

Strategic aspects of clinical R&D in a continuously changing environment

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Abstract

The basis for successful R&D in the pharmaceutical industry is rapidly changing and the currently predominant strategies are challenged. Conventional wisdom is questioned and many companies are seeking to find new ways of organizing and working. This paper brings forward strategic assumptions to be considered for clinical R&D.

Keywords: Pharmaceutical industry, clinical R&D, strategic change, new organizational models

Introduction

During the seventies and beginning of the eighties, working procedures in clinical research were characterized by a relatively stable situation based on conventional and well-accepted routines which were adopted by most companies. Over the following years these rules and procedures were continuously improved, including the introduction of formal methods for quality assurance (Good Clinical Practice). However, while many companies were able to gradually improve their R&D procedures, no real break-through thinking took place and the strategic assumptions about the way R&D should be done were hardly challenged. The same techniques, organization and competencies were used industry-wide and competition took place in the marketing arena.

In the long run, the adoption of these methods in large-scale clinical programs resulted in a dramatic increase in time and costs. Together with the quest for new indications and increasing demands for documentation, the established way of working turned clinical R&D into costly, time-consuming and large-scale efforts. With an increasing need of shorter development cycles, these factors became major driving forces behind a number of BPR-initiatives in virtually all pharmaceutical companies. This wave of change was probably also a major contributing factor to the restructuring of the industry through mergers, acquisitions and alliances.

We believe that the improvements gained so far are merely the end of this development, but rather a starting point for further, more radical changes. New indication areas, as well as new techniques for drug discovery combined with possibilities of utilizing new information technology makes it highly likely that working procedures and their organizational environment will look significantly different compared to today. However, while business forces within and outside the industry, as well as technological development, allow us to observe the ongoing change as such, it is far more difficult, if

not impossible, to predict the outcome of this process. Consequently, any valid and successful strategy for managing a pharmaceutical company needs to allow flexibility and enable the fast adaptation to changing environmental conditions. At the same time, it must provide a certain amount of stability in order to provide a work environment where daily activities can be performed without disruption. A major challenge for strategy development is to balance these, not obviously compatible, requirements.

An organization that successfully manages these requirements will be characterized by having a “standardized platform”, allowing the efficient handling of information but also high flexibility in procedures as well as organizational structure. Such an organization focuses on processes, projects and centers of excellence providing leading edge competencies and capabilities, rather than the functional model predominating today's pharmaceutical industry. In order to gain this position, it becomes imperative to implement and deploy effective mechanisms for knowledge management. This can be achieved through an organizational and technological infrastructure that enables access to information across space and time throughout the company without restraining local initiative and innovation.

Long-term strategic aspects

During the past decades, clinical research and development within the pharmaceutical industry has been subjected to considerable change. In the seventies, development and documentation of new pharmaceutical compounds was characterized by a relatively small number of patients in few centers with a limited number of countries involved. Since then, they have gradually increased both in size and complexity, primarily due to the scientific needs. Another contributing factor has been the introduction of Standard Operating Procedures (SOPs) that significantly extended the documentation of working processes in order to ensure the use of standardized, quality assured procedures. Furthermore, the use of contract organizations for the conduct of clinical studies has increased, resulting in higher needs for inter-organizational co-ordination. This continuous growth has resulted in a significant increase in time and cost for development of new compounds. Within the Astra group, the number of clinical studies has doubled from 30 trials in 1970 to 60 in 1990, a trend that has continued also during recent years. The average time to develop a drug increased from 11 to 15 years with costs raising by approximately 500%.

During the 1990s, most pharmaceutical companies have embarked on various Business Process Re-engineering (BPR) initiatives to meet demands for improved efficiency and cost control. The primary aim of these efforts has been to reduce time and costs in the clinical part of the R&D process. Although many of these efforts have resulted in shorter cycle-time and cost reduction, one can question whether they have really changed the basics of how clinical research is performed and to what extent they have had an impact on the basis of competition in the industry.

Stabilizers and de-stabilizers

As a framework for discussing process development within clinical research and development we have used a model that divides factors with a considerable impact into stabilizers and de-stabilizers.

Stabilizers are defined as *Improvements obtained by continuous development of existing processes*. They are based on historical experiences, they assume a stable environment and result in improvements of current processes. While the consideration of stabilizing factors can provide significant improvement under stable and predictable conditions, they may hamper the organization's ability to adapt itself in an unstable environment, characterized by a need for continuous adjustments, changing specialization, mergers, acquisitions and alliances.

De-stabilizers are defined as mechanisms for *Solving problems by utilizing new possibilities and thus creating new processes*. De-stabilizers are based on new seizable opportunities, assume an unstable environment characterized by high flexibility and effective communication and imply that problems are addressed by means of radical change, rather than incremental improvement.

Stabilizers

Considering clinical research, four main stabilizers can be identified. Basically, they are describing the factors governing how clinical R&D is currently performed within the majority of pharmaceutical firms. During improvement initiatives, these are also the aspects being most frequently addressed in order to achieve short-term operational elevations.

Scientific methodologies

The basic scientific theories behind the design and analysis of clinical research are today widely used throughout the entire industry. Furthermore, a terminology has been established, allowing efficient communicating of results. Thus it can be assumed that over the next coming years there will be only gradual changes, caused primarily by new medical entities and indication areas, as well as the developments in relatively new scientific areas, such as combinatorial chemistry and genomics.

Terminology

The terminology used in clinical research is of great importance for the efficient communication of results and provides a common platform for all individuals involved. Due to the standardization of terms, storage and analysis of data is made easier and for on-line accessibility in space and over time, the use of common terms plays an important role. The increasing number of arrangements with contracting organizations also requires the availability of a standardized set of terms, both from a scientific perspective and when considering inter-organizational process efficiency.

Current processes

In a number of areas and within most companies there are internal and external routines, such as SOPs and routine instructions for handling of clinical trials, established. In most cases, they are supported by information systems, either commercially available or developed in-house, being built to specifically support the current process. The people being involved in clinical R&D are trained and educated to work within the boundaries of these high-end processes and during the past years, score cards and other performance measurement systems have been introduced and are not widely deployed. All these factors are considered to be stabilizers, as they are supporting the current way of working, but can be a hurdle to overcome, if dramatic changes are needed or become available.

Cultural aspects

Cultural aspects include factors such as tradition, society and beliefs in the organization. They are a result of a long and continuous development taking place under a pre-dominating organizational paradigm and are probably the strongest stabilizer and also the one most difficult to overcome by traditional means of change, such as re-organizations and BPR initiatives. In companies with strong traditions and a successful past, it becomes extremely difficult to establish the sense of urgency and cultural prerequisites being necessary for radical change.

Another aspect requiring consideration is the initial cost and effort required for change exceeding the incremental improvement of current organizational structures and procedures. Even though not being a stabilizer in the sense of the previously used definition, this factor nevertheless constitutes an important barrier to radical change.

De-stabilizers

The de-stabilizing factors mainly represent drivers of change impacting the pharmaceutical industry, but being triggered from the outside. They include advancements in science, such as genomics, IT-development, changes in society and new methods of work, such as high-throughput screening.

Scientific aspects

From being quite small, focusing primarily on medical aspects clinical studies today regularly involve multiple scientific disciplines. New indications and chemical entities make it more important to have immediate access to the registered information, independent from where and when it has been collected. The objectives of the studies also affects their size and as a consequence, the patient materials are regularly collected on a global basis. Furthermore, it is likely that once collected material will not only be used for the actual study but also for generating new hypotheses both with respect to new research and development of technologies.

Technical aspects

The IS/IT-systems used for clinical studies have so far been primarily functional, i.e. they have been used for collecting, storing and analyzing data. Although systems have been developed for Remote Data Capture (RDC), their impact has been marginal, since their improvement potential has been limited to a narrow part of the clinical trial process and they, in return, brought other drawbacks into the process. A more substantial breakthrough can be expected from portal systems providing shared information spaces, since this technology offers the potential for a radical re-thinking of the basic assumptions about clinical R&D, rather than operational improvements.

Changes in society

It is likely that the information available in clinical studies will be of great interest also for groups, e.g. patient communities, that traditionally haven't taken interest in it. Today, pharmaceutical companies are starting to develop on-line communities for the users of their products, but those information sites do not yet allow access to clinical information. Also regulatory authorities are most likely to develop an interest in clinical information

going beyond the current demands for documentation of new compounds and drugs, since the data collected contains a large potential for re-use. Through the combination of data from multiple companies it becomes possible to develop knowledge bases that go far beyond what a single firm can achieve. At the same time, the consideration of clinical data as being a property owned by pharmaceutical companies is challenged and regulatory authorities might consider societal benefits as being more important than the pharmaceutical industry's interest in maintaining ownership of data.

New forms of working

The cost for running clinical studies today is significant also for large pharmaceutical companies. Considering the expected increase of clinical studies, with respect to scope, size and number, resulting from new discovery mechanisms, there is a latent risk for cost explosion that so far seems to be under-estimated. Costs of M\$ 100, or more, are not unusual today and with the increasing demands for documentation and new indication areas, these numbers can be expected to increase, if no cost control measures are taken. The development of new infrastructures and processes on organizational and technical level becomes imperative for pharmaceutical companies, if they want to sustain and improve their capabilities to conduct clinical studies. In addition to improved work processes and the deployment of standardized infrastructures, the trend towards alliances and different forms of networking will continue. The number of deals within the life sciences industry (pharmaceutical and bio-technology) has increased significantly over the past years and companies now pursue horizontal and vertical integration strategies.

It seems to us, that the traditional stabilizing factors have been dominating the mindset of decision makers in the pharmaceutical industry. As a result of a behavior influenced by these traditional factors, working procedures based on SOPs are continuously developed, including also routine instructions and different templates. The IT-systems follow the established routines with systems for data-management, data-capture monitoring systems as well as standardized tools for analysis. In order to make these routines and technologies work, organizational structures are also subjected to an often radical standardization, intended to ensure compliance with the rules and reduce deviations from the pre-designed process.

Information management

Although it's not meaningful to weigh or rank the factors presented above, there are good reasons to believe that those being categorized as de-stabilizers will be of great importance for changes of clinical R&D processes we are expecting to see over the coming years. These de-stabilizers will change the way pharmaceutical companies think about clinical R&D radically and will have a considerable impact on working procedures, organizational and technical infrastructures, as well as the required competencies and capabilities.

In order to cope with the challenges imposed, two main strategies are available. The first and more radical one is aiming to create balance between structure and flexibility, standardization and adaptation, procedures and flexibility, building on processes, projects and capability providing centers of excellence. The alternative, more conservative, strategy would be based on gradual improvements of stabilizers, following

the current path of improving existing processes, IT-systems and organizational structures. However, if the de-stabilizers will become as important and influential as we believe, the second strategy is highly hazardous, since major challenges are not addressed and the change required for successfully dealing with them will not be achieved.

In order to utilize the possibilities offered by emerging technologies, new organizational forms of cooperation and competition, it will be imperative to review the current processes, procedures and structures. Considering the current SOPs for clinical trials, based on batch processing of large amounts of data, we will see a transformation to a more parallel and less sequential handling of clinical data and project information. Common information spaces, delivering current and customized on-line information to all project participants - monitors, data managers, study centers, etc. - will reduce delays in the information flow and improve study management, e.g. with regard to patient recruitment and the handling of serious adverse events (SAEs). Subsequently, also external stakeholder, such as study contractor, regulatory authorities and patient organizations, can access the information space and receive customized information. Consequently, the accessibility of information across space and time, powered by on-line information infrastructures, is a major driving force for the change we are about to observe in the pharmaceutical industry.

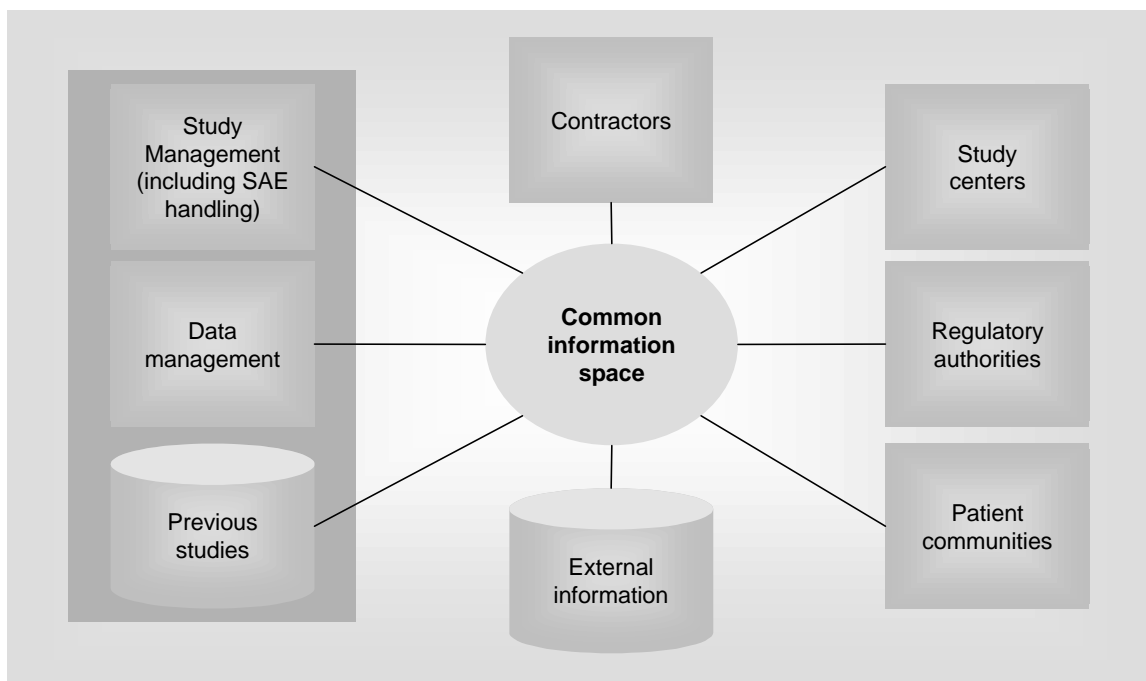


Exhibit 1: Common information spaces

The development, implementation and deployment of common information spaces is a crucial factor in the transformation of clinical R&D. However, a technological solution in itself will not elevate clinical R&D, unless certain critical success factors (CSFs) are satisfied.

- The technical system must be flexible in the sense that it does not prescribe a certain organizational behavior (business logic). Its use must be adaptable with regard to changes in the clinical R&D process. Possible changes in the process include SOPs, requirements for study documentation from regulatory authorities, and process variations due to locally determined environmental circumstances or requirements imposed by specific projects.

- The system must not depend on a high-end technology that prescribes the use of specific hard- or software. It should be based on open standards and enable the deployment of the installed base, but also allow changes of the underlying applications being used.

To be able to handle such a situation, it is essential to be as independent as possible from both processes and current systems. This perspective requires a strong focus on the information to be handled, rather than the organizational or technological environment.

Strategic implications

Today's pharmaceutical companies are under pressure from different factors. In order to sustain competitiveness, short term requirements for financial performance need to be balanced with long-term strategic development. These changes have to be achieved in a situation of fast scientific development and the establishment of new technological solutions that will have a dramatic effect on clinical research. Although the direction is clear there is uncertainty with respect to time and consequences.

Bringing new products to the market faster and more cost efficient, as well as reducing the number of terminated projects require new approaches to project management and prioritization. Moving new compounds through the pipeline more quickly, taking go/no-decisions faster and allowing resources to be (re-)assigned to the most promising projects is a crucial capability for fast pharmaceutical companies.

A second important aspect is the re-use of information and clinical data, once it has been obtained. Re-usable data can be used for developing and testing new medical hypotheses in further research programs, but also for developing and improving methodologies and working procedures. The use of IT for data collection and availability plays an important, which requires companies to develop capabilities in the bio-informatics field in order to deploy information efficiently and effectively.

An ideal strategy for coping with these demands would open-up for de-stabilizers in all areas, without disregarding the stabilizers that have been contributing to achieving current success. A major difficulty associated with this approach is the problem of actually achieving this transformation, given the strong impact of current stabilizers such as culture, terminology and established working procedures and organizational structures. Any strategy that is successful not only in the board-room, but also in the organization, needs to take into account the self-reinforcing power of current values and organizational and individual behavior. Cultural diversity in different countries and parts of the organization and the influence of third parties, such as contractors and authorities, will also contribute to making cultural change a major challenge.

For an organizational strategy addressing the aspect of culture it would be essential to allow the local adaptation of procedures, given that the generally defined standards for terminology and rules imposed by e.g. regulatory authorities are not compromised. Any attempt to standardize and predefine procedures, organizational and individual behavior in a top-down manner, is most likely predestined to fail. Either, the tension between local culture and behavior and the globally prescribed process will require a lot of energy to be resolved, or an inflexible organization, unable to change, will be created, staffed with de-motivated people.

In a long-term perspective, information accessibility in space and over time is the most important aspect of clinical research. For enabling information management over a period of many years, it is necessary to establish a common terminological framework,

including scientific parts, as well as a organizational and process aspects. Diverse cultures, different languages and interpretations of data constitute barriers to developing a common terminology. Within the scientific area, this development has started several years ago and a common terminology, even though not officially standardized, has been established as a part of clinical practice. Considering the area of processes and organizational aspects, however, we are still far from having access to common frameworks and what exists, is rather weak. The emergence of various forms of inter-organizational networks, alliances and cooperation will require a substantial development within this area.

The technological development within the field of clinical R&D support systems has attracted a lot of attention over the past years. Emerging technologies, such as systems for mobile and remote data capture, advanced data management and analysis systems and technology for decentralized management has opened the ground for a more efficient IT-deployment. However, the technical advancements have also started a costly race for new and better technology, requiring more frequent updates and replacements.

Considering the relation between technology and organization, we can conclude that technology contains stabilizing and de-stabilizing characteristics. The potential of IT for being a change agent when being employed properly is high. However, most systems used today are high-end systems, designed and implemented to support one specific process without allowing deviations from the original design. In that sense, technology also constitutes a significant barrier to change and adaptation with a risk for the organizational change pace to become dependent from the IT-systems' life-cycles.

A feasible technological strategy is the development of modular multi-tier systems, based on already widely diffused and adopted standards, such as WWW-technology. Using this technology, singular functional modules can be removed, replaced or included, without changing the overall architecture. In addition, the installed base can be included and previous investments are not lost. Platform independence at client level, intuitive interfaces reducing the time required for education and training, allow a faster diffusion and deployment process of new technology.

The organizational aspects also play an important role. So far, the functional organizational structures have been predominant. However, with an increasing amount of inter-organizational cooperation, e.g. with contractors specialized in clinical trials, the boundaries of the organization blur and become less important. This requires the consideration of cultural implications, when different local cultures meet and processes not only span over a variety of internal functions, but stretch into other organizations.

Decentralization of decision making, study management, data collection and other activities require new forms of networking and mechanisms for running clinical projects efficiently.

The consideration of the wide variety of factors we have identified - processes, projects, competence, information technology - leads us to the conclusion that there is a need for a strategic component, being responsible for the consistent and efficient development, deployment and improvement of the different elements: A meta-process. Within the meta-process, the different organizational and technical elements are balanced and converged. Also, the meta-process connects clinical R&D with the company's business strategy, the different therapy areas and the other parts of the overall R&D process - discovery, pre-clinical, pharmaceutical, and clinical science.

Four strategies for the future

The identification of stabilizing and de-stabilizing factors, together with the dimension of stability in the environment allows us to create a scenario model for strategic behavior. These scenarios also represent four alternative strategies that pharmaceutical companies can apply. Each of the scenarios assumes the focus of change to be on either stabilizers or de-stabilizers and the intended change to take place within a stable or unstable environment. Naturally, the borderlines between the scenarios are not clearly cut, but they allow us a clearer description of the implications for the strategy following each scenario.

- **Strategy 1: Go with the flow.** This strategy is building on the existing mind-set, assuming a rather stable environment and putting focus on stabilizers. Change is achieved through process improvements initiatives and the deployment of more efficient technological support systems. The driver for change is not experienced or expected external pressure and a need for adaptation, but organizational and process performance and internal ability to achieve change.
- **Strategy 2: Never mind.** This strategy is typical for companies that ignore environmental instability and attempt to maintain strategy 1 despite the requirements imposed by an unstable environment. As the environment becomes more dynamic, cost minimization is used in order to achieve cost leadership and ensure survival. Subsequently, an alternative strategy - either strategy 4 or a niche player role - must be adopted.
- **Strategy 3: Prepare to jump.** An intermediate strategy for companies in a currently stable environment where future instability can be foreseen. In this case, the company needs to make the necessary investments in organization and technology in a way that allows future adaptability without compromising operational performance.
- **Strategy 4: Always run.** This strategy is viable for companies in an environment characterized by instability and a high impact of external forces. Following this strategy, organization and technology infrastructure need to combine the capabilities to act and deliver efficiently in different forms of internal and external cooperation and organizational settings, but also to allow flexibility and adaptability to short-term changes.

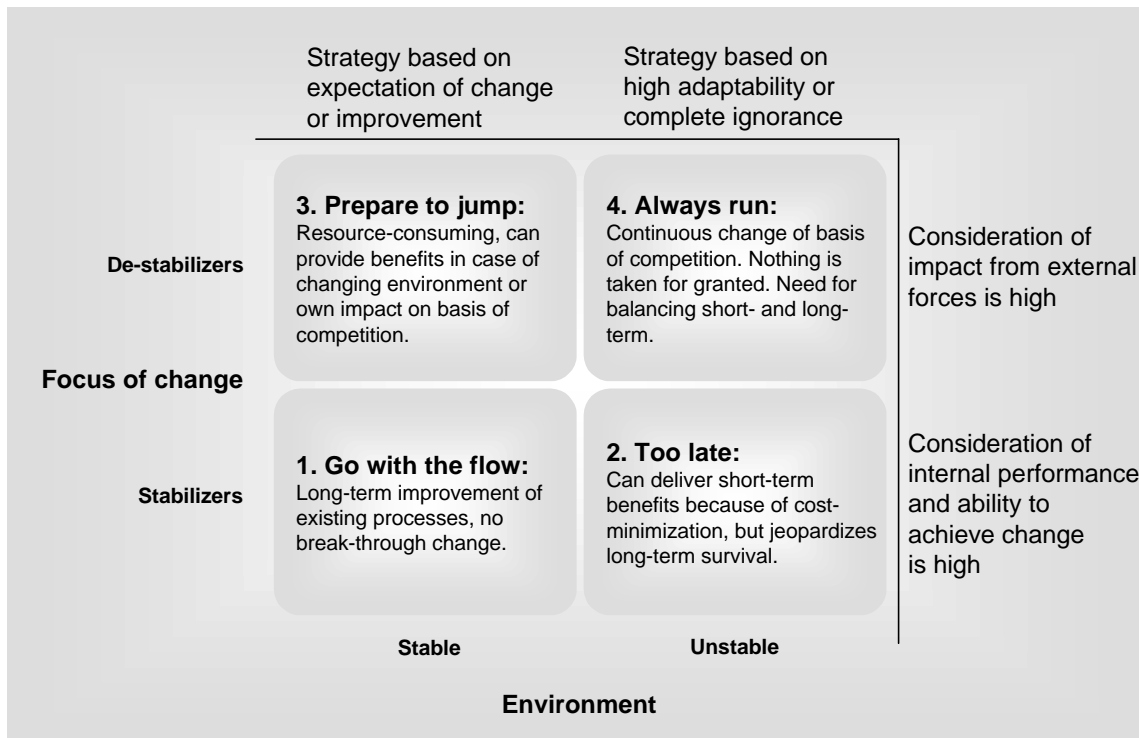


Exhibit 2: Four strategies for the pharmaceutical industry

The four strategies can also be categorized with respect to their viability over time. In accordance to this categorization, strategies 1 & 4 are viable in a long-term perspective, depending on the organizational environment. Strategies 2 & 3, on the other hand, are intermediately viable: Strategy 2 can be used for cost minimization under unstable conditions, but fails to ensure long-term survival without migration to a niche-player role. Strategy 3 is too costly to maintain in a long-term perspective, given a stable environment, but is feasible for preparing the organization for the migration into an environment of uncertainty.

A new model for organizing clinical R&D

Over the past years, pharmaceutical companies have been embarking on large scale change initiatives in order to improve their operational performance and reduce time-to-market in product development. These change programs, often conducted in the style of Business Process Reengineering, have allowed firms such as AstraZeneca to realize a significant improvement potential, especially with regard to cycle-time reduction. On the other hand, the rigid approach to process design and the implementation of standardized, high-end technology infrastructures does not allow the exploitation of the remaining improvement potential. Especially the concurrent introduction of high-end technology and standardized processes, that do not consider local infrastructure implementation and deployment contexts, does not seem to be a suitable approach (Cordella and Simon, 2000).

We argue, that it is necessary to revise the organization and technology strategies for the future and propose a model that, in our opinion, seems to offer a high degree of flexibility in organization design and technology use, without sacrificing operational efficiency. Following our proposition to focus on three core building blocks - processes,

projects and competence/capabilities - we can create structures that combine the advantages of consistently developed standards, practices and IT-use with the flexibility and adaptability required the an unstable environment.

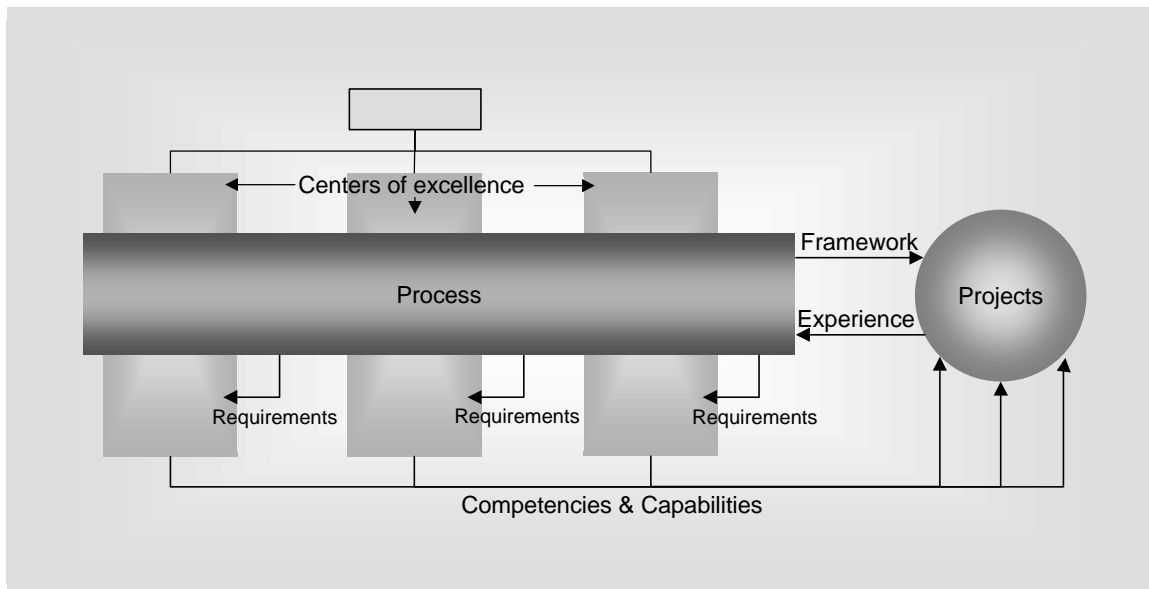


Exhibit 3: Organization built on Processes, Projects and Capabilities, with meta-process

Process

A process is a conceptual framework for clinical projects. It contains a collection of the practices, methods and tools being required for conducting clinical research in an efficient way. A process is developed by a process owner, i.e. a person being responsible for the improvement of the elements being part of the process, such as organizational procedures and the use of information technology. This development means to include the experience and knowledge gained from previous projects, but also to consider external developments, such as emerging technologies and developments in other firms. The content of the process also describes the competencies and capabilities to be provisioned from the competence areas to the clinical projects. While the concept of process ownership is similar to the one proposed in the business process improvement literature and methodologies, the term *process* has a different meaning. Instead of being a detailed prescription of work procedures, it must be seen as a collection of good practices, recommendations and experience, supported by Standard Operating Procedures only where they are required by regulatory authorities. For non-regulated activities, the process leaves room for local adaptation and improvement.

Projects

Today, clinical R&D is generally performed in project form, rather than by combining the activities of functional units within the line organization. A project is the instance of a process, where the methods and tools are deployed in a "real-world" setting, i.e. it contains the clinical research for an actual substance. Within a project, the framework provided by the process is used together with the competencies and capabilities provided by the organizational competence areas. The provisioning of services from competence

areas to projects takes place on the basis of a market model. From the projects, experience gained is brought back into the process, which can be improved continuously according to the feedback provided. Projects are run by a project manager, who is assigned on a temporary basis for the duration of the project.

Centers of excellence

Competencies and capabilities are provisioned to projects from centers of excellence or competence areas, which are based on the functional units of the "traditional" organization. Competence areas can also be described as defined communities of practice. In this setting, the role of functional managers changes from supervisor to coach. In the coaching role, the continuous development of functional expertise plays an important role and must be matched against process requirements.

Conclusions

In this paper, we have discussed some of the strategic aspects that need to be considered by pharmaceutical companies for managing their clinical R&D successfully in a turbulent and unstable environment. We have identified stabilizing and de-stabilizing factors that have an impact on the behavior of pharmaceutical companies.

Subsequently, we have discussed organizational and technological implications of this development and developed a model for organizing clinical R&D, based on three elements: Process, projects and centers of excellence serving a competence providers. We have also developed a set of four strategies that can be pursued, depending on the level of environmental stability and the company's ability to achieve change.

Our discussions have lead us to the conclusion, that very are about to observe a profound change in the pharmaceutical industry over the next few years. The current wave of mergers, acquisitions and alliances is a first indicator of what is about to happen, but so far, the predominant functional and hierarchical organizational paradigm has prevented an industry-wide break-through of new forms of organizing and working in clinical R&D. However, drivers such as emerging technologies and examples provided by high-performance companies, will fuel the transformation process taking place in the pharmaceutical industry.

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