

Phase IV Studies – A Market With A Proactive Approach For Growth Of A Pharmaceutical Business

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Summary

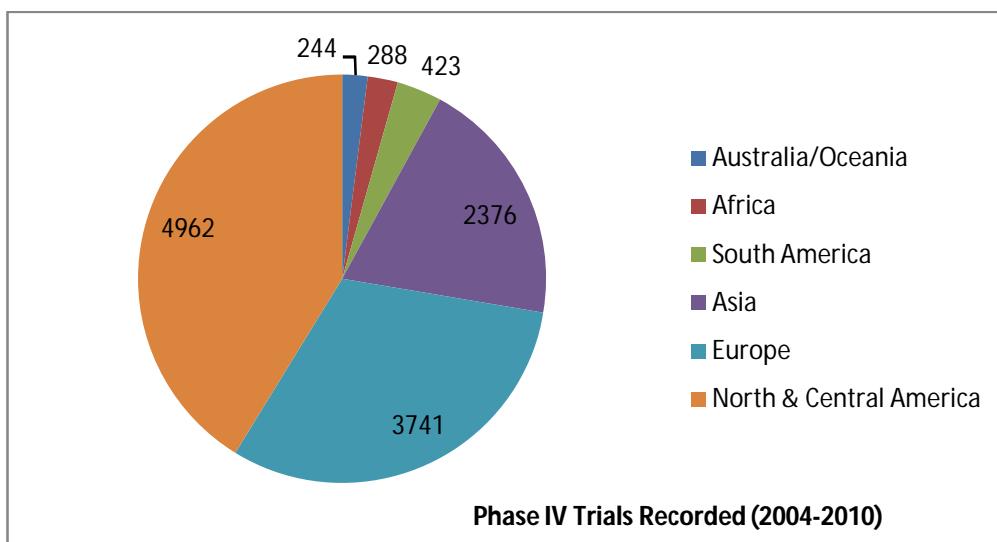
Phase IV studies are required as a condition of market approval. The companies look at venturing into Post marketing studies to improve the potential of the marketed product. This Phase has been the fastest growing segment in the area of clinical research. It supports in finding data for newer indications and new markets for which the drug product had not been initially approved. These studies should be randomized¹ and to maximize the informational value. The Phase IV research environment is driven by the varying regulatory environment, increasing safety concerns of new medicines, and the need for real-world data on the marketed drugs. This paper gives an overview of the Phase IV studies which form an integral part of the drug evaluation process and is a promising phase of advancement in the area of marketed drugs.

Introduction

Post Marketing Clinical (PMC) Research² studies or Phase IV clinical trials are executed after the regulatory authority has approved a product for marketing. The data gathered from the Phase IV studies determines the safety and efficacy of the drug in the market. Phase IV studies have become a key component in the pharmaceutical industry's product life cycle. This emerging area of clinical research is essential for the pharmaceutical firms to provide initiatives and assistance in areas such as client approvals, company expansion, and marketing. The potential to influence a viable advantage with post marketing research is reviewed by measuring the inferences for product marketing; expansion and a cost benefit advantage.

Clinical Trial Landscape

Bulk of clinical trials used to support drug approvals in the US are carried out outside the US, where site inspection is rare and regulations may be lenient. The number of countries involved in conducting clinical trials tracked by FDA increased from 80 in 1999 to 174³ in 2010. Phase IV clinical trials and Post Marketing Research are the fastest-growing area of clinical research today. Eastern Europe, Central and South America and Asia are the key regions involved in the trials outsourced. The scenario is due to the fact that the companies partaking in the trials do not have units within them to conduct Phase IV trials in comparison with the pre marketing studies.



Source: www.clinicaltrials.gov

The Phase IV trials are generally outsourced to Contract Research Organizations who look after the entire management of the trial and nearly 50 % of this workload is shared between the sponsor and the CRO. Formerly FDA used the term post marketing commitment (PMC) to refer clinical trials conducted by an applicant after FDA permitted a drug for marketing or licensing, that were intended to further refine the safety, efficacy and quality of the product.

Post Marketing Trial Requirements⁴

The main requirements for the PMC trials are covered in the new section 505(o) of the Federal Food, Drug, and Cosmetic Act, provided by section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA). The Section 505(o) allows FDA to conduct post marketing studies and clinical trials for prescribed drug and biological products approved under section 505 of the Act or section 351 of the Public Health Service Act. The applicant should compulsorily provide the following information to the FDA which includes:

Requirement	Deliverable
1	Periodic Reports on the Study Status <ul style="list-style-type: none">• Number of Participants enrolled• Estimated Completion Dates• Risks Involved during the trial• Registration Information
2	Detailed Timetable
3	Reports on Risk Evaluation and Mitigation Strategy

Source: www.fda.gov

Drivers for PMC Research

Emerging Market and Support of CRO Industry Advantage⁵

The PMC market is growing at an annual growth rate of 15-25 percent. The demand for the companies to be involved in the PMC trials is on the rise since it has been difficult for the sponsor community to concentrate both on the essential technological infrastructure and hire the required staff. The studies categorized as incomplete may in fact be finished and awaiting a review at the workload on the FDA. The industry is coping with the real pressure and the right mix of balancing the Phase IV research and the ability to create the infrastructure to be carried out during the drug

development cycle. Contract Research Organizations (CROs) are able to offer clinical trial services with a high level of expertise at a lower cost than the sponsor company. The key aspects of a outsourced CRO's include⁹:

- Global Portfolio of Clients
- Broad therapeutic expertise
- Efficient IT infrastructure
- Understanding of diverse regulatory demands
- Monitoring and Audit Services
- Tie ups with hospitals to develop own investigative sites
- Lower cost of operations.

The globalization of the market sets new requirements for the drug companies and while seeking approvals in a country in which the company has no previous experience, it is safer to turn to an experienced CRO for assistance.

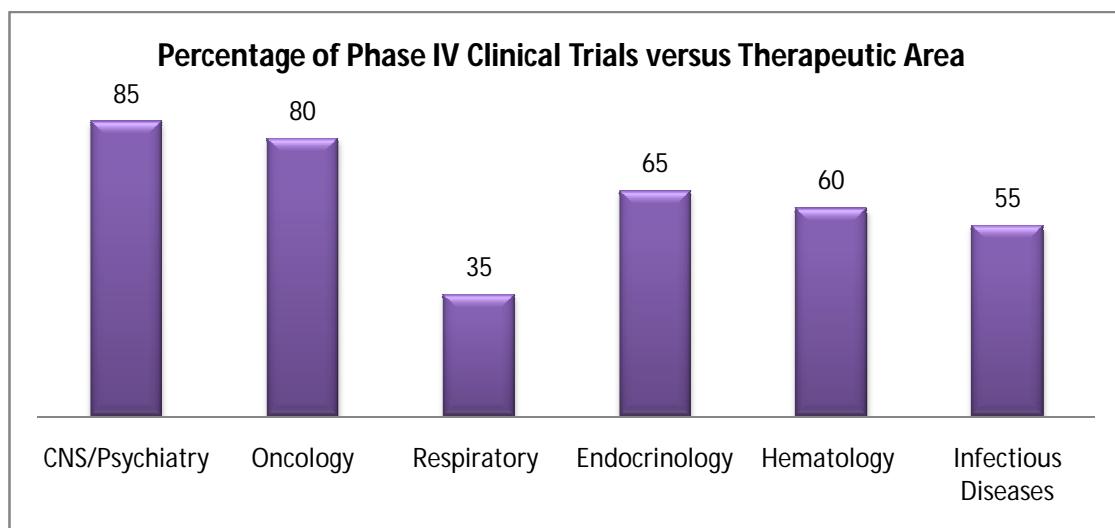
Emphasis on Post-Approval SOPs and Surveillance

The collaboration with the industry and the investigators for PMC studies is a challenge as the trials combine both marketing and scientific objectives that have to be clearly identified and pursued. The company can provide its customers a specialized set of standard operating procedures (SOPs). The company should focus on recruiting the right talent to carry out the phase IV research and be flexible in carrying on onsite monitoring for the SOP's with a futuristic market development perspective. The various methods of post marketing surveillance include spontaneous or voluntary reporting, cohort studies and case control studies. The chance that a particular study will discover a drug effect also depends on the study's sample size and the frequency of the drug effect. Marketed Health Products Directorate (MHPD) in Canada, Medicines and Healthcare products Regulatory Agency (MHRA) in United Kingdom ; MedWatch in United States; Drugs Controller General of India(DCGI)are responsible for coordination of post marketing surveillance studies . For designing postmarketing studies, the investigator must both be guided by the results of the premarketing clinical trials and this is a requirement for SOP's to be developed.

Awareness for Phase IV trials

The need for Phase IV trials has become mandatory. The evaluation of a new drug after it reaches the marketplace is a concern for pharmaceutical manufacturers and regulatory agencies. Many high profile recalls by sponsoring companies have drawn a lot of public attention to the shift for these trials. A few recent examples including recall of Tylenol, Benadryl by McNeil in Jan 2011⁶; Greenstone's recall of Citalopram and Finasteride in March 2011⁷ were taken as a precautionary measure to prevent supply of unhygienic medicines in the market. Companies are taking a positive approach in looking for data for alternative indications for existing products and the volume of patient registries help in supporting the development of these trials. Post Marketing Clinical research legally gives a chance to the medical community concern over performance and monitoring; complying or modifying with an existing regulatory body. The research gives information for future product development/improvement in turn supporting the strategic product/therapy initiatives of the company and facilitates in complying with relevant regulations for the testing of human subjects.

Analysis of Phase IV studies and Therapeutic Areas



Source: www.clinicaltrials.gov

Most of the Phase IV therapeutic areas are out sourced .The chart shown above depicts the relation between the percentages of Phase IV trails outsourced in relation to key therapeutic areas. We see here that 85% of the Phase IV trials outsourced in the area CNS/Psychiatric disorders with the lowest in the respiratory therapeutic area.

Conclusion

The need for a solid archetype in Phase IV research involves unique level of cooperation between marketers and clinical scientists. Phase IV data can be essential for responding to regulatory⁸ mandates for additional post-approval safety information; for extension of product marketing approval; and for developing the essential therapeutic role and benefit of a product for physicians. Trends in this market are intermittent¹⁰ but the stakes are high for patients and the pharmaceutical healthcare sector as a whole. The success of these studies will determine the ability to meet the needs of patients, payers, prescribers and decision-makers.

Research Methodology

The article gives a strategic insight into the post marketing clinical research market. Scientific Journals, Company websites and G7 Synergon analysis were the sole source of data points for all the analysis featured in this report. References were made to multiple secondary resources, in-house data, during the course of the due-diligence on data-aggregation to derive strategic insight on initiatives to be taken during Post Marketing Studies.

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