutical industry has increased; however, some of the decisions made during drug development today are not supported by high-quality evidence. This paper summarises and challenges evidence generation opportunities across the drug development process.

Early Development Stage

This stage includes pre-clinical/animal models and phase I clinical trials. During this stage, little is known about the product and/or marketplace. There is a challenge in making informed decisions for allocating resources to guide further development. To support making evidence-based go/no-go decisions on further product development, evidence generation activities should focus on:

- Prioritising information-gathering on disease burden, market, and competitive landscape
- Identifying market feasibility requirements for payer acceptance
- Supporting the design of observational studies to close gaps in the evidence base (e.g., retrospective cohort and cross-sectional studies)
- Informing Phase II and III trial design and implementation

Mid-stage Clinical Development

This stage predominantly includes Phase II and Phase III trials. The main challenges herein may entail a difficulty in determining indication, if there are multiple potential indications (e.g., oncology drugs), as well as selection of trial endpoints. Furthermore, considering that trial data are needed for regulatory submissions and health technology assessments, acquiring this information may delay submissions and result in a change in the competitive landscape. This is especially true when there is uncertainty as to target markets and patient populations and when entering a crowded and competitive marketplace. Evidence generation strategies should focus on:

- Identifying internal priorities to facilitate a timely product launch
- Defining needed evidence to position and support future product launches

- Leveraging existing data from interventional, observational, and cost-of-illness studies, as well as from ongoing clinical trials/studies
- Conducting supplementary data collection and interpretation
- Establishing stakeholder audiences (e.g., payer, provider, patient)

Examples may include

Define optimal pricing bands

Initial payer value proposition

Gap analysis

Plan activities focused on securing favourable access and pricing

Assessment of reimbursement and HTA submissions by competitors for all major markets

Building upon the payer analysis conducted in the early development stage

Late Clinical, Approval, and Market Access Stage

This stage includes Phase IIIb and Phase IV trials, as well as new Phase III trials for additional indications. There are numerous challenges during this stage, including resistance from payers if currently available comparators are well established and available at a low cost in a crowded marketplace, and availability of generics. In addition, it may be difficult to effectively communicate potentially attractive product attributes (e.g., improvements in adherence, cost-savings, etc.) to stakeholders, especially when the product in question has no clear advantage over comparators. Evidence generation strategies are especially important at this stage to allow effective navigation through competitive and regulatory pitfalls and hurdles, as well as responding to

competitive challenges and changing market dynamics.

These include:

- Defining evidence needs to ensure optimal positioning and market uptake alongside other products in the market, as well as in the product portfolio
- Leveraging body of existing evidence
- Conducting supplementary data collection and interpretation, e.g., payer research, surveys, focus groups, etc.
- Integrating new evidence into pricing and marketing strategies

Examples may include

Refine pricing strategy with the use of clinical data

Use data from payer research to address strategic challenges in preparation for launch

Regulatory/HTA submissions

Use new data to achieve a narrower price band with an optimal launch price

Conduct payer research to understand the receptivity to product and to test value proposition

Incorporation of Real-world Evidence

The traditional process for evaluating new medical products does not produce the evidence that patients, clinicians, and payers require for real-world decisions. The volume and complexity of information about individual patients is greatly increasing with use of both electronic medical records and personal devices. The possibilities and opportunities for medical product development

in the context of this wealth of real-world data are great, ranging from the ability to determine both large-scale and patient-specific effects of treatments, to assessing how therapeutics affect patients' lives through measurement of lifestyle changes and impact.

Mechanisms to facilitate efficient use of real-world data to meet the decision-making needs of a multitude of stakeholders are yet to be firmly established. There are, however, numerous opportunities and, indeed, challenges associated with incorporating real-world evidence in evaluation of medical products.

The quality of data arising from real-world sources must be considered, including the relevance and validity of different sources of real-world data (e.g., user-collected, practice-based) in the context of different clinical/scientific questions, and the strengths and limitations of different data sources at different stages of drug development and the licensing process.

There exists a pressing need to consider re-evaluation of traditional distinctions between goals and methods of pre-approval and post-approval research. Novel methodologies and approaches that may be considered to improve development and evaluation of products using real-world evidence may include the use of web-based or digital technologies to enhance clinical evidence collection and interpretation.

Aligning Stakeholders

A major challenge for regulatory and HTA bodies is to find an appropriate trade-off (or balance) between earlier/affordable access whilst ensuring overall benefits exceed risks sufficiently to approve new medicines. This balance has shifted in the last decade towards an increase in benefit-risk evidence requirements and more evidence generation for marketing approval decisions. Recently, studies have been conducted on different elements of these regulatory systems,

such as evidence generation for initial marketing approval and benefit-risk assessments. The EMA Adaptive Pathways pilot scheme is an example of such a study and elements of this paradigm are now incorporated into the new PRIME scheme, where there is an increased focus on patient groups with the greatest unmet medical need. In addition, various new trial designs and analysis techniques are being piloted having had input from both regulators and HTAs via Scientific Advice.

Different stakeholders will have their own perspectives on acceptable trade-offs or uncertainties throughout the full, drug development life-cycle. Regulators may have a different view as to what is acceptable to that of the patient, HTA body, payer, caregiver, or society (as-a-whole). Stakeholders, including the EMA and NICE, among others, have recognised the need to involve patients in dialogue around development and marketing approval of medicines. They have introduced varying instruments to respond to this need. Patient involvement and real-world evidence will be relevant in adaptive approaches to help define acceptable levels of risk and uncertainty.

Conclusion

It is important to note that the pursuit of high-quality, data-driven evidence should not detract from the significance of expert opinion and qualitative information as a complementary source of knowledge to inform decision-making; indeed, the former enhances the latter, and vice versa. We believe there is much opportunity to utilise qualitative methods to supplement and enhance high-quality quantitative data, with a more focused approach, throughout the drug development process.

The need for high-quality evidence will continue to increase, as regulators and payers require more long-term data on product safety and effectiveness, as well as demonstration of the product's value in treating disease. Huron has a global, in-house team of multidisciplinary experts

in pharmacoepidemiology, pharmacovigilance, regulatory affairs, pricing, and market access. Our digital team develops and implements informatics/web-based tools and applications for disseminating information and/or gathering data from healthcare professionals and patients, including interactive communications, surveys, and more formal study-based collection. We optimise evidence generation strategies on any scale, ranging from highly specialised, local activities, to large global studies.



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