Organizational Design: The Integration of Pharmaceutical Discovery and Development

by

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Abstract

The decline in Pharmaceutical R&D productivity has been attributed to high clinical failure rates suggesting that targets, leads and clinical candidates may be of lower quality in recent years. Senior R&D management generally believes that a greater integration of drug discovery and development will improve the selection and optimization of clinical candidates.

I demonstrate the different nature of discovery and development with discovery tasks seen as more uncertain, having more reciprocal work flows and more under the control of management than development tasks. Discovery and development personnel have different characteristics and motivations, with discovery staff having greater creative skills and development staff greater planning skill. Following a congruence approach to organization design these differences imply that a complete merging of discovery and development functions would lead to poor fit between organizational design elements. This leaves an ongoing requirement for integrative systems which can preserve the important characteristic of discovery and development functions yet provide knowledge integration at key decision points to improve the quality of clinical candidates.

A wide range of integrating mechanisms was found to be in use with an emphasis on cross functional teams. Information Technology was viewed as necessary infrastructure but not an important component of knowledge integration. No strong links were found between pipeline maturity and the integrative mechanism deployed. I speculate that company R&D performance could be better matched to internal and external circumstances by a more active approach to managing integrative systems. I propose a conceptual model of integrative systems to guide a more dynamic management approach to organizational design of R&D and suggest further work to formalize the model through an agent based simulation.

Table of Contents

Table of Figures

1.0 Introduction

1.1 Pharmaceutical Industry environment

At the beginning of 2004 the pharmaceutical industry finds itself amidst one of the most challenging periods of the last 50 years. Patent expiry, political unease about drug pricing, and the rising cost of drug discovery and development are some of the pressures weighing on the industry. The industry structure is also in transition with major M&A initiatives and the arrival of more than 2000 new and diverse biotechnology companies since 1983. These firms account for significant proportion of pharmaceutical R&D activity and have become embedded in the industry through equity transactions and drug licensing deals.

1.2 Productivity Crisis

Over the last 10 years the process of creating new pharmaceutical products has become more technologically intensive, more regulated and more expensive. The most recent study from the *Tufts Center for the Study of Drug Development* suggested that the cost of taking a drug to the point of marketing approval is $802 million (Year 2000 dollars) and is rising at an annual rate 7.5% above general price inflation (DiMasi et al, 2003)

Large pharmaceutical firms have found themselves caught in a productivity gap where looking forward they are unable, from their own research efforts, to

replenish their development pipelines fast enough to replace the anticipated lost value from patent expiries.

In 1998, the biggest drug makers each announced that they aimed to produce three new chemical entities (NCEs) a year; indeed, some companies now claim they need to produce three or more billion-dollar blockbusters a year (IBM, 2003). It is estimated that there are a total of just 14 blockbusters in the industry pipeline between 2003 and 2008 (Datamonitor, 2002) which will result in a major productivity gap. The high levels of M&A and licensing activity are part of the industry response to this shortfall however these initiatives do not directly address the performance of R&D.

Just a few years ago industry commentators were forecasting research productivity gains from the genomics and other related new technologies, suggesting that in the best case the cost of drug development could be halved (The Boston Consulting Group, 2001) There are indeed more targets, larger compound libraries, more extensive informatics, greater diversity of chemical synthesis, more sophisticated screens and higher resolution in measuring patient physiology than there was five years ago. However, this has failed to improve drug development productivity which has declined during recent years. Several theories have been put forward to explain this contradiction. These include more stringent FDA regulations, easy targets having been previously addressed and the high cost of using the new genomic technologies. Some

traditionalists believe that the industry has become too obsessed with high throughput technologies and cell-based assays and would do better to return to the low throughput but information rich whole animal testing. Another contributing factor to the productivity dilemma might be that R&D teams are fragmented and adjusting to new positions due to human resource turbulence during the last five years. The high valuations of biopharmaceutical companies during the pre March 2001 bubble economy generated the financial resources for them to recruit R&D staff from more experienced companies. The rising level of M&A activity and frustration with large company remuneration schemes have also encouraged movement of personnel across the industry.

Notwithstanding the above difficulties, significant therapeutic advances have been made in recent years including the discovery of important new targets particularly in oncology and inflammatory disease and the development of pharmaceuticals based on rational exploitation of these targets, whether based on traditional medicinal chemistry or protein based biologics. Amidst these signs that the new science is able to deliver therapeutic advances the pharmaceutical industry continues to grapple with the issue of R&D productivity.

The purpose of this study is to explore the organizational architecture of R&D as a means to improving R&D performance. Its aim is to provide insights and guidance to CEO's and R&D managers overseeing drug discovery and development operations. The intention is to understand how industry has

configured the design of drug discovery and development units and to develop a conceptual framework to help senior mangers think about the effects of design on the performance of their R&D operations. Special emphasis will be placed on the way discovery and development organizations integrate knowledge since this has the potential to help mitigate the effects of high technology discovery becoming isolated from human data. This issue is an important component of the industry discourse on the productivity dilemma.

2.0 Literature Review

I have focused the literature review on topics which are most relevant to the organization and productivity of drug discovery since my goal is to seek out connections between organizational design and R&D performance. I have categorized the literature to facilitate the development of hypotheses and to underpin the modeling framework I use to examine organizational architecture.

2.1 Dynamic Capabilities

Dynamic capabilities have been defined as a firm's ability to integrate, build, and reconfigure internal and external competences to address rapidly changing environments and thus reflect an organization's ability to achieve new and innovative forms of competitive advantage. (Teece, Pisano and Shuan, 1997) This concept is important at this stage of the pharmaceutical industries development since the extensive range of new technologies available to drug companies has given firms the opportunity to find architectural advantage in

discovery technology by selecting and combining and managing the technologies in unique ways.

2.2 Knowledge Absorption

Outside sources of knowledge have been shown to be critical to innovation and a firm's ability to value absorb and commercially apply this knowledge has been labeled 'absorptive capacity'. Absorptive capacity is dependent on a firm having prior related knowledge which increases the understanding and assimilation of new knowledge with commercial value (Cohen and Levinthal, 1990). The uptake of this external information does not occur evenly across all employees and studies have shown that technical managers rely on organizational colleagues as the major source of outside information. This knowledge enters the firm through "Gatekeepers" who are individuals who keep abreast of technological development through reading more literature and maintaining a greater range of external contacts than most of their colleagues (Allen, 1971)

Further support of the importance of external interactions is provided by the correlation of research performance with the extent and nature of linkages between private firms and publicly funded research groups (Cockburn and Henderson, 1995).

2.3 Project Teams and Networks

In a multidisciplinary business like modern drug development teamwork allows the coordination and integration of many specialists towards a common goal.

Teams are a collection of individuals with different needs, backgrounds and expertise who are transformed into an integrated work unit with shared goals (Thamhain and Wilemon 1987). The literature on building team performance is extensive. An important distinction has been made between a team and an ordinary working group which might be called a committee, council or task force. A working group is a function of what its members do as individuals whereas a team's performance includes individual contributions and collective contributions which require the two or more members to work together (Katzenbach and Smith 1993). It is important from a performance perspective for managers to understand whether their organization has true project teams which integrate information discuss and decide work together. In contrast to work groups true teams produce work which is more than the sum of the parts. Teams tend to progress through a lifecycle which has been described in three phases; socialization, innovation and stabilization (Katz, 1997). During socialization employees are primarily concerned with getting to know the new social and task environment. The innovation stage follows when team members now familiar with their environment can divert their energies towards achievement and influence and finally stabilization occurs when work patterns become routine and team members less involved. Team productivity peaks through the innovation phase and declines as stabilization sets in.

Members of a project teams or functional departments require a rich source of supporting information to function. In addition to information entering the

business from external sources, information arrives from interaction with colleagues in the team and other groups inside the business. It has been shown that physical location of individuals and teams is a very strong determinant of interaction patterns and can promote or inhibit communication (Allen, 1971). The ability of a firm to integrate information within and across boundaries has been shown to be an important source of competitive advantage and depends on a complex set of interlinked factors (Henderson 1994).

2.4 Fit

The concept of fit has been considered to be an important component of organizational design for at least 40 years. A firm's strategy, its structure and managerial processes have to fit with one another (Chandler, 1962). Competitive advantage comes not from a collection of individual activities within a firm but from the way the whole set of activities fit and reinforce each other rather than from a collection of parts (Porter, 1996). Underlying the concept of fit are complementarities; activities are complementary if doing more of one of them increases the return of doing more of another (Milgrom, 1995). Competitive advantage is likely to be more sustainable if it is based on activities that are strategy specific and that have contextual interactions with other activities (Porter, 2002). These concepts can be applied to help understand the interdependencies which arise in organizational design.

2.5 Interdependencies

A significant body of organizational literature suggests that organizational design elements affect one another (Mintzberg, 1979, Nadler and Tushman 1997). The interaction of a number of elements of formal organization design has been studied through agent based simulations with some surprising results. One such simulation contradicts conventional wisdom by suggesting that when managers are highly capable and there are rich decision interactions between departments firm performance is improved by an active vertical hierarchy. The simulation also suggests underlying tensions between design elements with some combinations of elements favoring organizational search and others favoring stability around a set course of action (Rivkin and Siggelkow 2002). In the setting of pharmaceutical R&D it may be beneficial to set the 'search' capacity at a higher level for a discovery unit facing a changing technological landscape, and organizational 'stability' at a higher level for a development unit focused on efficiently moving projects through clinical trials.

3.0 Drug Discovery and Development

Drug discovery and development is complex, diverse and dynamic and as such is not uniformly described in academic literature or by industry managers. An average drug costs in the order of $1 billion to develop and takes around 15 years from initial discovery to approval. For the purpose of our study we will outline some of the key components to facilitate the analysis and discussion of our findings. This is not intended to be a detailed technical review of drug

discovery and development but an illustration of the types of management challenges faced by operating discovery and development units.

3.1 Drug Discovery

3.1.1Target Selection and Validation

A drug target is usually a protein linked to a disease and is either an enzyme or a receptor. There are estimated be less than 500 targets currently in pharmacological use, a surprisingly low number given the estimated 500,000 different human proteins. The selection of a target depends on many factors and is closely linked to the business strategy of the firm. The selection of a target disease and ultimately a drug target will depend upon the external environment such as socio-political factors, epidemiology and on the competitive landscape. It also depends on economic factors including the scale of the business opportunity and on scientific considerations such as the target's drugability. Ideas for targets can come from basic scientific insights, gene expression analysis, articles published in the literature, patent databases and reviewing competitive activity. Target selection will also need to be matched to other drug development and commercial capabilities in the company. Overall target selection is a multi leveled and complex process conducted through a wide exploration of available opportunities.

Target validation is necessary to ensure the target has a biological role linked to the disease process and is unlikely to trigger unacceptable toxicity. This work is carried out in cell based systems and animals where the effect of suppressing the production of the target molecule and observing the effects on the whole animal or cell line. Many of the targets originally derived from studying the human genome have subsequently failed to be validated as drug targets.

3.1.2 Screening

Screening involves developing an assay with the ability detect biological activity of compounds against the target. Compounds which 'hit' the target may then be selected as starting points for designing a drug. Research scientists have many available options when designing a screen and often draw on the latest scientific advances in cellular and molecular biology. The term high throughput screening (HTS) came about during the industrialization of screening during the 1990s following advancements in automation and miniaturization technology. During this period industry placed great emphasis on the number of molecules screened per day which ran into the hundreds of thousands. HTS was also a response to the large number of targets generated from genomic technologies and the greater number of small molecules produced by combinatorial synthesis. The current emphasis is shifting from quantity to quality of molecules passing through the screen. This trend places emphasis on thoughtful assay selection and metrics and the filtering out of molecules known to have chemical properties which are unlikely to develop into safe and effective therapeutics.

(Walters and Nanchuck, 2003)

3.1.3 Lead Evaluation and Optimization

Once a compound has passed the screen it is known as a hit and undergoes further assessment before becoming a lead. This designation 'lead' can be achieved without testing in animals. However there is usually a requirement for evidence that a molecule has selective activity and reason to believe that it will perform sufficiently well in terms of adsorption, distribution and excretion (ADME).

A lead or a series of leads is optimized methodically by medicinal chemists to improve its performance in these areas. A high quality standard for leads is critical since major flaws are unlikely to be smoothed out through lead optimization which is a chemical tuning rather than radical restructuring. One criticism of lead optimization in recent years is that the affinity of lead to the target has been optimized at the expense of other aspects of its performance. ADME and the development of viable synthetic route became secondary considerations in discovery and then often insurmountable problems in clinical development.

3.2 Drug Development

3.2.1 Pharmacokinetic (PK) Studies

The chemical structure of a drug affects its physical properties which have a significant impact on its utility as a therapeutic. Organisms process drugs differently according to these properties and this influences the dosage and route

of administration and whether the molecule is suitable as a pharmaceutical at all. Small changes in structure can affect how a drug is absorbed, how it is metabolized and the products of that metabolism and how it is distributed throughout the body and excreted from the body. The only effective method of determining these pharmacodynamic properties is to test the drug at different dosage levels in animals and then in humans.

3.2.2 Pharmacodynamic (PD) Studies

The drugs impact on the body through its interaction with the intended target and other sites are known as its pharmacodynamic properties and the desire here is to have maximum therapeutic benefit at a dose where there are no significant side effects. Given the complexity of biological networks it is often difficult to determine all the effects of a drug even after animal and early human trials. In fact in most cases animals do not predict well the activity of a drug in human subjects. Even between different humans there may be different responses to a drug based on their genetic makeup and disease state. This gap in our ability to connect biological knowledge to drug response can lead to problems in later trials when issues are observed for the first time in larger patient populations and longer timescale of later trials. It also creates an impetus for the physicians and managers involved in clinical development to connect their analysis of a drug candidate as closely as possible to the biological understanding developed by the discovery group.

3.2.3 Clinical Trials

The actual running of clinical trials is a complex logistical feat involving precise coordination of trial centers, patient recruitment and data collection. The fieldwork is outsourced by most early and traditional stage companies to contractors know as Clinical Research Organizations (CRO's). The cost of a major trail is typically $10,000 per patient and may involve several thousand patients.

3.2.4 Manufacturing Process Development

The drug needs to be available at a high level of purity and in a stable form for use in clinical trials over the course of its development and then finally will need to be manufactured to supply the market once it is approved. In the case of small molecule drugs, a synthetic route will be devised which will consist of a series of chemical reactions leading towards the final drug structure. Alternative routes have to be assessed in terms of the quality of their output and the likely costs when the drug is produced on a commercial basis. In the case of biological drugs which are usually identical or very similar to naturally occurring human molecules the process development is viewed a more challenging step than overcoming ADME and toxicology issues which are more difficult hurdles in small molecule development. The production of biological drugs takes place in large vats of genetically engineered bacteria or mammalian cell cultures.

3.2.5 FDA Documentation

The FDA is the government agency which has the responsibility for approving new drugs. The FDA is not only involved in reviewing data which supports the request for human trials (IND) and new drug approval (NDA) but is also involved in specifying the type, the level and formatting of data it wishes to review. This in effect determines the characteristics of many of the tests performed during the drug development process. Dedicated managers are employed by most firms to handle the communication with the FDA and to ensure the contents of the dossier submitted by the company are sufficient.

3.3 Integration

As the drug discovery process became more mechanistic and industrialized during the 1990s the higher volume of targets and hits from HTS did not translate into clinical success, and New Drug Applications (NDAs) to the FDA began to fall. Apparently, as the quantity of targets, leads and drug candidates has risen their quality has fallen with many molecules failing in the later stages of clinical development through unforeseen toxicities or lack of efficacy. A widespread view is that in order to improve the quality of leads and candidates destined for the clinic a greater level of integration of activities is required both within the discovery process and between discovery and development activities.

Three key decision gates in drug discovery which have a high impact on downstream clinical performance have been identified (Pritchard et al, 2003): (1)

Is the target validated? (ii) Are leads identified? (iii) Is the lead developable in the clinic? These questions are complex and require multifunctional co-ordination and highly integrated decision making. Figure 1 summarizes and simplifies some of the most obvious interactions by outlining some of the questions which should be asked by the main functional specialists at each of the decision gates.

Figure 1 Functional interaction at decision gates in drug discovery

Function	Department	Target ?	Lead?	Clinical Candidate?
Biology	Discovery	Role in disease pathway and other pathways?	Is it specific? Is it active?	Is there any new published data since we began this project?
Chemistry	Discovery	Is it druggable? Is there a credible start point for ligand design?	Affinity, solubility, permeability, stability?	What else could we (or a competitor) have done to make it better?
Pharmacology	Discovery and Development	How can it be accessed?	Toxicology? ADME?	Are we comfortable with the dose ranges and animal PK results?
Process Development	Development	Biologic or Small Molecule?	What synthetic route? Formulation?	Can we make enough for trials?
Clinical Development	Development	What genetic / phenotypic factors will influence the response? Are there any biomarkers we can measure? Have there been previous clinical difficulties with this class of target?	Have there been previous clinical difficulties with this type of molecule? Administration? Dosage?	Is the animal safety data good enough to prepare an Investigational Drug Request (IND)?

Some managers might view these decision points are arbitrary and the process should be a continuous multifunctional assessment of the molecule. The decision gates outlined however involve the commitment of additional resources and usually will involve activating a senior management input which provides a clear punctuation to the process at the decision gates we have considered. One hypothesis on the decline in pharmaceutical R&D productivity is that the highly complex interdependencies in this process were neglected during the 1990s and lax decision making allowed poor quality candidates to slip into the clinic.

4.0 Hypothesis Development

4.1 Hypothesis 1

Most of the academic literature treats R&D as one functional unit (Cohen, 1989) or separates research from development and explores the properties of one or the other (Pisano, 1997). There is also a significant literature on the relationship between exploration and exploitation (March, 1991) and radical versus incremental innovation (Utterback, 1994) There is however surprisingly limited discussion on the relationship of research to development within organizations and the management challenges involved with their integration.

I contend that within the pharmaceutical industry research and development are fundamentally different entities and this has implications for their organizational design. It is certainly obvious that the tasks undertaken by each unit are different. It is less obvious whether this difference is meaningful in terms of the assembly of effective organizational structure for each unit.

One possible difference between discovery and development is in the level of control managers in each unit have over the design of the tasks they undertake. The external regulatory environment set by the FDA greatly impacts development activities while drug discovery research remains largely unregulated. The final decision on the design of a discovery activity rests with the company management and not the regulators. There is an increasing variety of technology options and process architectures available to a modern discovery organization. On the other hand in drug development FDA regulations and guidance documents stipulate standards for conducting clinical trials, data collection, statistical standards and presentation of documentation. The pharmaceutical industry has also adopted norms and standards perceived to be necessary for the smooth running of the development process and to meet the expectations of managers at the FDA.

A second difference stems from the nature of scientific discovery which involves information flow across firm boundaries through contact with other professionals and publishing papers in scientific journals. It is true that within the development arena clinical results are published in leading medical journals, however in this case the principal investigators and the medical institution involved are the recognized source of the work. The scientific community will also tend to attribute any great successes in the clinical to the discovery of the molecule itself rather than the design of the clinical program.

A final potential source of difference is that drug development is a more expensive process than drug discovery with large financial investment made in

the running of clinical trials. If a project fails during the latter stages of development all the accumulated costs to that point are in effect lost. Any mistakes in drug development are therefore costly and this leads managers to be extremely cautious and risk adverse in the way they design and manage development programs.

The net result of lack of regulatory control and the need for discovery scientists to explore within and across firm boundaries is a task profile which is less routine, less expensive and more uncertain than that in development.

There are arguments that drug discovery and development have become more similar in recent times. Drug discovery has become a more systematic and industrialized process particularly in discovery of small molecule therapeutics. Drug development has become a more networked activity with the necessity to coordinate multiple outside contractors and medical experts and committees. I maintain that these arguments are insufficient to overcome the case for a clear division of discovery and development.

If my conjecture is correct that there is a fundamental difference in the nature of discovery and development tasks is correct it follows that the organizational architecture of an optimized discovery unit should be different from the architecture of an optimized development unit. This connection is based on the link between task certainty and organizational design (Mintzberg, 1979). The concept of organizational fit or congruence has been linked to organizational effectiveness. A congruence approach to this issue would suggest that to optimize the effectiveness of an organization, formal and informal organization

elements should be congruent with the tasks, processes and workflows (Nadler and Tushman, 1997). This suggests that if discovery and development have different levels of task certainty they will require different formal and informal organizational design components to manage their inherent uncertainty effectively. This leads to the question of how far discovery and development organizations are currently differentiated and how congruent are their constitutive elements. Thus I hypothesize:

H1: There are fundamental differences between drug discovery and development which have led to separate organizational design solutions.

4.2 Hypothesis 2

The decision gates outlined in section 3.3 are critical points in the drug discovery and development process. One reason for high clinical failure rates is the poor ability of organizations to predict the odds of downstream failure at these decision gates. A wide held belief is that better application of knowledge generated by development activities at these decision gates would improve the quality of candidate molecules and increase the probability of those molecules reaching the market and generating revenues. The integrative systems connecting discovery and development may therefore have a direct impact on clinical failure rates and overall R&D productivity.

It follows that in addition to the requirement for organizational congruence around the different tasks and process associated with discovery and development, there will be a need for integrating systems running between discovery and development units. Alternative integrating systems will have properties which modify organizational competence in different ways for example some integrative configurations may promote early stage technological search to provide new targets whilst others may promote rapid progression of lead compounds through the pipeline. The type of integrative system adopted by organizations will therefore depend on the objectives and project mix within a firm. Thus I hypothesize:

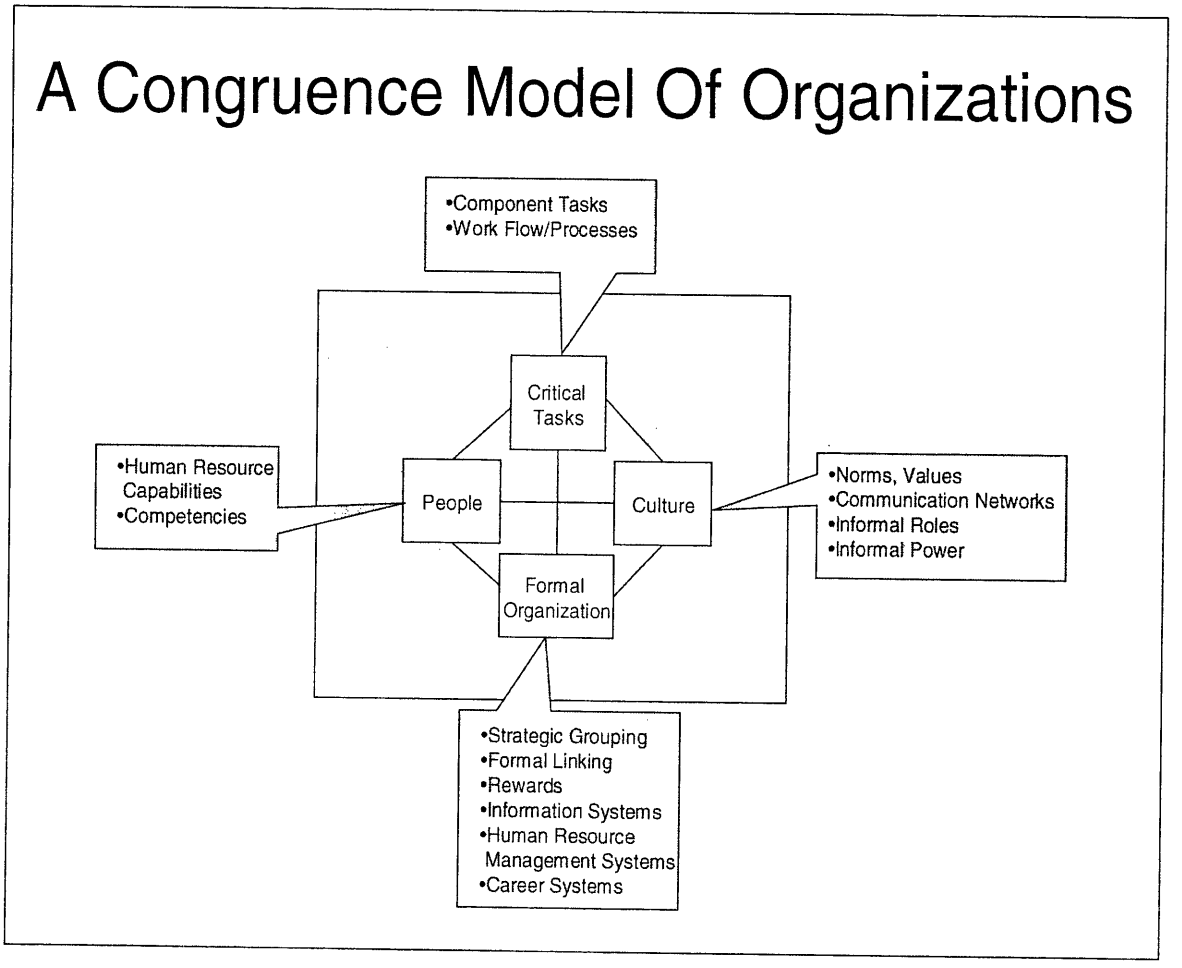
H2: Drug discovery and development's integrating system will be dependent on the status of a firm's development pipeline.

5.0 Methodology

5.1 The Congruence Model

Tushman and O'Reilly, and Nadler and Tushman have described in detail a congruence model which considers the alignment of 4 organizational building blocks; critical tasks and workflows, formal organization arrangements, people and culture (Tushman and O'Reilly 1996, Nadler and Tushman, 1997) Figure 2.

Figure 2



The organization whether a whole company or a department is divided into four principle components:

Critical tasks and processes - The activities engaged in by the organizational unit under analysis. The nature of the tasks performed and patterns of workflow.

People - The characteristics of people employed to conduct the critical tasks in terms of their skills, knowledge and behavior patterns

Formal Organization - The explicit structures and procedures used to organize work and guide activity of individuals.

Informal Organization (Culture) – Unwritten guidelines and the values, behaviors, norms and beliefs of the individuals at work in the unit.

The model allows design components to be assessed and categorized in a way which creates a high level of transparency of their level of fit. Fit or congruence is defined as how well the needs, demands and goals of one component are consistent with those of another component or in other words how well pairs of components fit together. The basic hypothesis of the original model is that the greater the total degree of fit among the various component the greater effectiveness of an organization. In the context of this study I use the model to construct a description of drug discovery and development units in a sample of pharmaceutical firms

5.2 The Survey

I conducted a series of interviews with senior executives in the pharmaceutical and biopharmaceutical industry during March and April, 2004. These executives were selected because they had an intimate knowledge of the R&D operations of their firms and were in a position of direct responsibility for their organizational design. In one firm, two senior executives were interviewed and the results combined to get a result for the firm as a whole. The aim of the survey was to profile the discovery and development organizations in terms of the 'Congruence model' described in the previous section. The full questionnaire is attached (Appendix1). In addition to the specific questions on the questionnaire the

interviews probed for a deeper understanding of the answers put forward to the quantified questions. Particular attention was paid to soliciting a full description and rationale for the linking mechanisms used to foster collaboration between discovery and development units. I label the recipe of integrative measures adopted by a company an 'integrative system'.

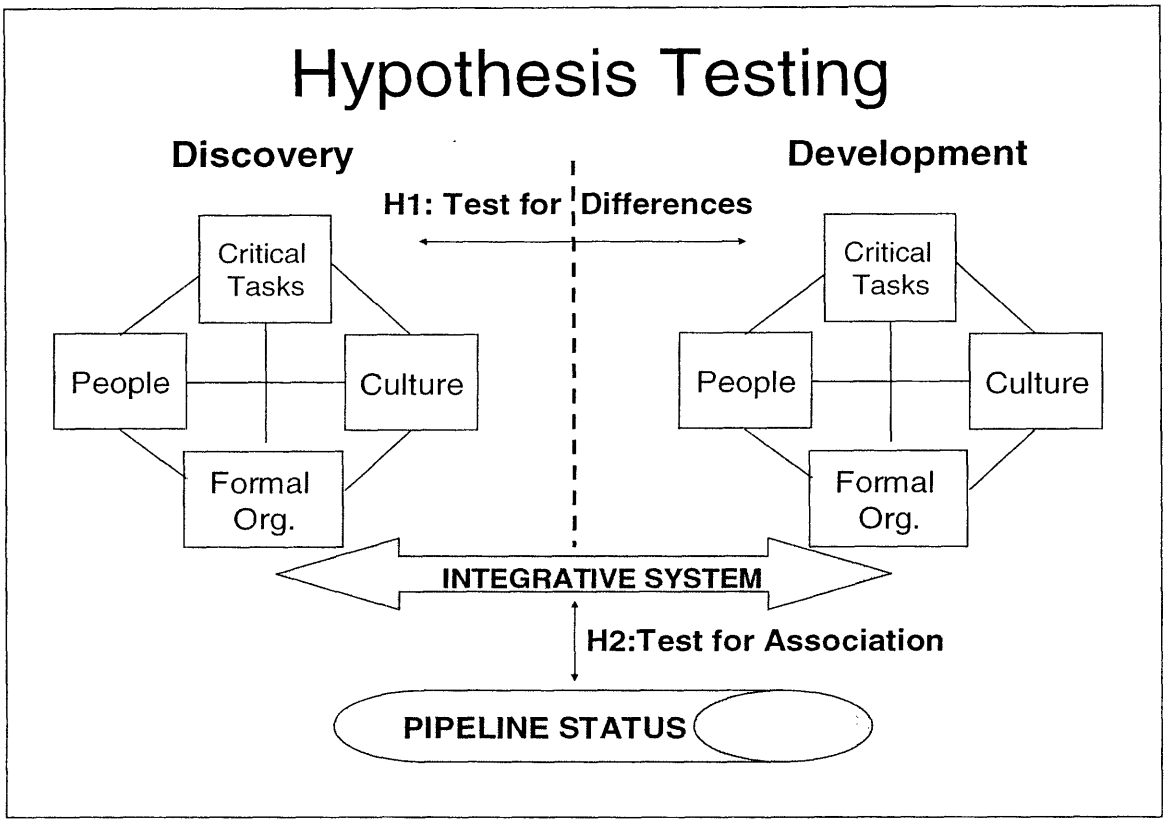
5.3 Testing the hypothesis

To accept H1 I need to show the tasks and other design elements specified in the congruence model are different for discovery and development departments. The case for accepting this is stronger if the differences are consistent with our precept that drug discovery tasks are fundamentally more uncertain than drug development tasks.

To accept H2 I need to show that companies are using different integrative systems and that their choice of integrative system is associated with the status of their development pipeline. We define the development pipeline in terms of whether the company has only discovery projects, a mix of discovery and development projects and no marketed drugs, or discovery and development projects and marketed drugs (Figure 4). This information was obtained from company websites and 10K reports.

Figure 3 summarizes the methodology and approach to hypothesis testing.

Figure 3



5.4 The Sample

A sample of 7 firms of varying size and development stage was randomly chosen from the pharmaceutical industry in the state of Massachusetts. The sample composition included local and geographically spread organizations, and those focused on developing small molecules, biological drugs or both.

The sample can be broadly classified into three groupings.

Figure 4

Pipeline Classification	R&D Personal	Discovery Programs	Development Programs	PROFIT	No of firms interviewed
Early Stage	> 100	YES	NO	NO	3
Transitional	100– 500	YES	YES	NO	2
Mature	> 500	YES	YES	YES	2

6.0 Results

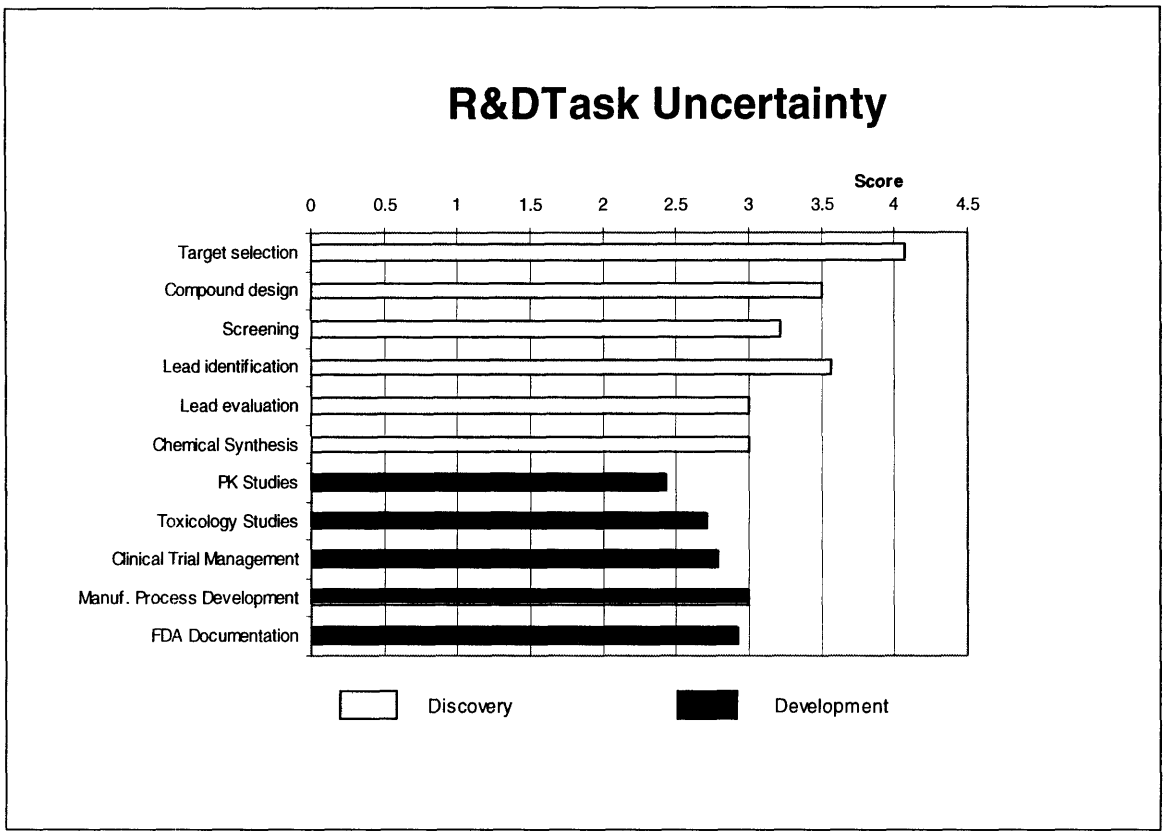
A full set of quantitative scores from the survey is provided in Appendix II

6.1 The nature of discovery and development

It is well established that drug discovery and development have different goals and different tasks supporting their progress towards these goals. The questionnaire was not designed to identify the different tasks but to assess whether the nature of drug discovery is different from drug development in a fundamental way. A difference in fundamental nature, according to the principle of congruence, would require a different response in organizational design to maintain congruence.

The questionnaire asked respondents to rate the major task grouping of discovery and development in terms of their uncertainty. An uncertain task is one which may vary from one project to another whereas a routine task would tend to be always executed the same way. Figure 5 summarizes the responses for each of tasks.

Figure 5



A significant difference is apparent between the uncertainty perceived by the respondents for discovery and development tasks with mean scores of 3.5 and 2.8 respectively.

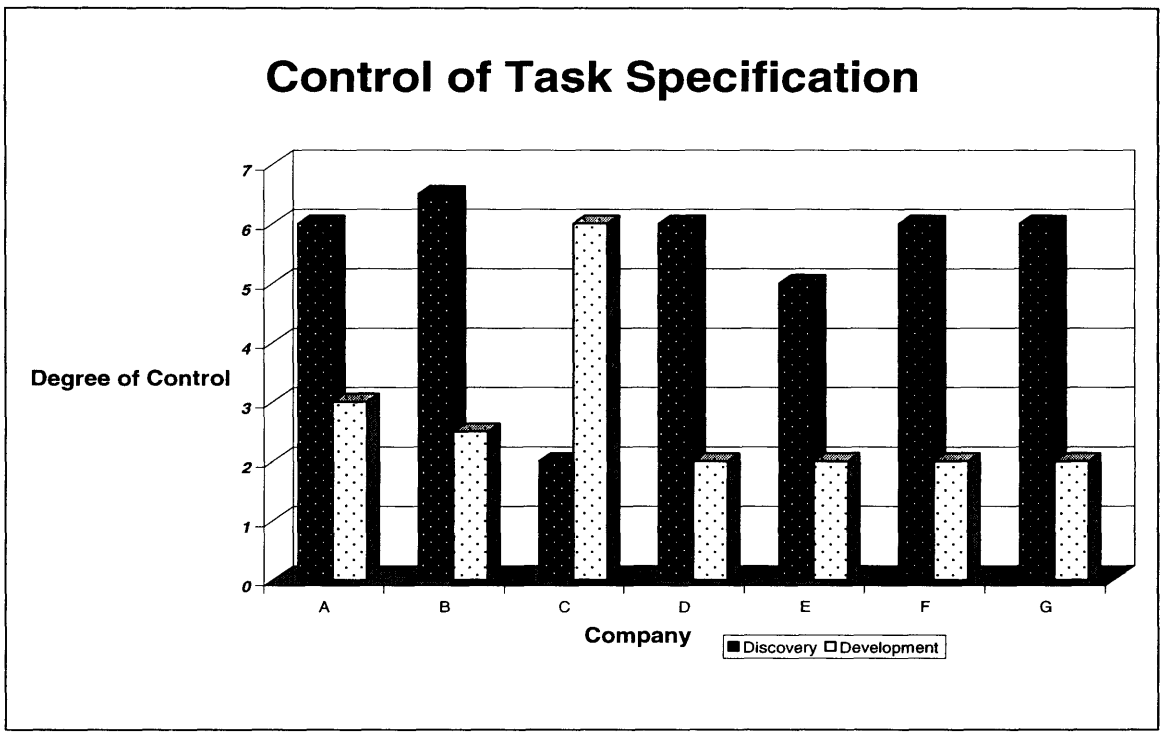
Target Selection and validation stood out as the most uncertain of all the tasks which may be reflective of the complexity of biological systems and wide range of effects elicited by modifying the activity of a biological target.

Within discovery, compound design, screening and lead identification were also seen as more uncertain than any single development task with lead evaluation rated as the most routine of the discovery tasks.

Within development chemical synthesis and manufacturing process development were seen as the most uncertain tasks reflecting the wide variety of options synthetic chemists and process engineers have in designing the production route for a molecule. The development items most closely under the influence of FDA regulatory control such as PK and Toxicology studies were rated as the most routine.

A further question probed how much control managers had over the design of tasks in discovery and development units, this was to test whether the higher levels of FDA regulation guiding development are perceived by managers as limiting freedom to innovate and specify new processes in their pursuit of efficiency. Figure 6.

Figure 6



Six of the seven firms interviewed expressed that they had a higher level of control over drug discovery than development. The higher uncertainty and higher degree of control of development tasks strongly suggest fundamental differences in the nature of discovery and development tasks and support H1. This was summed up qualitatively by one interviewee who stated; "*if something unexpected happens at the research stage it is a discovery and if it happens in development it is a disaster*".

Following the congruence approach this difference should lead to differences in the other organizational design elements which should be set to optimize the congruence of each unit to the tasks it undertakes. In addition, any techniques deployed to optimize integration of knowledge and decision making will need to

take account of the differences in discovery and development tasks and the organizational units which surround them.

6.2 Formal Organization

All the organizations interviewed had a separate individual heading the discovery and development units. In all cases these two managers reported to a head of R&D, a chief operating officer or a CEO responsible for the entire R&D system. The number of people employed by the organizations seemed to be the main determinant of the structural detail rather than any contrasting philosophy on the role of hierarchies.

All the sample companies had formal management reviews every year and some had interim reviews two or three times a year. There were no differences highlighted between the review system for discovery and development departments. The measures were generally different however with more clear milestones in development such as completing a clinical phase.

6.3 Physical location

The physical location of research and development also varied with each of the following represented in the sample:

- *Discovery and development together in a single building in different areas*

- *Discovery and development together in a single building with some groups intermingling*
- *Discovery and development on the same site in different buildings*
- *Multiple R&D sites with separate buildings for discovery and development*
- *Multiple R&D sites with discovery and development sharing buildings*

The wide range of physical configurations of the R&D units was in part a function of size and history and also in part a lack of obvious policy on this aspect of organizational design. The impact of physical design on communication patterns does not appear to have been a major consideration.

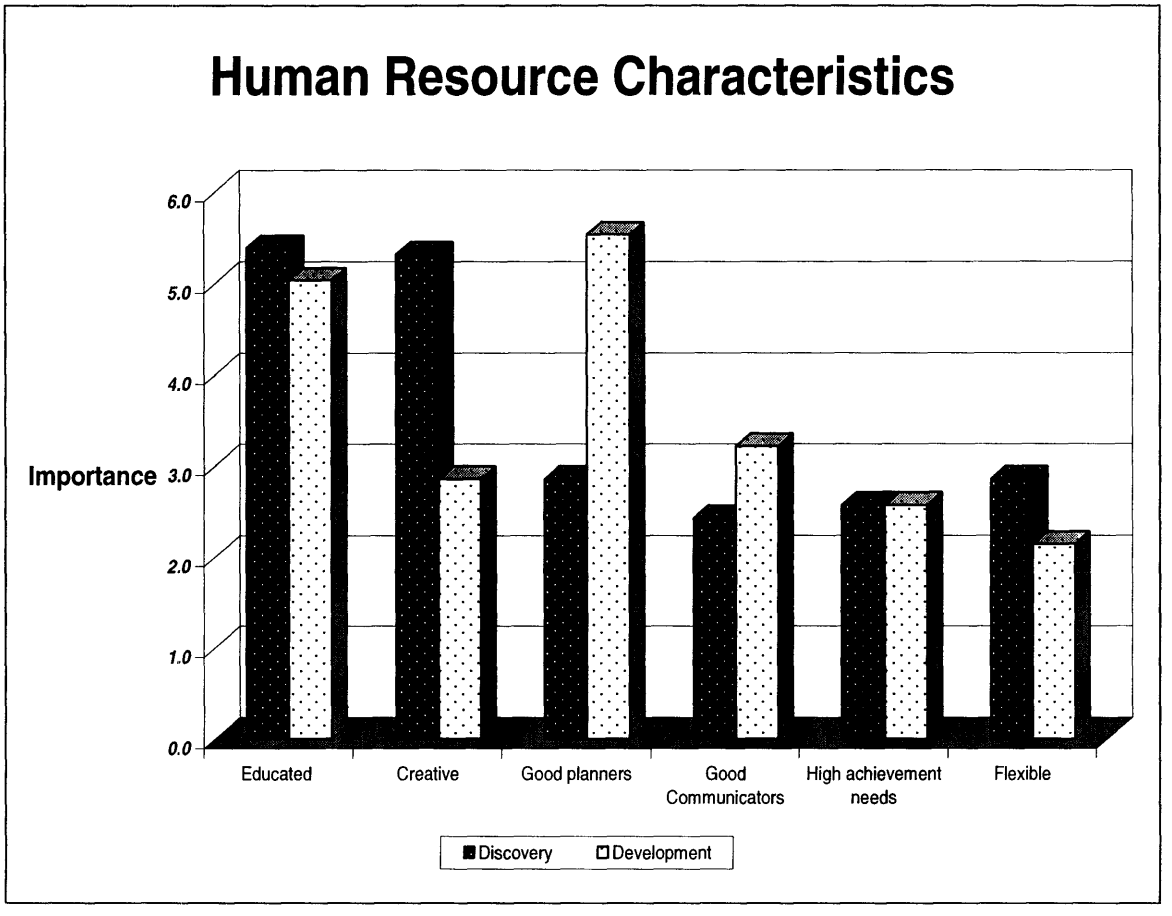
6.4 People

6.4.1 Profile

The interviews revealed that development scientists who were both attracted to and selected for roles in drug development had distinctive characteristics. The highest ranked quality was their level of education with a high proportion of personnel qualified to an MD or PhD level. This level of advanced qualification was seen by some as entry level necessity to become an R&D professional in the pharmaceutical industry. Secondly and in contrast to the rankings for development people they were seen as creative and thirdly flexible.

Development people were ranked highest on their planning ability with level of education close second. They had higher ranked communication skills and lower ranked creativity and flexibility than their colleagues in discovery. Figure 7.

Figure 7



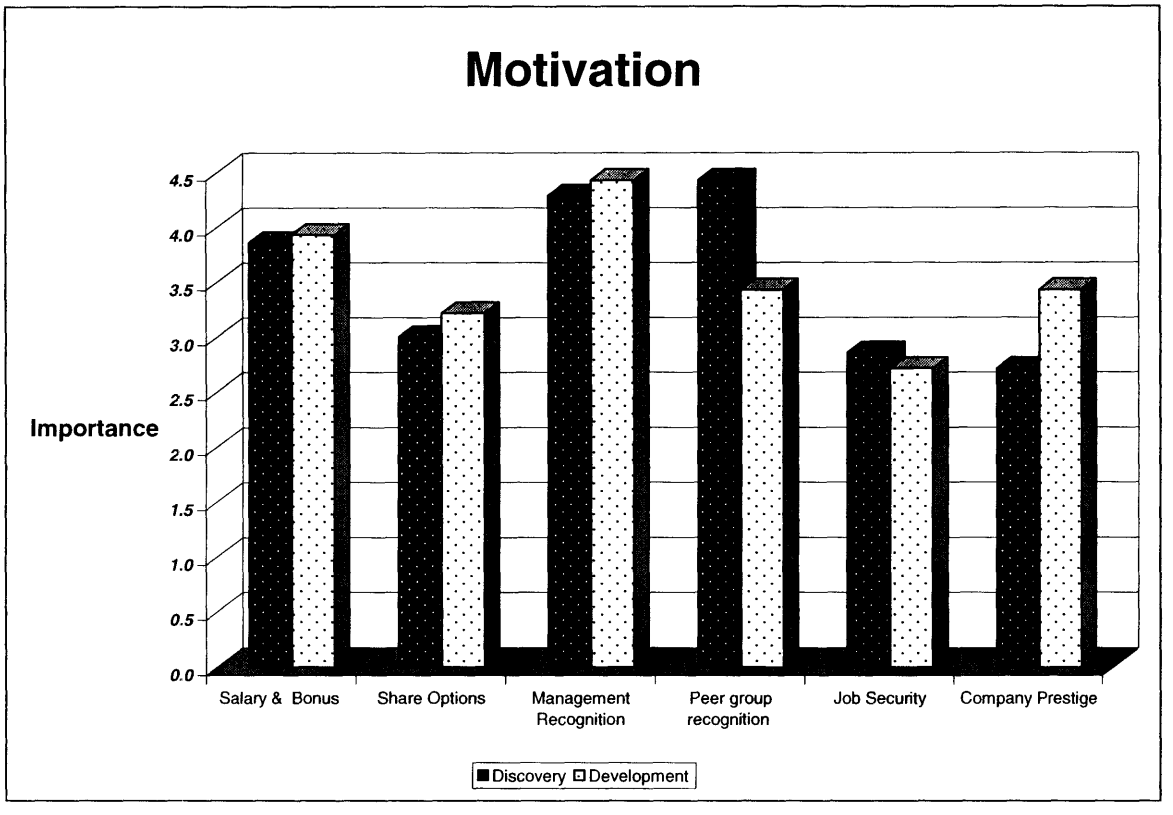
6.4.2 Motivation

A point made spontaneously by several of the respondents was that the attributes listed in the questionnaire did not cover a very powerful and overriding driving force behind scientists; the passion for the work itself as a search for scientific discovery.

Within the motivations listed on the questionnaire there were few differences between discovery and development with salary and bonus and management recognition coming at the top of the rankings in both cases, Figure 8.

The most prominent difference between discovery and development was the higher ranking of peer group recognition within discovery. The impression given was that the endorsement of an individual's work by the scientist managers in the discovery unit would count for more than the endorsement of general management from outside the R&D function.

Figure 8

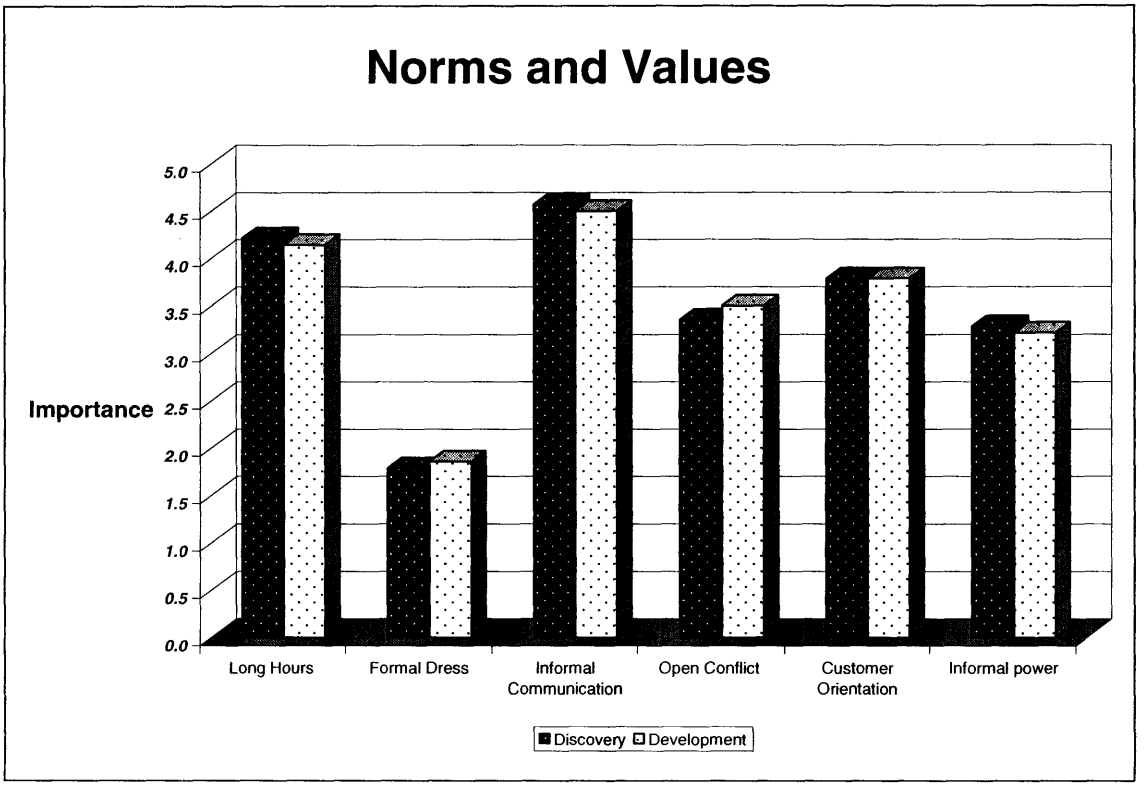


6.5 Informal Organization (Culture)

This was the area of the analysis respondents found most difficult to discuss and provide precise rankings and they felt some discomfort with the lack of rationality

of this organization feature. Consequently it is difficult to draw a firm distinction between the informal attributes of the two units. Customer orientation is ranked more highly within development. Formal dress was universally ranked the lowest. The discussions confirmed the concept of gatekeepers in discovery where individuals informally assume the role of absorbing external knowledge and disseminate it around the organization. Overall culture as a concept did not feature strongly in the minds of the respondents. There was no strong dependence on individual company mission statements. The motivational quality of the generic mission to create human therapeutics and advance science dominated the cultural slant of most companies. Figure 9.

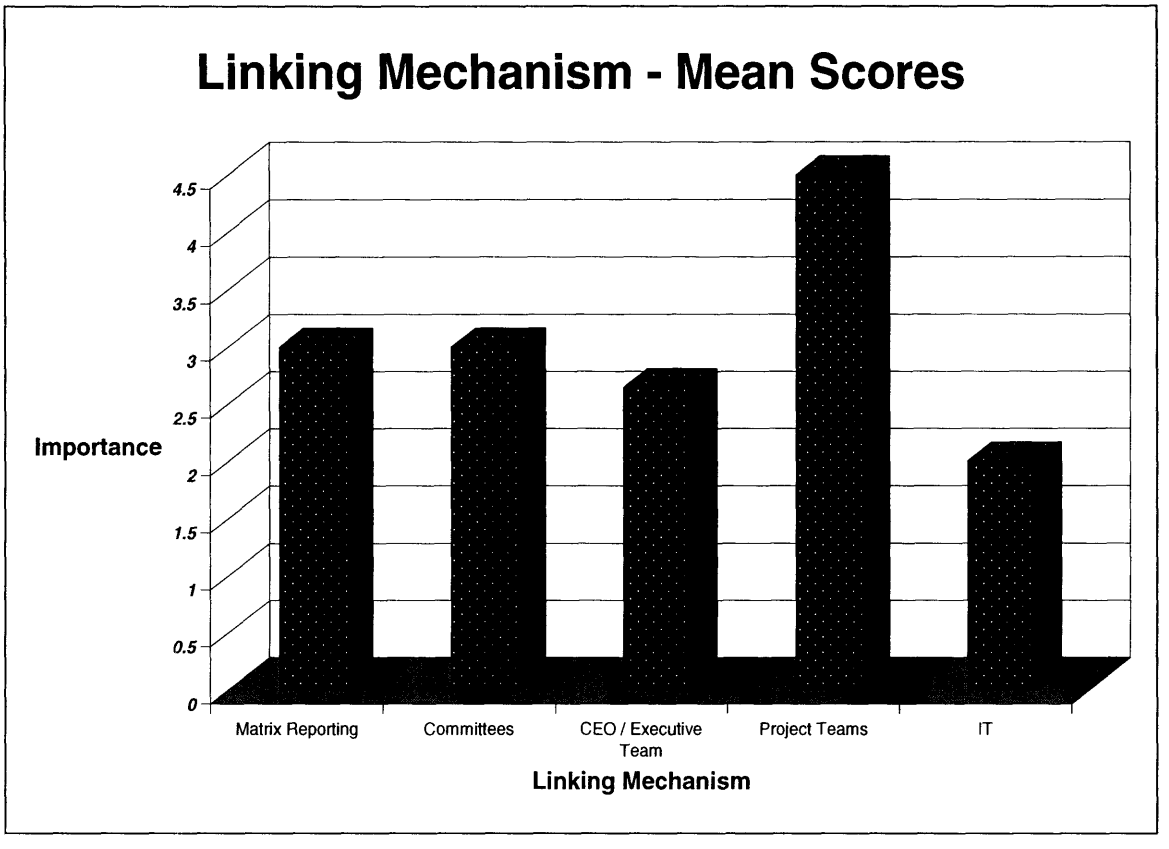
Figure 9



6.6 Linking Mechanisms

Universally the respondents were proponents of increasing the linkages between discovery and development. The importance of the linking mechanisms specified in the questionnaire is detailed in Figure 10.

Figure 10



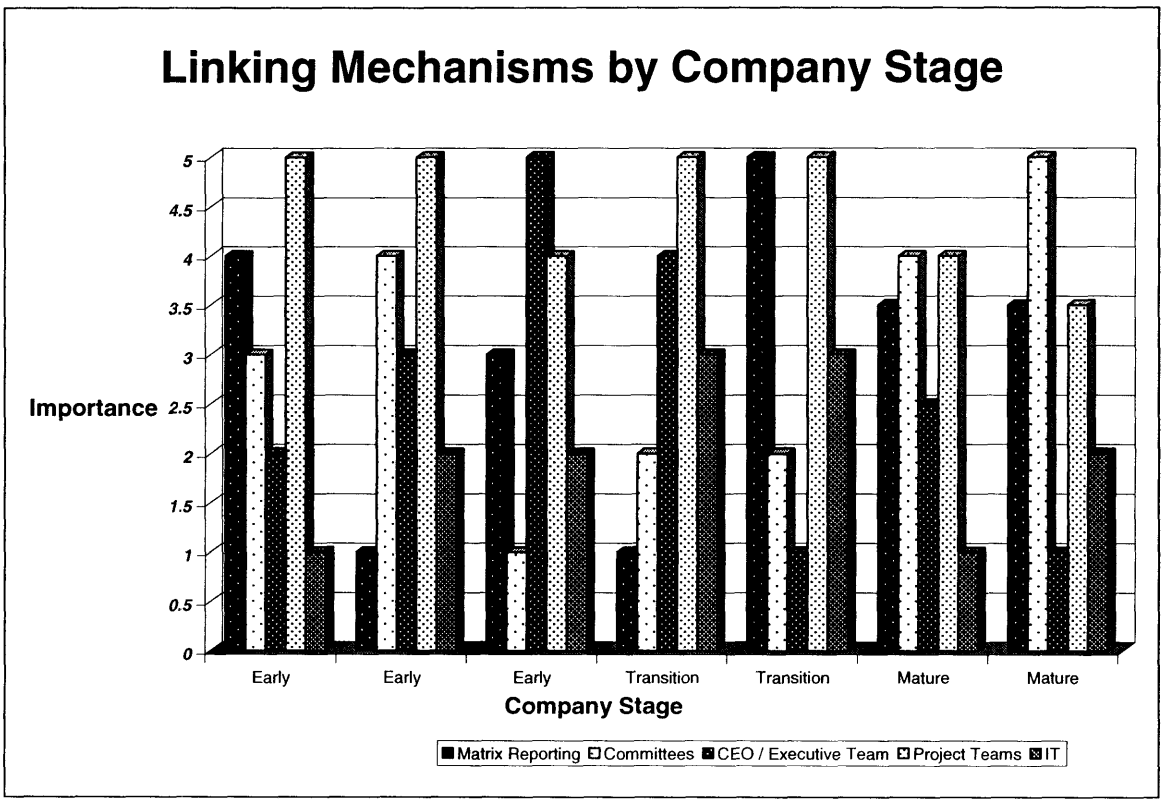
In addition to the linking mechanism specified in the questionnaire the more established companies within the sample made use of task grouping and formal reporting as a technique to fuse discovery and development processes. This involved some of the personnel conducting development tasks reporting to discovery management and being physically located within the discovery unit. In

the most extreme case, the discovery management had responsibility for Phase I and Phase II clinical trials with the later phases controlled by a separate development unit. In several companies toxicology and chemical synthesis were at least partially located within discovery. As a linking mechanism project teams were ranked first or second in importance by every respondent and were regarded as essential components of pharmaceutical R&D and the main technique for coordinating activities and integrating knowledge. Other than the premise that selecting the right people is critical to team performance there was no set formula for setting up teams. Some respondents talked about team composition in terms of a continuum evolving through the advancement of a drug project from being predominantly composed of discovery personnel in the early stages and transitioning to being predominantly composed of development personnel in the latter stages. There was a polarized view of matrix reporting with some managers seeing it as an important part of teamwork and others viewing it as an alternative to teamwork. There was little evidence that any true formal reporting lines existed between team members and the team leader, with formal connections remaining inside the function. Committees were seen as important to set priorities between projects and make major decisions such as the decision to allow a molecule to enter clinical development. They involved senior people and were involved with issues of strategic importance or major resource allocation. They were generally more important in the larger organizations in the sample substituting for the direct involvement of the CEO in earlier stage companies. The importance of the CEO and executive team to link

discovery and development was ranked significantly below the use of project teams at a similar level to committees and matrix reporting. Information Technology was seen as a necessary supporting infrastructure and was thought of more passively than other linking mechanisms. There was a recognition that knowledge creation and new insights came out of the richness of human contact and that IT could not substitute for this.

The acceptance of hypothesis 2 depends on finding an association between the importance of the alternative linking mechanisms and company pipeline status. Figure 11 illustrates this comparison and does not immediately reveal any strong connection between company stage (and pipeline status) and linking mechanism.

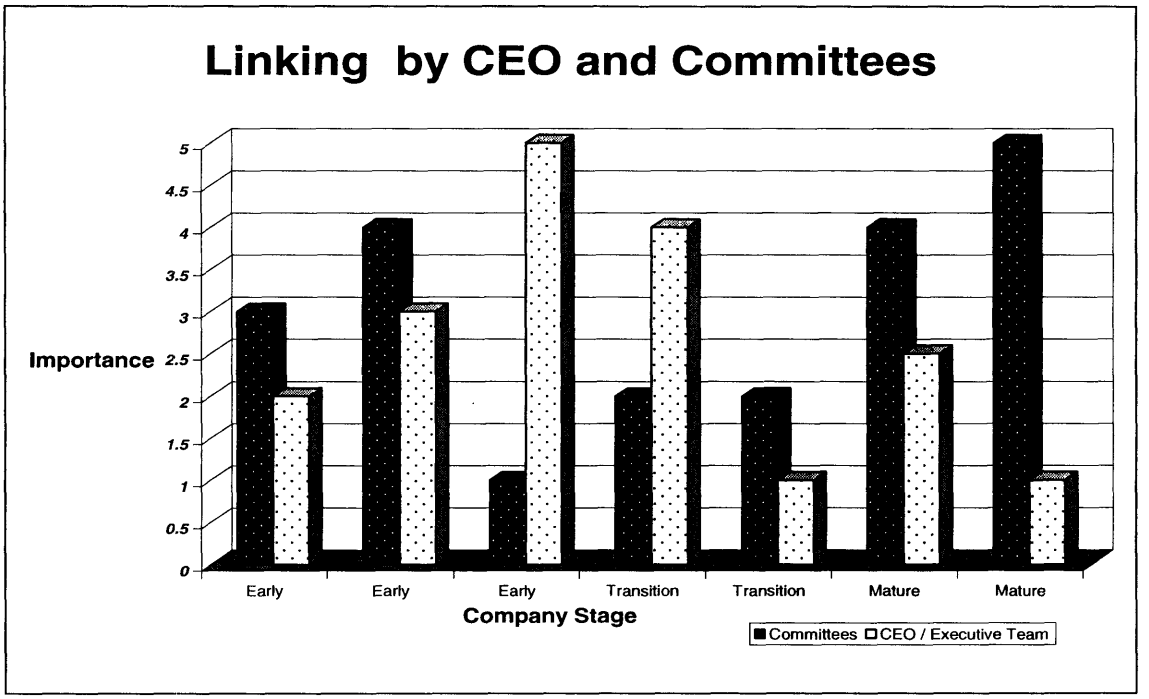
Figure 11



A closer look at the importance of the CEO and committees (Figure 12) reveals a degree of trade off in most of the companies between hierarchical coordination through committee and the CEO i.e. when one of these components is seen to be important the other is seen as significantly less important. This is consistent with the idea that both CEO and committees are alternative forms of centralized control and to a degree they are mutually exclusive.

A second observation is that in the transitional stage companies use of committees is less important than in the early or late stage companies. One possible explanation for this is that in the early stage companies are more science driven, the CEO may be a scientific founder and the style adopted may reflect the collegiate nature of a scientific research organization which is more likely to be formally coordinated by committees than an overbearing CEO. The mature stage companies are too large for a CEO to perform an effective coordinating role and therefore rely on committees to represent senior management in the business process. Transitional companies however are more likely to have a venture investor backed professional CEO who appointed to steer the company to marketable products and profitability. This type of CEO is more likely to take a personal and active role in key decisions.

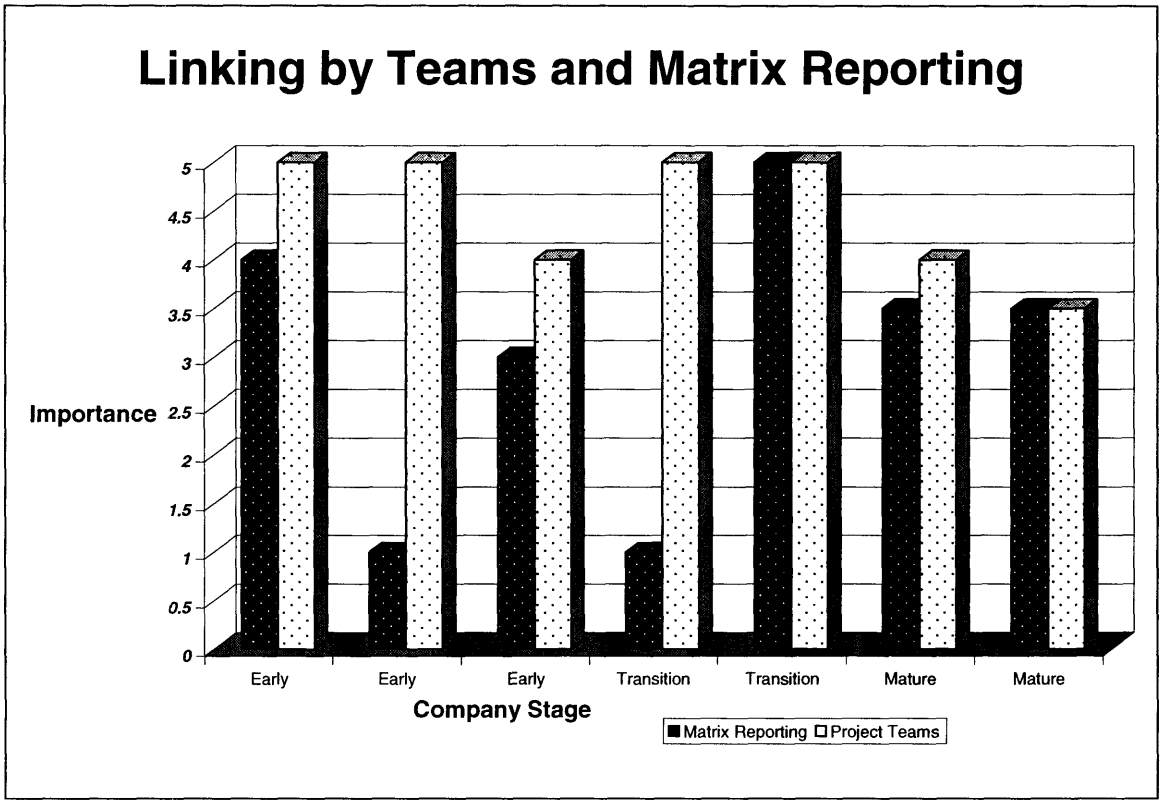
Figure 12



A closer look at the two horizontal forms of linking mechanism, teams and matrix reporting (Figure 13), does not suggest the trade off we see in the case of CEO and committees. The pattern is consistent with matrix reporting being used to reinforce team activities rather than substitute for them. It may also reflect some degree of confusion over the meaning of matrix reporting in our survey where no formal examples could be cited by respondents.

The overall pattern suggests that teams are universally important across our sample whereas matrix reporting is used by a subset of companies to reinforce team working.

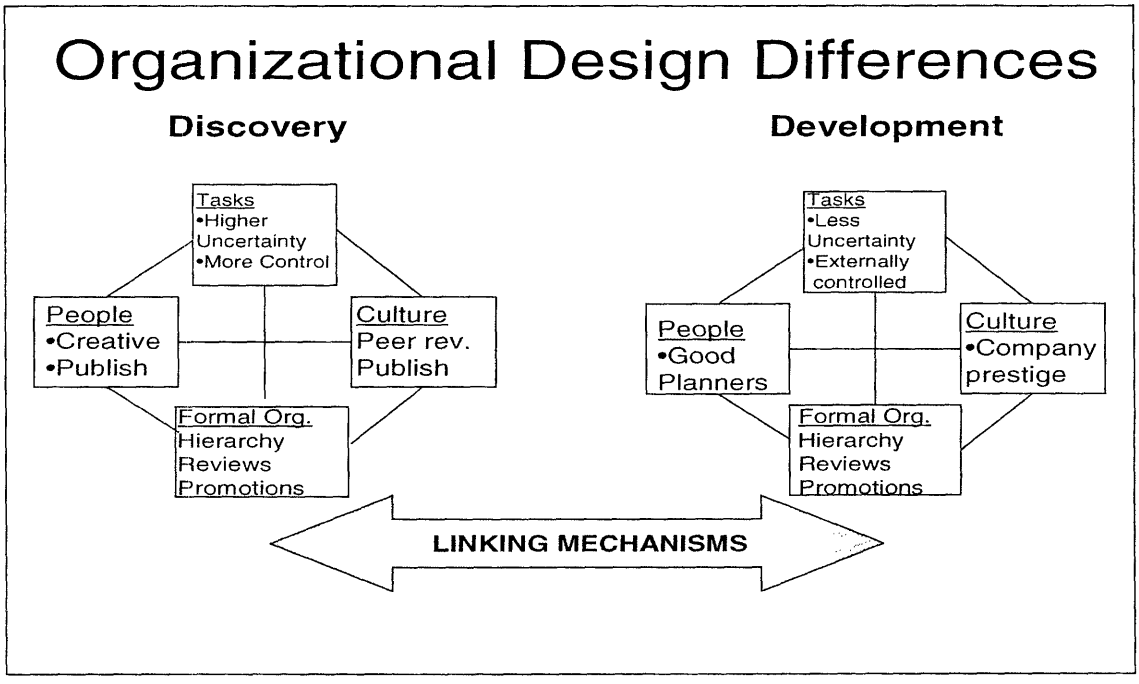
Figure 13



7.0 Discussion and Conclusions

Figure 14 summarizes the organizational design of discovery and development as derived from the survey data. The fundamental differences in uncertainty and ability to control tasks in design and development have contributed to different human resource characteristics in each unit and some differences in values. The following section considers the implications of the findings in terms of the congruence model and the choices managers face in designing appropriate integrative systems.

Figure 14



7.1 Alignment of Discovery

Discovery work tasks and processes are uncertain and research scientists have a wide range of freedom in their design and implementation. The discovery unit's people qualities of creativity and flexibility appear to be well aligned to these task characteristics. Similarly a culture of publishing externally is consistent with the need to exchange information in order to solve the complex issues which surround the design of discovery tasks and with the motivational requirement of peer group recognition. The formal discovery organization in discovery in overall structure was found to be the same as development and other departments in the company. The common features were annual revues and promotion of top performing staff. There were some indications that detailed measurement of progress was less formalized in discovery than other departments.

7.2 Alignment of Development

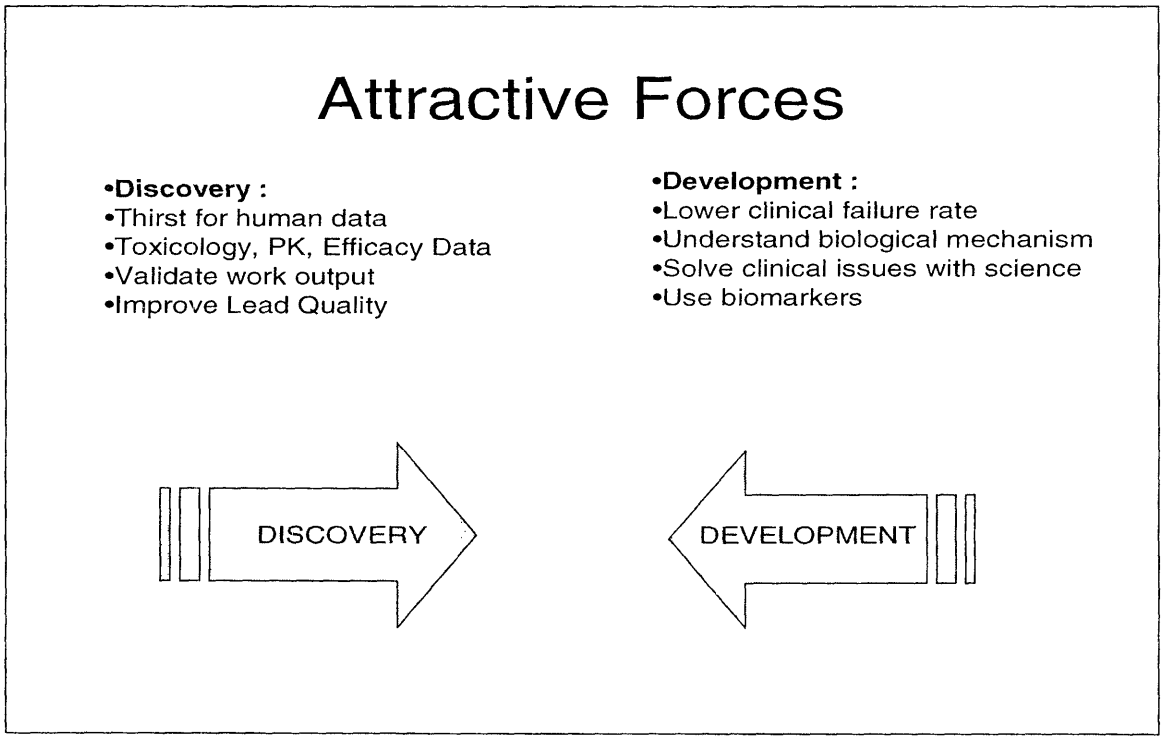
The tasks and processes in development are heavily formatted by FDA regulations and industry standards and although the task outputs are uncertain the designs of the tasks themselves are more formulaic. The planning skills of the managers and their motivations attached to the prestige of the company fit with this task profile. They suggest a tighter integration to other company units such as manufacturing and marketing than is the case with the discovery design. There would also appear to be a good match between the formal review system and the timelines and checkpoints inherent to the development process.

7.3 Integrative pressures

All the senior managers interviewed were of the opinion that discovery and development should be more closely integrated and were taking action to achieve this objective. The underling reason for this trend stems from the awareness that the economics of drug development have become unworkable given the prevailing industry productivity levels. Measures to sharpen the discovery and development processes through streamlining workflow and better planning of clinical trials were viewed as insufficient to overcome the performance gap. The improvement of failure rates of clinical projects was seen as a better route to solve the productivity problem. Given that the majority of products fail in clinical trials because of toxicity or lack of efficacy the companies were striving to get a better understanding of the interaction of the molecule with human biology in the early stages of the process. This has created a strong

requirement for human clinical data to be used as comprehensively and as early as possible in drug discovery projects. Development groups are trying to find higher resolution methods to understand the interactions of drugs with human biological pathways through the development of biomarkers which often arise from the biological insights derived from discovery programs. As summarized in Figure 15 there are pressures from both units to exchange knowledge and jointly manage projects.

Figure 15

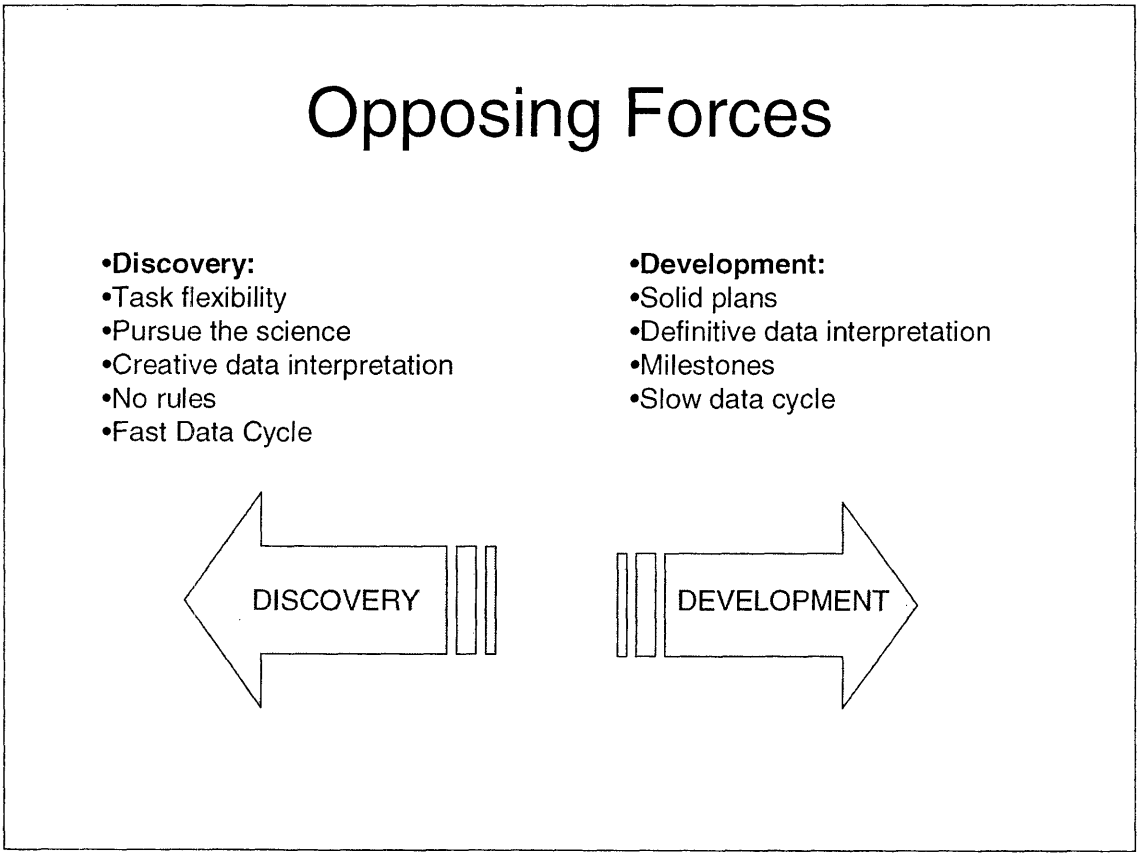


7.4 Opposing Forces

As discussed in the congruence analysis there are some components of development organizations which are in direct opposition to those in discovery

organizations. These opposing elements have their root cause in the fundamentally different nature of discovery and development tasks. As discovery and development organization architectures are pushed together the tension increases between the open organizational landscape required for creative discovery and the gated precision landscape required for operationally effective development processes. This tension results in an opposing force which works to keep separate the key elements of both organizations as outlined in Figure 16.

Figure 16



7.5 Alignment of linking mechanisms

The linking mechanisms which run between discovery and development units are the organizations attempt to resolve the opposing attractive (integrative) and

opposing pressures outlined in the previous section. The desire to increase drug development productivity through lowering clinical failure rates and to improve the characterization of molecules in the early stages of the process means that linking mechanisms are a critical feature of pharmaceutical R&D. I contend that some linking mechanisms will function more effectively than others and that there will be interdependencies amongst linking mechanisms which complicates the choice and emphasis when combining several mechanisms within an organization.

7.6 A Model of Integration

Based on the responses to our survey it is possible to streamline the view of linking mechanisms by grouping and refining the list in the questionnaire. To provide meaningful and actionable data to industry manages a clear cut understanding of the choices and properties of different systems for integrating discovery and development work is required. The information from the survey can be distilled into three distinct groups which I have called integrative systems. The term integrative is defined as the coordination of activities and synthesis of information across the two departments. The distillation process involved the following steps:

Step 1: Information technology was considered by the majority of the sample as a prerequisite for being in the discovery and development business and was

regarded as the basic infrastructure rather than any unique source of capability. I therefore disregarded it in the analysis.

Step 2: An integrative procedure which I had not originally treated as a linking mechanism became apparent in discussion with several of the surveyed companies; the regrouping of tasks by formally placing traditional clinical tasks within the discovery organization. This was a clear and purposeful step to bring together discovery activities with the development activities associated with phase I and phase II clinical trials in particular. I propose taking this concept forward as the first types of integrative system. I label this architecture as *re-grouped.*

Step 3: Use of active co ordination through an overseeing CEO or Executive Team was frequently observed in the sample companies. Other formal committees to oversee important decisions were composed of senior executives and behaved as an extension of an active hierarchy. I grouped CEO and committee linking mechanisms into a second grouping and labeled this form of integrative system as *centralized.*

Step 4: It proved difficult to find a clear distinction between teamwork and matrix reporting with some respondents believing they were the same thing and some believing that one supported the other. Conceptually both teamwork and matrix reporting involve allegiance to a leader outside a manager's functional reporting

line, and horizontal interaction across departments so we propose combining teams and matrix reporting as the third integrative system termed *team*.

Figure 17 summarizes these constructs in terms of the underpinning linking mechanisms and Figure 18 illustrates the dynamics of interaction within them.

Figure 17

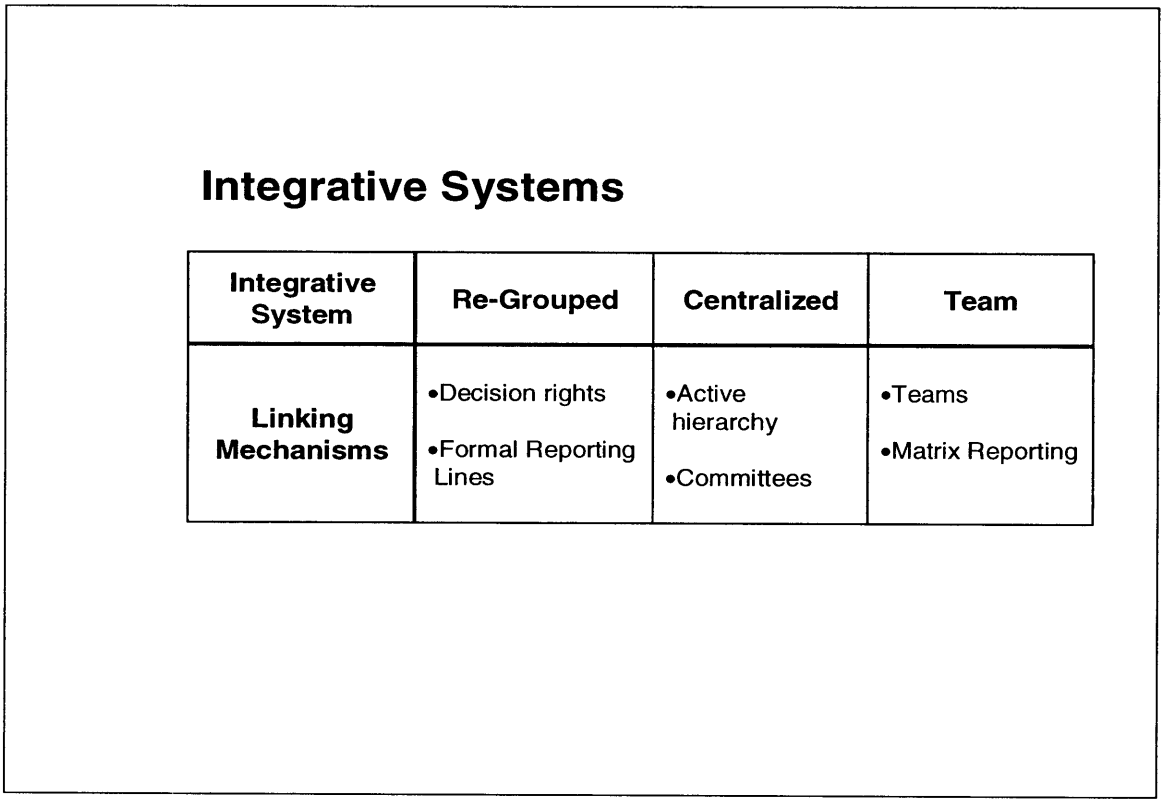
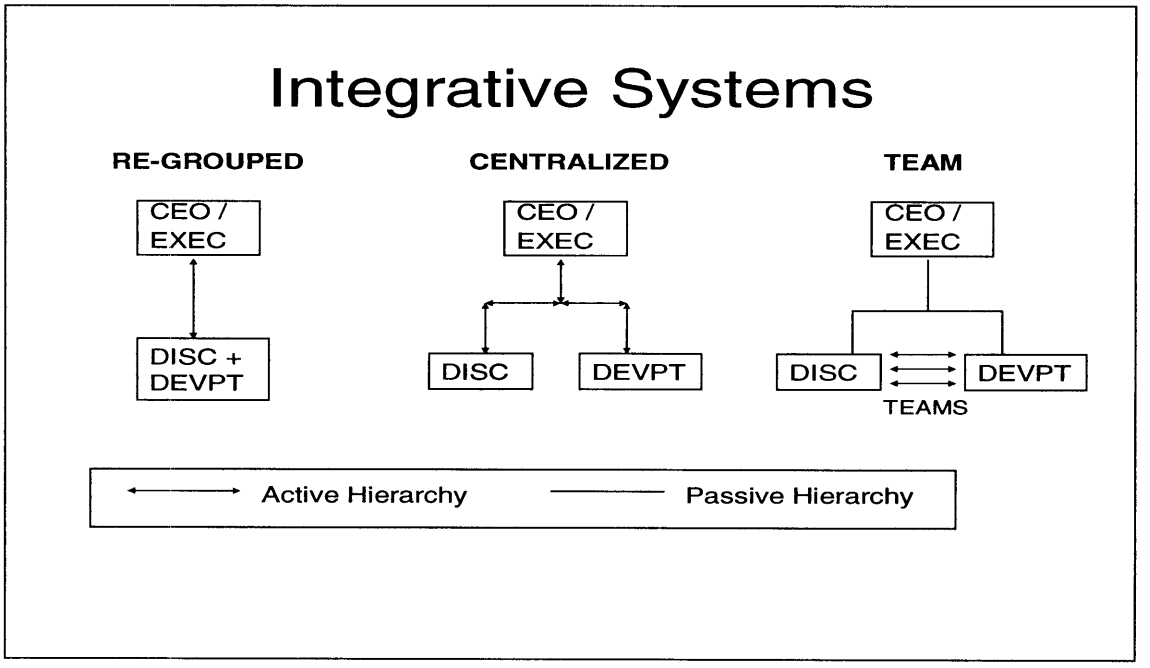


Figure 18



7.7 Evaluation of Integrative Systems

Before considering the value of the our three proposed integrative systems it is worth considering some of the general properties of linking mechanisms and the relevance of these to design choice. Linking mechanisms and their properties are discussed in a long line of literature (Mintzberg, 1979; Nadler and Tushman, 1997; Rivkin and Siggelkow, 2003). I have simplified this discourse to allow easy access to these concepts by industry managers and to allow their incorporation into a conceptual scheme of R&D performance. I suggest the set of parameters outlined in Figure 19 to evaluate linking mechanisms.

Figure 19

Measures of Integrative Performance

Parameter	Definition
Knowledge Processing	The ability of the system extract meaning from data
Decision Speed	The speed at which critical decisions are made
Low Resource	The management hours devoted to the cross functional integration of knowledge
Motivation	A function of the level of ability of individuals to influence decisions effecting their work
Search	The ability of the R&D organization to find new and relevant ideas
Stability	The ability of the R&D organization to focus on progressing selected projects.

This framework provides a means to speculate on the properties of the three integrative systems in the model:

Re-Grouped

The *re-grouped* system is in it's extreme form the fusion of two departments into one. In other word the tasks are grouped together and a formal reporting system installed which deals with research and development tasks through one department head.

In its extreme this system would essentially destroy the individual discovery and development functions. Although this may seem to be radical departure from the general industry paradigm there was evidence from our survey that a less

extreme form of this is occurring in at least three of our sample companies. In these companies some elements of the development organization are physically located within the discovery workspace and formally report to the head of discovery. In the most advanced case of this all development activities associated with Phase I and Phase II clinical trials were located in the discovery organization, in this situation the discovery unit is responsible for developing drugs to proof of concept. In practice re grouping would require a variety of technical specializations within a department with individuals dealing predominantly with either discovery or development issues.

The *re-grouped* organization form can be considered in terms of the integrative performance measures I have defined. Firstly it is likely to have high speed and high quality processing of knowledge since the same group is conducting discovery and development work. This would allow discovery scientists to be intimately involved with the design and interpretation of early stage clinical trials and it would allow development mangers access to the richness of biological data from the bench top to help guide their pharmacological and clinical investigation. It is probable that these groups would become close colleagues exchanging information informally and taking social time together. Camaraderie is likely to emerge uninhibited by departmental rivalries which will facilitate a fusion of research and development inputs.

At another level however there is likely to be some loss of functional congruence and task specific expertise. The trade off of increased integration is that the

experts in a specialty are no longer shoulder to shoulder vying for the intellectual high ground. From a more task based perspective the presence of creative biological scientists may distract development people from their timelines and benchmarks, and conversely the biological scientists may feel less able to desert their more down to earth colleagues in search of an exploration new terrain. The re grouped organization in its extreme is likely to be highly integrative and highly disruptive to functional congruence.

Centralized

A *centralized* design in our exploration is represented by a structure where discovery and development decision rights have been clearly separated between the two departments however there is an extremely active hierarchy where both departments submit decisions upward to a head of R&D or a CEO can make choices based on the information received from both departments. This structure has historically featured strongly in the design of large pharmaceutical companies and was not found within our survey sample in this pure form however it may be helpful to consider the ramifications of this type of structure on the functioning of R&D.

Centralization has a low capacity to transfer and process information. The senior manager who links the two departments will have finite cognitive capacity and will eventually be unable to convey all the relevant knowledge to the departments under his jurisdiction. Given the time constraints of the overseeing manager the way information is conveyed will primarily be in the form of decisions from above

with limited time for integrating or molding knowledge through discussion. *Centralization* is an extremely fast way to make decisions and move projects forward, it avoids much of the time for consensus building and iteration. Time is important in drug development, for a patented molecule with projected sales of $1 billion the cost of one days delay in getting the drug to market is around $2 million lost profit. *Centralization* is also resource efficient in that it reduces the time taken for managers to plan and hold meetings and it provides clear focus on objectives and priorities.

Team

This is a form of decentralized organization where discovery and development activity is located in separate units and the active hierarchy of the previous centralized structure is replaced by cross functional teams. Targets and objectives are set by an executive team however project management is primarily achieved through project teams which span the two units, and other units in the organization. This type of organization will have some of the properties of the *re-grouped* design in that it will allow a richness of knowledge processing and a motivational team commitment through the buy-in process that discussion brings. It will not be as fast or a resource efficient as the re-grouped design in that teams need to arrange meeting and are more prone to indecision than formal units. This organizational form will provide a higher quality of information processing and greater people involvement than the *centralized* form, however again it will not be as fast or resource efficient.

Figure 20 summarizes of the inherent properties predicted for each of our three integrative systems.

Figure 20

Evaluation of integrative systems

	Knowledge Processing	Decision Speed	Low Resource	Motivation	Search	Stability
GROUP	+	+	+	+	-	-
CENTRAL	-	+	+	-	-	+
TEAM	+	-	-	+	+	-

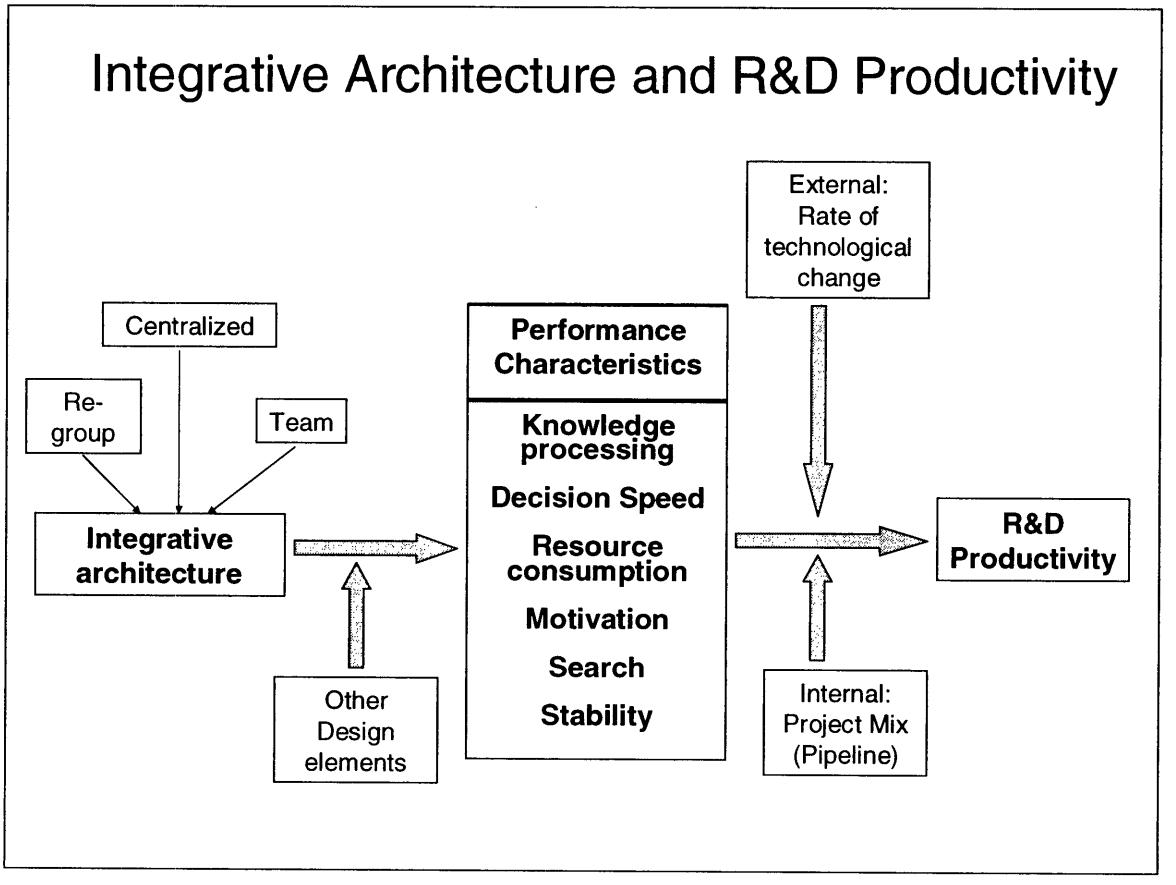
+ = Promotes

Each of the firms in our survey had blended all three of these systems to form an 'integrative architecture'. Although predicting the properties of each of the integrative systems in their purest form can provide some guidance to managers responsible for designing R&D organizations it is insufficient to be able to fully define the relationship between integrative architecture, performance characteristics and R&D productivity. This relationship is not one of simple proportions and is complicated by the interdependencies between design

elements, task objectives and environment. The response of any given performance characteristic will therefore vary unevenly as design elements are adjusted.

It follows that Integrative systems will exhibit contextual properties in addition to the generic properties discussed in the previous section. The conceptual model of integration can be extended to include some of the interdependencies and interactions governing the translation of organization design into performance characteristics and productivity, Figure 21

Figure 21

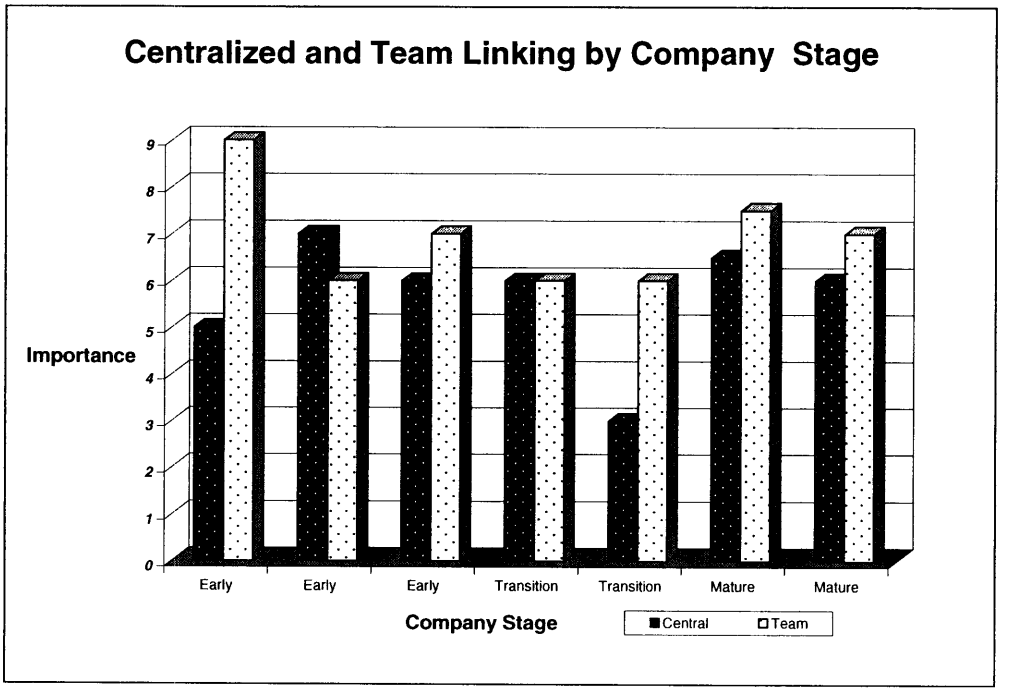


In the extended model the integrative architecture is considered to provide output at two levels. The first level is the performance characteristics I have discussed which provide the firm with capability; the second level is the translation of this capability into productivity. R&D productivity will be optimized only when the performance characteristics fit well with the mix of projects in the pipeline and the external technological environment.

7.8 Implications of the model

Although there was evidence of firms using 'regrouping' to varying degrees in our survey our data suggests there was a more passive deployment of *centralized* (CEO+ committee) and *team* (project team +matrix reporting) systems with most companies relying equally on each (figure 22).

Figure 22



According to our basic model it would be beneficial for firms wishing to increase their 'search' for targets and leads to emphasize *team* and *regrouped* systems and for those wishing to efficiently progress expensive development assets (molecules in the clinic) through a pipeline to adopt a more *centralized* approach. Similarly in periods of high technological change where it is desirable that basic scientific information crosses firm boundaries to specialist groups it may be best to focus on *team* based integration so the discovery scientists are unencumbered by the formalities of *regrouping* or an active hierarchy. In this case once the desired knowledge has been captured from outside the firm the integrative mix may be shifted to provide more stability and exploit the knowledge. A dynamic control of the mix of integrative systems will lead to an appropriate tuning of organizational performance in response to changing external and internal requirements.

7.9 Further work

Aspects of the extended model of integrative systems could be formally tested using techniques such as NK simulations. Alternative integrative architectures could be simulated in different contextual settings. A more robust model would expand our understanding of the interdependencies surrounding integrative architecture and provide firms with more confidence to adapt organizational design to meet specific R&D challenges.

References

Allen, T. (1971),Communication Networks in R&D Labs, R&D Management,Vol.1,14-21.

Chandler, A.D. (1962), Strategy and structure: Chapters in the history of the industrial Enterprise, MIT Press, Cambridge MA.

Cockburn, I. and Henderson R. (1996), Public–private interaction in pharmaceutical research, Proc. Natl. Acad. Sci. USA Vol. 93, pp. 12725–12730.

Cohen, W.M. and Levinthal D.A. (1989), Absorptive Capacity: A new perspective on learning and innovation, The Economic Journal, 99, 569-596.

Datamonitor, (2002), The New Generation of Blockbusters: Pipeline Potential, 2002-2008

DiMasi J.A. et al. (2003), The price of innovation: new estimates of drug development costs, Journal of Health Economics, 22, 151–185.

Goldman Sachs (October 2002), Global Pharma Sector Update.

Henderson, R.(1994), The evolution of integrative capability : innovation in cardiovascular drug discovery, MIT, Sloan School of Management, Program on the Pharmaceutical Industry ; #5-92.

IBM (2003), Pharma 2010, The Threshold of Innovation.

Utterback J. (1994), Mastering The Dynamics of Innovation, Harvard Business School Press.

Katz R. (1997), Managing Creative Performance in R&D Teams, The Human Side of Managing Technological Innovation, oxford University Press, p 177.

Katzenbach J.R. and Smith D.K. (1993), The Discipline of Teams, Harvard Business Review,Vo.17,pp.111-120.

Levitt, B. and J. G. March (1988), Organizational Learning, Annual Review of Sociology, 14 319-340.

March, J. G. (1991), Exploration and Exploitation in Organizational Learning, Organization Science, 2 71–87.

Milgrom, P. R., and Roberts J. (1995), Complementarities and fit: Strategy, structure, and organizational change in manufacturing. Journal of Accounting and Economics, 19: 179-208.

Mintzberg, H. (1979), The Structuring of Organizations, Englewood Cliffs, NJ: Prentice Hall.

Nadler, D. and Tushman M.L.,(1997), Competing by Design: the Power of Organizational Architecture, Oxford University Press.

Pisano, G. P. (1997) The development factory: unlocking the potential of process innovation, Harvard Business School Press.

Porter, M. E. (1996), What is Strategy, Harvard Business Review, 74, 6 61–78.

Porter, M. E. and Siggelkow N. (2002), Contextual Interactions within Activity Systems and Sustainable Competitive Advantage, working paper, Wharton School, University of Pennsylvania, Philadelphia.

Pritchard et al (2003), Making Better Drugs: Decision Gates in Non-clinical Drug Development, Nature Reviews: Drug Discovery 544 Volume 2.

Rivkin, J. W. and N. Siggelkow (2003), "Balancing Search and Stability: Interdependencies among Elements of Organizational Design," Management Science, 49 290-311.

Teece,D., Piasano,G. and Shuen (1997), Dynamic Capabilities and Strategic Management, Strategic Management Journal, Vol. 18:7, 509–533.

Thamhain, H. J., Wilemon, D. L. (1987), Building High Performing Engineering Project Teams, IEEE Transactions on Engineering Management. New York: Vol. EM34, Iss. 3; p. 130.

The Boston Consulting Group (2001), A Revolution in R&D.

Tushman, M. L. and O'Reilly C. A. (1996), "Ambidextrous Organizations: Managing Evolutionary and Revolutionary Change," California Management Review, 38, 4 8–30.

Walters W.P. and Namchuk M. (2003), Nature Reviews: Drug Discovery 260 Volume 2.

APPENDIX I

CONGRUENCE QUESTIONAIRE

1.1 **Strategy**

How would you summarize the strategy of your company in two or three sentences?

[Therapeutic areas, small molecule vs. biologics, out-licensing vs. self-development, discovery platform.]

What is your company's vision or mission statement? What does it mean to you?

1.2 **Component Tasks**

How unpredictable are the key tasks within the discovery organization?

	Extremely Routine						**Extremely Uncertain**
	1	**2**	**3**	**4**	**5**	**6**	**7**
Target selection							
Compound design							
Screening							
Lead identification							
Lead evaluation							
Chemical Synthesis							

How unpredictable are the key tasks within the development organization?

	Extremely Routine						Extremely Uncertain
	1	2	3	4	5	6	7
PK Studies							
Toxicology Studies							
Clinical Trial Management							
Manuf. Process Development							
FDA Documentation							

How much freedom do you have to specify tasks and their outputs internally vs. dictated by regulatory and industry standards?

	Totally Externally Determined						Totally Internally Determined
	1	2	3	4	5	6	7
In Discovery							
In Development							

Workflows

What type of workflow exists within and between drug discovery and development in your organization?

	Mostly Sequential						Mostly Reciprocal
	1	2	3	4	5	6	7
Within Discovery							
Within Development							
Between Discovery and Development							

What do you see as the key differences between drug discovery and drug development?

.....

1.3 Human Resources

How would you describe the human resource characteristics within discovery and development units, please rank the following?

	Discovery Rank	Development Rank
Educated		
Creative		
Good planners		
Good Communicators		
High achievement needs		
Flexible		

What motivates you and members of your discovery and development teams, please rank the following?

	Discovery Rank	Development Rank
Salary & Bonus		
Share Options		
Management Recognition		
Peer group recognition		
Job Security		
Company Prestige		

How centralized is the decision making in your discovery and development units?

	Fully Centralized						Fully Decentralized
	1	2	3	4	5	6	7
Discovery							
Development							

1.4 Formal Organization

What is your unit's formal structure?
[Organogram]

What are the formal linking mechanisms between drug discovery and development units in your organization please rank the following?

Linking Mechanism	Rank	Detail	Reason
Matrix Reporting			
Committees			
CEO / Executive Team			
Project Teams			
IT			

How much is progress in discovery and development units is dependent on set procedures vs. individual empowerment and motivation?

	Mostly procedures						**Mostly Individual empowerment**
	1	**2**	**3**	**4**	**5**	**6**	**7**
Discovery							
Development							

What is formally measured and controlled within your organization?

Discovery –

Development -

How do your formal career and promotion systems operate?
[Annual, quarterly reviews, with boss, with grandfather]

Discovery –

Development -

1.5 Norms and Values

What are your discovery and development units' norms and values, please rank the following?

	Discovery Rank	Development Rank
Long Hours		
Formal Dress		
Informal Communication		
Open Conflict		
Customer Orientation		
Informal power		

APPENDIX II Part (a)

COMPANY	A			B			C			D		
	Discovery	Development	Link	Discovery	Development	Link	Discovery	Development	Link	Discovery	Development	Link
Discovery Components - Uncertainty												
Target selection	3.00			6.50			3.00			5.00		
Compound design	3.00			3.50			3.00			4.00		
Screening	1.00			3.50			4.00			3.00		
Lead identification	2.00			4.00			2.00			4.00		
Lead evaluation	4.00			3.00			2.00			4.00		
Chemical Synthesis	3.00						N/A			4.00		
Mean	2.67			4.40			2.80			4.00		
Development Components - Uncertainty												
PK Studies		3.00			2.00			2.00			3.00	
Toxicology Studies		5.00			2.00			2.00			3.00	
Clinical Trial Management		5.00			2.50			2.00			2.00	
Manuf. Process Development		4.00			3.00			3.00			2.00	
FDA Documentation		4.00			2.50			2.00			2.00	
Mean		4.20			2.40			2.20			2.40	
Task Specifiation - Freedom	6.00	3.00		6.50	2.50		2.00	6.00		6.00	2.00	
Workflows- Reciprocal	6.00	2.00	4.00	4.00	3.50	2.50	5.00	5.00	4.00	6.00	4.00	6.00
Human Resource Characteristics												
Educated	3.00	3.00		1.75	2.25		1.00	1.00		1.00	1.00	
Creative	2.00	6.00		1.25	3.50		3.00	6.00		2.00	4.00	
Good planners	4.00	1.00		4.50	1.75		2.00	2.00		5.00	2.00	
Good Communicators	5.00	4.00		3.50	3.00		6.00	3.00		3.00	3.00	
High achievement needs	1.00	2.00		6.00	6.00		5.00	4.00		6.00	6.00	
Flexible	6.00	5.00		4.00	5.00		4.00	5.00		4.00	5.00	
Motivation												
Salary & Bonus	1.00	1.00		2.50	3.00		2.00	3.00		6.00	6.00	
Share Options	3.00	3.00		3.50	4.00		1.00	1.00		5.00	5.00	
Management Recognition	2.00	2.00		3.00	3.00		4.00	5.00		3.00	3.00	
Peer group recognition	4.00	5.00		2.00	2.00		5.00	6.00		1.00	1.00	
Job Security	6.00	6.00		4.00	4.00		3.00	4.00		3.00	3.00	
Company Prestige	5.00	4.00		6.00	5.00		6.00	2.00		3.00	3.00	
Centralization- Decentralized	4.00	3.00		4.50	3.50		4.00	4.00		7.00	4.00	
Linking Mechisms												
Matrix Reporting			2.00			2.50			5.00			2.50
Committees			3.00			2.00			4.00			1.00
CEO / Executive Team			4.00			3.50			2.00			5.00
Project Teams			1.00			2.00			1.00			2.50
IT			5.00			5.00			3.00			4.00
Individual Empowerment	3.00	2.00		5.00	2.00		5.00	5.00		4.00	4.00	
Norms and Values												
Long Hours	1.00	1.00		3.00	2.50		3.00	4.00		1.50	1.50	
Formal Dress	5.00	4.00		4.00	3.50		5.00	6.00		4.50	4.50	
Informal Communication	2.00	2.00		2.00	2.50		2.00	2.00		1.50	1.50	
Open Conflict	6.00	3.00		4.50	5.50		4.00	5.00		4.50	4.50	
Customer Orientation	3.00	6.00		4.00	4.00		6.00	3.00		4.50	4.50	
Informal power	4.00	5.00		3.50	3.00		1.00	1.00		4.50	4.50	

APPENDIX II Part (b)

COMPANY	E			F			G			ALL		
	Discovery	Development	Link	Discovery	Development	Link	Discovery	Development	Link	Discovery	Development	Link
Discovery Components - Uncertainty												
Target selection	1.00			5.00			5.00			4.07		
Compound design	4.00			3.00			4.00			3.50		
Screening	4.00			3.00			4.00			3.21		
Lead identification	5.00			5.00			3.00			3.57		
Lead evaluation	3.00			3.00			2.00			3.00		
Chemical Synthesis	N/A			3.00			2.00			3.00		
Mean	3.40			3.67			3.33			3.47		
Development Components - Uncertainty												
PK Studies		3.00			2.00			2.00			2.43	
Toxicology Studies		3.00			2.00			2.00			2.71	
Clinical Trial Management		3.00			2.00			3.00			2.79	
Manuf. Process Development		3.00			2.00			4.00			3.00	
FDA Documentation		5.00			2.00			3.00			2.93	
Mean		3.40			2.00			2.80			2.77	
Task Specifiation - Freedom	5.00	2.00		6.00	2.00		7.00	3.00		5.50	2.93	
Workflows- Reciprocal	5.00	5.00	5.00	5.00	7.00	4.00	7.00	7.00	7.00	5.43	4.79	4.64
Human Resource Characteristics												
Educated	1.50	1.50		2.00	2.00		1.00	3.00		1.61	1.96	
Creative	1.50	3.50		1.00	3.00		1.00	3.00		1.68	4.14	
Good planners	3.00	1.50		5.50	1.00		5.00	1.00		4.14	1.46	
Good Communicators	4.00	3.50		5.50	5.00		5.00	5.00		4.57	3.79	
High achievement needs	6.00	6.00		4.00	6.00		3.00	1.00		4.43	4.43	
Flexible	5.00	5.00		3.00	4.00		3.00	5.00		4.14	4.86	
Motivation												
Salary & Bonus	1.00	1.00		4.00	2.00		5.50	5.50		3.14	3.07	
Share Options	6.00	6.00		4.00	2.00		5.50	5.50		4.00	3.79	
Management Recognition	3.00	3.00		3.00	1.00		1.00	1.00		2.71	2.57	
Peer group recognition	2.00	2.00		1.00	5.00		3.00	4.00		2.57	3.57	
Job Security	5.00	5.00		6.00	6.00		2.00	2.00		4.14	4.29	
Company Prestige	4.00	4.00		2.00	4.00		4.00	3.00		4.29	3.57	
Centralization- Decentralized	4.00	4.00		6.00	6.00		4.00	3.00		4.79	3.93	
Linking Mechisms												
Matrix Reporting			5.00			3.00			1.00			3.00
Committees			2.00			5.00			4.00			3.00
CEO / Executive Team			3.00			1.00			5.00			3.36
Project Teams			1.00			2.00			1.00			1.50
IT			4.00			4.00			3.00			4.00
Individual Empowerment	6.00	6.00		1.00	1.00		6.00	6.00		4.29	3.71	
Norms and Values												
Long Hours	1.00	1.00		5.00	5.00		5.00	5.00		2.79	2.86	
Formal Dress	6.00	6.00		6.00	6.00		6.00	6.00		5.21	5.14	
Informal Communication	4.00	4.00		3.00	3.00		2.50	2.50		2.43	2.50	
Open Conflict	2.00	2.00		2.00	2.00		2.50	2.50		3.64	3.50	
Customer Orientation	3.00	3.00		1.00	1.00		1.00	1.00		3.21	3.21	
Informal power	5.00	5.00		4.00	4.00		4.00	4.00		3.71	3.79	