

Transforming Drug Development with a Fully Outsourced Model: Lessons Learned for Biopharmaceuticals

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Introduction

The pharmaceutical industry is exploring alternative drug development models to address the persistent decline in productivity. One transformation model that has been implemented successfully in early phase development is Eli Lilly and Company's Chorus. Chorus is an example of research and development (R&D) transformation rather than a corporate downsizing exercise. Lessons learned from Lilly's Chorus outsource model may be applied to biotechnology and pharmaceutical companies, as well as Contract Research Organizations. Application of Chorus principles could result in similar productivity gains in both the early and late phases of drug development.

When the Tufts Center for Study of Drug Development (CSDD) published its 2008 Outlook report, they stated the most successful drug developers in the coming years would be those who radically change their entire approach to business – from R&D to project management, manufacturing, and marketing [1]. Given that the pharmaceutical industry has made only incremental changes to their R&D paradigm in the last four decades, there is skepticism the industry will transform anytime soon. With the rising cost of drug development and continued shortage of new molecular entities entering the marketplace, it appears transformation is not occurring fast enough.

Eli Lilly and Company Created Chorus to Radically Transform Pharmaceutical R&D

Chorus, an independent division of Lilly Research Laboratories, is empowered to quickly and cost-effectively advance a portfolio of candidate molecules from discovery through clinical proof of concept (PoC) [2]. The model is simple: Chorus tests new molecule hypotheses in man by addressing key scientific questions at the earliest possible time before embarking on the more expensive, late-stage development activities. In this model, traditional pre-PoC development activities including large-scale manufacturing, extensive formulation work or long-term toxicology testing are delayed until data are developed to support the mechanism of action (MOA) and the specific candidate [3]. This approach alters the balance of risk across the portfolio and enables Lilly to pursue many more

leads at a fraction of the time and cost, while advancing molecules with an enhanced probability of technical success into later phases of development [4]. In the seven years since inception, Chorus has taken more than two dozen assets into development from discovery to clinical PoC at a mean cycle time and cost per asset of just under 32 months and \$4.5 million, respectively [5]. Data from a 2000 Tufts report placed the cost of Phase 1 development without getting to a PoC at US \$15.2 million [6]. In a subsequent analysis published in early 2006, Adams and Brantner place the mean cost of Phase 1 development at US \$32 million [7].

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Chorus Performance Efficiencies are Attributed to Its Business Model

Chorus operates much like a lean biotechnology company within the walls of a larger pharmaceutical company. Chorus is a flat structured, multi-functional R&D organization with an experienced internal staff. The 30 drug development and operational experts that make up Chorus average 15 years of industry experience and are responsible for the core functions of Medical, Statistics, CM&C, Toxicology, Regulatory, Clinical Operations, ADME, and Quality. This nimble structure, along with the responsibility for a substantial independent portfolio of molecules, has created an “act like an owner” work environment. Doing whatever it takes to complete work rapidly, without compromising patient safety or quality, has contributed to Chorus’ impressive productivity results. Chorus’ internal staff is responsible for the design of drug development plans and then implementing the work product through a fully outsourced network of third party providers (TPP) and external consultants. This minimal infrastructure enables lower costs of operation and creates a business model where the ratio of fixed to variable costs at Chorus (25%/75%) is more favorably weighted than traditional drug development paradigms.

Matching Organizational Structure with a Flexible, Simplified Outsource Strategy is Essential

For any outsource model to work efficiently, there needs to be an appropriate balance of internal and external resources on the project. The art of successful outsourcing within the Chorus model is to avoid duplication of effort in order to keep resources to a minimum. This concept sounds straightforward, but has proven to be difficult for most pharma companies to execute. Chorus reduces complexity by assigning a single functional expert to direct/lead the integrated work product for a given functional area. For example, a Chorus research manager is accountable for all operational aspects of a molecule’s clinical plan, including the outsource strategy, project management, and technical oversight. Chorus will not assign additional internal functions to assist in specialty clinical disciplines such as medical writing or data management; in fact, Chorus does not staff these rules-based disciplines internally. Instead, the Chorus single source accountability model requires that all internal staff have a broad understanding of their discipline so they can navigate projects, as well as possess technical skills to be able to dive deep into functional issues when vendors require additional guidance. Chorus encourages TPP experts to make implementation decisions and has a well-defined, yet flexible, change control process that supports this practice. For strategic issues that have a major impact on project scope or milestone delivery and require sponsor input, Chorus has a straightforward governance structure designed to facilitate quick decisions within a few days, thereby decreasing lag time in implementation of scope or timeline changes.

In addition to the flexible change control approach, Chorus has also eliminated routine process complexity by developing a set of streamlined standard operating procedures (SOPs) that permit delegation of authority. While Chorus is fully compliant with Lilly corporate policies, as well as all applicable laws and regulations, Chorus has created a streamlined set of purpose-fit, early phase research SOPs aligned directly with GCP, GLP, and GMP requirements as described in International Conference on Harmonisation (ICH) guidelines. After a vendor passes an in-depth vendor/site qualification and ICH audit inspection, Chorus and the outsource partner may use the outsource provider’s SOPs, templates (such as protocols, study reports and Case Report Forms), and/or information technology platforms for data management. For outsourced work that requires sponsor approval, Chorus confirms regulatory guidelines are followed through the utilization of quality checklists. Overall, this practice minimizes imposed sponsor burdens onto its partners and has resulted in improved cycle times and consistency of externally delivered

work product. While this process speeds work flow, it requires the sponsor to be flexible and willing to work through multiple database formats and templates. This can pose integration challenges later if the data is expected to be consolidated for submission activities.

The Chorus Outsource Strategy: Selection of the Right Vendor, at the Right Time, for the Right Project

The Chorus business model was built on the foundation of flexible outsource staffing through TPPs, offsetting fixed internal costs. Tactical outsourcing such as staff augmentation, functional outsourcing, and full-service outsourcing is being pursued more aggressively by pharmaceutical and biotech companies to reduce R&D fixed cost. Each of these tactics has its own merits and purpose, and anyone who has worked in pharmaceutical operations can most likely recite an actual success story (and failure) for each. Rather than dealing with inefficient Pharma outsource models, such as relying on a small exclusive group of providers, Chorus recognizes the need to leverage a wider group of external global implementation expertise to deliver multifaceted services. This external network provides Chorus the flexibility to match unique needs of each project and strategic integration requirements to a wider array of global and niche TPPs. Chorus then has the ability to not only try out multiple providers, but also move quickly from one to another if expectations are not met or harmonization is not achieved. Under traditional preferred provider contracts this flexibility can be difficult to achieve. To support this more inclusive model, Chorus has developed a large and growing network of providers to support each functional area (i.e., Chorus worked with 75 clinical TPPs in 2008). While this greater flexibility is desirable, it places an increased burden on procurement, contracting and quality groups.

In Chorus, selection of the right vendor goes beyond the standard technical requirements such as indication experience, geographic presence, and big pharma references. The right vendor also means close alignment and strategic fit with the Chorus business philosophy. Counter to big pharma practice, Chorus works with many niche and smaller sized vendors. This not only benefits Chorus with the specialized knowledge these vendors offer, but their agility and focus on Chorus work typically results in exceptional performance metrics. Chorus does have de facto preferred vendors that have consistently performed and collaborated well under this business model. Repeat business has rendered faster contract and budget negotiations, as well as simplified business processes.

Technology is Essential to Enabling the Implementation of the Outsource Model

When Chorus was formed, it could not function effectively within this new outsourced model given the information technology (IT) solutions available at the time such as e-mail, e-rooms, and timeline management tools. Also, corporate business tools were not designed to support a virtual drug development paradigm. In particular, they did not support a broad collaboration site capability with appropriate security, privacy and firewall safeguards suitable for use with external parties. As a result, Chorus had an immediate need for a single, integrated tool to address the unique communication and management challenges associated with the Chorus business model and to facilitate collaboration with TPP’s. This tool needed to have the following characteristics:

- Robust security to control internal and external access to intellectual property and proprietary information
- Global access via the internet, via any computer
- No special software requirements for external collaborator’s computers
- Compliance to FDA 21 CFR Part 11 for electronic records and electronic signatures

- Integration of high-level project plan information with detailed implementation plans
- Role-based functionality for Chorus, vendors, and sponsor stakeholders (i.e., Lilly)

Given these unique requirements, Chorus teamed with an external IT partner to develop a web-based enterprise management system. This system, which has been in active use since 2005, enables small, virtual, drug development teams to globally and securely collaborate on all aspects of a project, including broad planning, detailed implementation, document development and approvals. It also provides Chorus with administrative solutions to numerous internal portfolio challenges. Overall, the system has facilitated quicker, strategic decision-making by leveraging defined processes to integrate collaborative information across a development plan.

Lessons Learned for the Industry

As a response to increased pharmaceutical R&D spending and its flagging productivity, pharma is experimenting with transformation solutions to reduce the cost and time to develop drugs. The Chorus group at Eli Lilly and Company has implemented an alternative approach to drug development that utilizes a full implementation outsource strategy which has proven to be very cost-effective to the advancement of molecules from discovery through clinical PoC. Barely seven years into existence, Chorus has successfully implemented over two dozen early phase plans at substantial savings and cycle time reductions compared with a traditional development model. As the industry transforms traditional development into flexible outsource models for both early and late-phase development, several key outsource practices from Chorus can be applied. These include, but are not limited to:

- Maintain a minimal organizational infrastructure, staffed with experienced drug developers and operations experts, to enable effective decision making with a low fixed operating cost.
- Outsource the bulk of actual work (e.g., clinical development, toxicology, CM&C) to a global vendor network to decrease direct costs and cycle times versus comparable work conducted internally.
- Implement a flexible change control process and push decision making down to the lowest appropriate level, removing the need for belabored governance reviews and facilitating decisions in a few days rather than weeks or months.
- Conduct functional operations on a streamlined set of SOPs and processes, as well as utilize TPPs' processes, tools, and templates to minimize imposed sponsor burdens to partners and improve quality of work product.
- Provide a flexible global technology platform to bring key information together in a comprehensive, accessible format, to enable multiple external parties to collaborate on a project in a virtual global environment.

As the industry leader in this early phase transformation model, Lilly has taken initial steps to extend these concepts downstream into later stages of product development, completely reforming a paradigm that has dominated the industry for nearly forty years.

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