CRITICAL SUCCESS FACTORS IN BIOMEDICAL RESEARCH AND PHARMACEUTICAL INNOVATION

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The joint impact of management control and contingencies on performance and effectiveness in research laboratories in medical faculties, health research institutes and innovative pharmaceutical companies

by

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Printed on acid-free paper

to Frances, my wife
to Anne Willem and Ilonka, my children

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PREFACE

This book presents the findings of a study into management and organization in biomedical research in universities and institutes and pharmaceutical innovation in company laboratories. It aims at providing a sound empirical basis for a number of ideas and statements about research management in general. The backbone of this monograph is formed by a number of articles in scientific journals and contributions to scientific congresses and workshops. The findings also have served as a platform for discussion with managers in R&D.

The study was performed at the Institute for Research in Extramural Medicine (EMGO-Institute) of the 'Vrije Universiteit' in Amsterdam and the Department of Business Development and Business Research Methodology of the Faculty of Management and Organization in Groningen. It would not have been possible without the support of researchers from many different disciplines. I would like to thank the professors and the directors of the institutes and the R&D directors in pharmaceutical companies who gave their time for interviews about research management, and whose advice enabled me to evaluate the results. I am also indebted to the senior scientific staff for their willingness to complete the research questionnaires. My special thanks go to Jo van Engelen and Lex Bouter for all their help in conducting the study and to Lou Feenstra and Hans Valkenburg, who encouraged me to start it. Felix Janszen was willing to share his theoretical and practical knowledge of pharmaceutical innovation, I have good memories about the discussions we had in Miami about technology management.

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Abcoude, March 1995 Onno Omta

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INTRODUCTION

For the several employments and offices of our fellows, we have twelve that sail into foreign countries under the names of other nations (for our own conceal), who bring us the books and abstracts, and patterns of experiments of all other parts. These we call Merchants of Light. We have three that collect the experiments which are in all books. These we call Depredators. We have three that collect the experiments of all mechanical arts, and also of liberal sciences, and also of practices which are not brought into arts. These we call Mystery-men. We have three that try new experiments, such as themselves think good. These we call Pioneers or Miners. We have three that draw the experiments of the former four into titles and tables, to give the better light for the drawing of observations and axioms cut of them. These we call Compilers. We have three that bend themselves, looking into the experiments of their fellows, and cast about how to draw out of them things of use and practice for man's life and knowledge, as well for works as for plain demonstration of causes, means of natural divinations and the easy and clear discovery of the virtues and parts of the bodies. These we call Dowry-men or Benefactors. Then after divers meetings and consults of our whole number to consider of the former labours and collections, we have three that take care out of them to direct new experiments, of a higher light, more penetrating into Nature than the former. These we call Lamps. We have three others that do execute the experiments so directed and report them. These we call Inoculators. Lastly, we have three that raise the former discoveries by experiments into greater observations, axioms, and aphorisms. These we call Interpretators of Nature. We have also, as you must think, novices and apprentices, that the succession of the former employed men do not fail; beside a great number of servants and attendants, men and women. And this we do also: We have consultations, which of the inventions and experiences which we have discovered shall be published, and which not: and take all an oath of secrecy for the concealing of those which we think fit to keep secret: though, some of those we do reveal sometimes to the State, and some not.

Nova Atlantis (Sir Francis Bacon [1625] in Allen 1977)

In around 1625, Sir Francis Bacon magnificently described a research organization in the ideal world of Nova Atlantis. These days, research organizations can be found in the everyday world. This book will bring you into this world. It describes the unclear situation of everyday research management. It will show you the publish-or-perish world in universities, the struggle for market orientation in institutes, and the competitive fight for market share in industry. This book aims at answering such questions as: 'Are there universal factors of management and organization determining success in research and experimental development (R&D), or are these factors merely dependent on the organizational setting you are dealing with? Which types of management and organization will give the best results, and which incentives and instruments should be used to achieve this?'

This monograph concentrates on the research floor level, the research unit (the professors with their scientific, technical, analytical and administrative staff in universities, or the department heads with their staff in institutes), and the system of research units which together form the R&D process in industry. What are the secrets of the best performing units? Is it only the brilliancy of the supervisor(s), or are there other factors dividing the outstanding from the average performers? In industry questions arise about the coordination and structuring of the R&D process. How is optimal coordination achieved if one part of the R&D process is carried out in the USA, whereas at the same time another part is done in France. And how do we get coordination if in a multi-centred clinical trial the same study design must be followed by physicians in Norway, France, and Germany? This study is based on a comparative study of 40 biomedical research units in 8 medical faculties, and 17 research units in 5 large Health Research Institutes in the Netherlands. This is combined with the findings of a European survey of the main R&D laboratories of 14 large and medium sized pharmaceutical companies.

Unfortunately, this book will not give you the definite answers. In the world of research it is often unknown what is cause and what is effect. For instance, if is found that an outstanding research unit has many international contacts, is this then one of the causes of its excellency? By communicating intensively with colleagues abroad, researchers do get a better idea of what is new and interesting in their research field. Or is it an effect of excellency? The outstanding research units may attract more attention from the scientific community, for instance, in the form of proposals for cooperative projects or presentations at international congresses as the institution behind a keynote speaker.

Or is it cause and effect simultaneously? The latter could very well be the case. In many places in this book, reinforcement loops such as, doing good research, getting interesting results, attaining more attention from the outside world, getting more international contacts, developing more innovative ideas etc., will be encountered. If it were possible to provide clear-cut relationships, then management would be (or become) a formalistic system, which would eliminate the need for scientific enquiry. The fact that it is not leads us to the second unfortunate point. At the very moment the secrets of success are revealed, they no longer apply. A certain strategy which is a competitive advantage for the few, will turn into its opposite if it is used by all. Therefore, it might sometimes be better to proceed in the opposite direction than the one which is suggested by the empirical data. Although this book does not provide the reader with clear-cut relationships, it does provide him or her with a comprehensive list of features which separate the outstanding from the average research laboratories. Discussions with research managers in the strata universities, institutes and company laboratories revealed that most of the suggestions were judged fruitful for everyday management.

This book is aimed at research managers at different levels in universities, institutes and companies. Policy makers in the field of research and experimental development may also find useful ideas and concepts in it. Researchers in the field of management studies may be interested in the research model and the interpretation framework used. Because the field of management and organization is a broad one, all of the methods and techniques presented will not be appropriate for the individual reader. Still it can be assured that it contains sufficient relevant information for his or her purpose. This book is divided into two major parts, each of which is designed to achieve a different objective. Readers primarily interested in management practice and advising may find useful concepts and ideas in the sections 1 and 4. Researchers in management studies will find an account of the design, conduction and results of the empirical study in the sections 2 and 3.

Section 1 (chapters 1 to 3) supplies the theoretical foundation for the study. The first chapter deals with the research methodology and the study domain. The empirical part of this book follows the trajectory of theory construction, whereas the evaluation of the possible impact for management practice follows the heuristic methodology of theory application. It is argued that success of application depends heavily on the context (situation) one is dealing with. Then the chapter turns to the study domain. It classifies research and experi-

mental development in universities, institutes and companies, and gives a factual overview at the current state of biomedical research in the Netherlands. Because of its multinational character, industrial pharmaceutical R&D is described on a global level. The second chapter focuses on the concepts of systems theory. Different aspects of organizational structure and behaviour are described, using the contingency theory and the organizational typologies elaborated by Mintzberg (1979). The systems theory of control is introduced, based on the broad paradigm of control ('any form of goal directed influence') as defined by De Leeuw (1990). It provides the theoretical foundation for the analysis of the control situation in the three strata, and it is used as a checklist on the completeness of the variables used. The chapter ends with an outline of the expected relative strength of the different system variables in the three strata. Chapter 3 focuses on the research floor level. It introduces the concept of circular learning to describe the research process in terms of value adding learning loops. The conceptual model of the double unity cell (Van Engelen 1989) is discussed, which integrates the concepts of value adding learning and a control situation. Finally, the model of the double unity cell is applied to the three strata.

Section 2 (chapter 4 to 6) focuses on the study design. Chapter 4 describes the different elements which are used in the theory structure; i.e., the concepts, observational relationships and operationalizations of the variables, and the measures taken to provide for complete coverage of the relevant relations and entities, and for internal and external validity. The 'triangular' model is developed to cover the dynamic associations of management control (control by the research management) with performance and effectiveness, while different contingencies are used to fine-tune for situational differences at the research unit level. Chapter 5 concentrates on the expected associations between management control and the contingencies on the one hand, and performance and effectiveness on the other. The general hypotheses regarding the differences in management control and more specific hypotheses about the different contingencies are formulated, and different cross-sections of the industrial study population are made. Chapter 6 concentrates on the methods of data collection. Structured interviews regarding research management in general, and specific questionnaires regarding qualitative and quantitative aspects of structure and control, have been designed to measure the dependent variables. The attention is focused on the sampling procedures, inclusion criteria and the measures taken to provide for the representativeness of the study population. In addition, the bi-variate and multi-variate methods

of data-analysis are discussed. This chapter ends with a description of the methods used to approach the study population.

Section 3 (chapters 7 to 9) presents the results of the empirical study. Chapter 7 concentrates on the actual data collection, specifically on the representativeness of the response and the reliability of the instruments. Because of the difference in the level of analyses (single research units in universities and institutes versus systems of research units in industry), the results found in the universities and institutes are presented separately from those found in company laboratories, in chapter 8 and chapter 9, respectively.

Section 4 (chapters 10 to 12) discusses the results and draws the conclusions. In chapter 10 the main conclusions for universities and institutes are given, and in chapter 11 those for companies. In the final chapter, chapter 12, the management control situation is compared in the three strata. The main findings are placed in a broader context, and suggestions are made for further research. Also, practical implications for research management, administration and research policy are given, taking into account the differences in the applicational contexts.

SECTION 1

THEORY

CHAPTER 1

RESEARCH METHODOLOGY AND STUDY DOMAIN

This Section provides the theoretical foundation for this monograph. This chapter concentrates on the research methodology and study domain. A distinction is made between the trajectories of theory construction and theory application. The attention is then focused on the study domain. A broad definition of R&D is given, and it is classified into basic research, applied research and experimental development. After a factual overview at Dutch R&D in general, it focuses on biomedical research in particular. Because of its multinational character, the features of industrial pharmaceutical innovation are discussed on a more global level. In the next two chapters, the concepts of systems theory on which this study is based, are discussed in more detail. Chapter 2 concentrates on structure, behaviour and control at the level of the whole organization, and chapter 3 focuses on the object of study, i.e. the research unit level.

1.1 THE METHODOLOGY OF THE STUDY OF MANAGEMENT AND ORGANIZATION

The study of management and organization is one of the empirical sciences, because the discipline is concerned with the physical and social reality. The design of most empirical management studies follows the methodology of the empirical sciences, in which quantified variables are explained (in strict statistical sense) by other quantified variables (see § 3.2). This is mathematically expressed in the following general equation:

Equation 1.1 $$y_i = f(x_i) \qquad (1 \leq i < n)$$

By convention y_i is taken as the dependent variables (effect) and x_i represents the independent variables (cause). However, in trying to find the above causal relationship, the researcher in management and organization studies may encounter a number of methodological and contextual problems, connected with

the subject of the study, which are not present in other empirical sciences. They are considered below in more detail (based on Bagozzi 1983 and Van Aken 1994).

- Conceptual variables are sometimes difficult to operationalize in quantitative measures.
- Errors in measurements occur as a result of the imperfect correspondence between constructs and operationalizations.
- Multi-causality, y may be influenced by more factors than x alone, and it is often a certain combination of factors which causes a certain effect in y. These other factors might have been overlooked or omitted for practical reasons.
- A degree of randomness exists, such as might be reflected in the natural variability in the responses of individuals or in data collection and coding.
- It is often difficult to find the number of observations necessary for statistically justified conclusions.

Additional problems arise because managers and management consultants have to deal with complex questions and situations in which a large number of mutually correlated effects are at work simultaneously, or where an integrated approach is necessary because a specific problem cannot be isolated from its context, for instance:

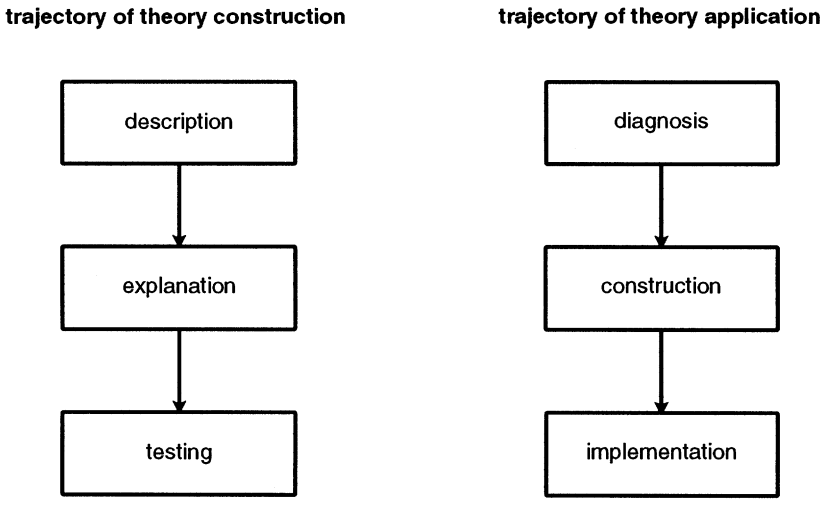
- Situation and time dependency means that a relationship may be found in organization A but not in B, and might also disappear in A after some time.
- The effect of an alteration (an organizational change) may take a longer period of time then expected.
- An implementation effect may apply, i.e. the effect of a measure does not only depend on the measure itself, and the situation and moment of implementation, but also on the person(s) who implements it. It is often observed that 'good' measures may fail by poor implementation, whereas 'bad' measures can be successful in the hands of a skilled consultant.

Therefore, a manager or management consultant has to work with heuristic knowledge based on the study of comparable cases. On the basis of such studies the most promising applications or measures are chosen.

1.1.1 The Trajectories of Theory Construction and Theory Application

In order to address these problems systematically, Van Engelen and Van der Zwaan (1994) have distinguished the trajectories of theory construction (TC) and theory application (TA). The trajectory of theory construction is directed towards the confrontation of the theory with reality via description (or measurement), explanation and testing. Based on this confrontation the theory can be confirmed, rejected or (re-)designed. The trajectory of theory application is directed towards the creation of the artificial in the theoretical and/or practical context. The two trajectories are outlined in Exhibit 1.1.

Exhibit 1.1 THE TRAJECTORIES OF THEORY CONSTRUCTION AND THEORY APPLICATION



source: Van Engelen and Van der Zwaan 1994

The trajectory of theory construction starts with the definition of concepts and constructs which give a theoretical description of part of reality. This description aims at providing explanations for the observable phenomena, combined with a high level of predictability. By use of formal testing procedures, the level of explanatory and/or predicting power is investigated on reality. If such a test is positive (or negative) than a contribution is made to the body of scientific knowledge. This new body of knowledge may lead to new investiga-

tions, new propositions (hypotheses) and thus to further 'theory production' or will be used in the trajectory of theory application. In the trajectory of theory application the sequence of steps is quite the opposite from that in the trajectory of theory construction. In this trajectory, an undesired situation is observed in reality (a disease or organizational problem). In the diagnosis phase the reality is theoretically assessed in order to choose which theory should be used to improve the situation. After that, a solution for the problem is designed and implemented (therapy or organizational redesign). If implementation does not lead to the desired situation this may lead to additional measures in the domain of theory application or to new research questions in the domain of theory construction.

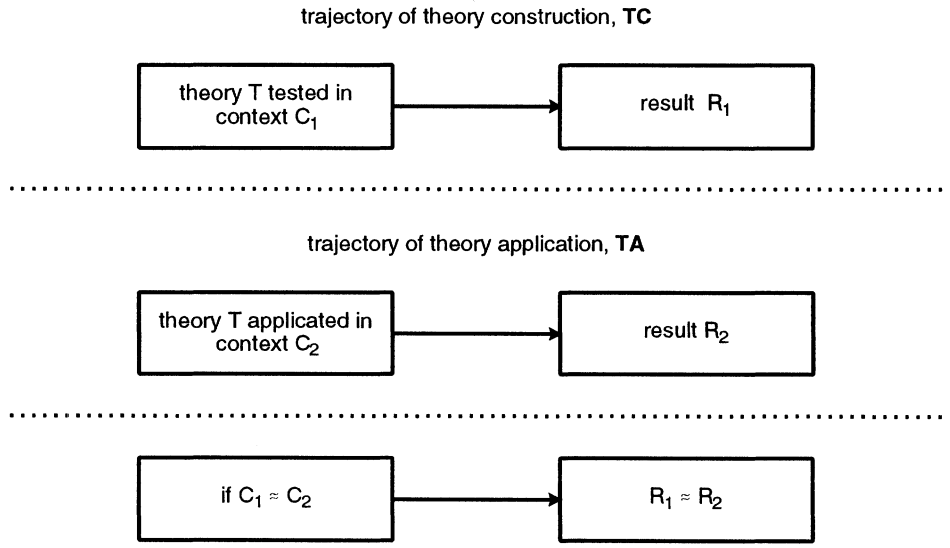
One of the most well-known examples of theory application is the therapeutic action of the physician. The physician will start with taking down the general anamnesis of the patient. He/she then chooses a suitable diagnosis procedure, for instance, one that is sufficiently wide-reaching (a physician will examine a patient with pain in his/her fingers, not only for fractures, but also for a possible deviation of the heart function). He/she will end with establishing the probable cause of the complaint and searching for a therapeutic action. If more methods are available, the physician will have to choose the best (an evaluation problem), for instance a drug therapy or an operation. Sometimes a new method has to be developed (a construction problem), for instance, the use of a new type of synthetic pin to heal a hip fracture. Thereafter the chosen therapy is implemented. An implementation effect may also apply, it is often established that the success of a therapy partly depends on the confidence of the physician in his/her treatment.

1.1.2 The TC/TA matrix

Exhibit 1.2 depicts the idea that in scientific fields, which encounter large contextual variation, a theory tested in one specific context (C_1), may give quite different results if applied in another context (C_2). However, a theory will only have practical merit if it leads to comparable results in similar contexts. The design of this study is based on the concept of 'context-comparison'. If for a certain phenomenon (management control) in one technology field (biomedical research, chosen for the similarity of the overall context) but in three different (sub-)contexts (basic and strategic research in universities,

applied research in institutes and R&D in industry) consistent relationships with outcome are found this phenomenon is considered to be fundamental for these relationships and may therefore be generalized to related contexts in other technology fields.

Exhibit 1.2 CONTEXT-DEPENDENCY OF THEORY CONSTRUCTION AND THEORY APPLICATION



The reliability and the generalizibility of the results both are depended on the size of the study population. The TC/TA matrix (see exhibit 1.3), which couples the trajectories of theory construction and theory application to the size of the study and the target population, might therefore be a helpful tool for taxonomy purposes and as a paradigm of completeness for empirical management studies.

If a case study is conducted in one or a few organization(s) or a rare illness is described in a small group of patients, the sample size is small in the trajectory of theory construction. In general, no statistical techniques can be applied, and the findings have only a limited generalizibility, because of the very specific context. Nevertheless, if carefully designed, such a study can provide significant descriptive, explorative and even explanatory power (see, for instance, Yin 1989 and Biemans and Van der Meer 1994). The strength of the case

Exhibit 1.3 TC/TA MATRIX AS A TAXONOMY FRAMEWORK FOR MANAGEMENT STUDIES

		TC			examples
		s	m	l	
TA	s		X		reorganization, comakership
	m				industrial marketing
	l				consumer marketing
examples		case study	group interview	statistical survey	

TC = theory construction
TA = theory application
X = this study

s = small sample size
m = medium sample size
l = large sample size

study is its high resolution. Specific aspects of the organization, patient or situation can be analyzed in great detail. The sample size is medium if a small survey is conducted into a group of 10 to 50 organizations, or an interview group is selected for market research into individual buyer behaviour, or a patient group is followed in a double blind clinical trial. In general, only specialized statistical techniques, designed for use in case of weak statistical power can be applied. The generalizibility is larger than for case studies, but the resolution is less. The sample size is large, for instance, in a survey into consumer behaviour in the general population or a nation-wide epidemiological programme on cancer research. The statistical power is high, and even small differences in the study population can be traced. In a lot of cases the contextual situation is well-known and can therefore be generalized. By comparing several contextual situations, relevant characteristics can be defined more precisely. This makes it more accurate and easier to diagnose the applicability of a theory in a certain context. However, the level of resolution of specific aspects outside the statistical domain is low. In the trajectory of theory application the same separation can be made. Examples of small target samples are, for instance, a reorganization carried out in a company, the establishment

of a co-maker relationship between two companies, or a new drug being tested on a small number of healthy volunteers. Just as with the case study, the management consultant or physician will put much emphasis on the special context of the organization(s) or patient(s) involved. If the sample size is medium, the results from the interview group are used in industrial marketing aimed at a limited group of (industrial) customers, and the results of a case study into communication improvement in one project team are applied to all the project teams in the company. Examples of large scale application are, for instance, the use of the results of a statistical survey in consumer marketing.

Empirical studies conducted for their relevance in the domain of application will have to pass through the trajectories of theory construction and theory application. The succeeding steps in the process will roughly be, theory description, formulation of hypotheses, empirical testing, analysis of results and enrichment of the theoretical domain in the trajectory of theory construction, and diagnosis of context of application, design of the improved situation and implementation in the trajectory of theory application. Therefore, such a study has to appear in one (or more) position(s) in the TC/TA matrix. If not, the study design is incomplete. For instance, a large epidemiological study into the incidence of cancer may reveal that a specific form of cancer can be healed if discovered at an early stage. If so, a group of patients may benefit tremendously. In terms of the TC/TA matrix such a combination of a large population in the trajectory of theory construction and a small (or medium sized) target group in the trajectory of theory application can be referred to as TC_{large} / TA_{small} (TC_{large} / TA_{medium}) or, in short, ***LS (LM)***.

This study is an example of a TC_{medium} / TA_{small} or a ***MS*** combination (indicated by ***X*** in exhibit 1.3). The total study sample is large (271 respondents in 71 research units), but because of the focus on the contextual differences it has to be analyzed in the three strata, separately. Therefore, the sample size per stratum is medium (40 research units in universities, 17 in institutes and 14 in companies). It can therefore be looked at as a combination of several case studies of which the results can be applied, to some extent (in relation to the contextual differences), to the individual organization. Section 4 of this book aims at bridging the gap between theory construction and application. There is much included which divides successful biomedical research units and innovative pharmaceutical companies from their less successful competitors. A major objective of this book is to provide practical guidelines for those who

have to develop new product and research strategies, or have to devise new innovative structures. They are invited to select those which look potentially fruitful for application. The reader is urged to consider the specific context of their organization as a separate parameter in the selection process, by asking the question: 'Does this information apply to my type of organization?'

1.2 RESEARCH QUESTIONS AND MAIN HYPOTHESIS

The fundamental question behind this book is: 'Why are some research organizations more effective than others?' Is this only due to the quality of the supervisor and the individual researchers, or are there other aspects of management and organization determining the success or failure of a research laboratory? In fundamental research especially, the traditional idea of creating excellency by bringing some brilliant people together, providing them with the best facilities, and letting them work in a 'creative' - possibly remote - environment, leaving them alone and waiting for the break-through articles to come, is still very popular. An inspiring example of this concept of creating excellency by leaving alone is given by Maddox (1988) for the field of theoretical physics. According to Roussel et al. (1991) this strategy is still very common in industrial R&D too, especially in larger firms. As Hamel and Pralahad (1989) put it: ' ... *put a few bright people in a dark room, pour in some money and hope that something wonderful will happen.*' Of course, good researchers are a necessary condition for success, but is it the only thing that matters? In fact, there is a general feeling that it is not. Most people working in the field of research management, have experienced, or know from observation, that bringing some brilliant people together often ends up in an argument, rather than producing good results. All the 'How to manage, how to organize' literature starts from the underlying assumption that management and organization do make a difference between success and failure. Up to now, only very few studies are available to test this underlying assumption at the empirical evidence.

The specific questions which will tried to be answered in this study are: 'Can management control (control conducted by the research management) positively influence the performance and effectiveness of the research organization? And if so, to what extent can it enhance performance and effectiveness, and which instruments should it use to do so? For instance, tight control, with

strict planning of every step of the research process, or loose control, leaving the individual researcher room for manoeuvre? And what is the impact of the organizational setting on this relationship?' These general questions can be converted into the following three research questions:

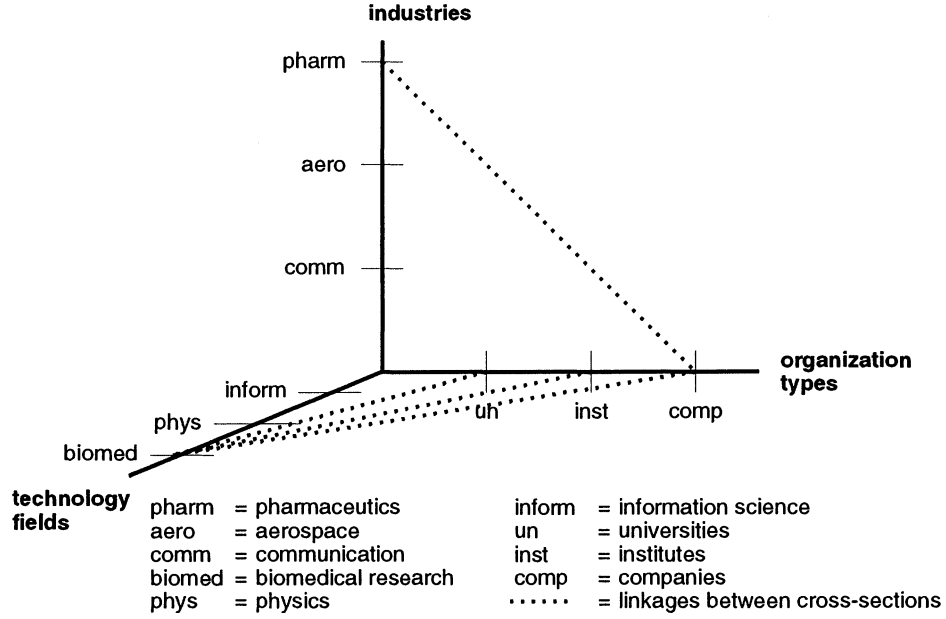
1 *Do certain aspects of management control relate to R&D performance and effectiveness in a positive way?*
2 *If so, to what extent do these aspects relate to R&D performance and effectiveness, and which instruments should be used to increase R&D performance and effectiveness?*
3 *What is the impact of the organizational setting (universities, institutes and company laboratories) on this relationship?*

In order to answer these questions, a comparative study has been conducted in biomedical research units in medical faculties and large health research institutes in the Netherlands. This was combined with a European survey in the main R&D laboratories of fourteen large and medium sized innovative pharmaceutical companies. The research management (the heads of the research units and their senior scientific staff in universities and institutes and the heads of the different research departments constituting together the R&D process in industry) was asked to judge a number of items regarding the management control situation in their organization in general and their unit in particular (i.e. regarding personnel policy, pace of administrative procedures, advancement of laboratory equipment). To fine-tune for the differences at the research unit level (for instance between preclinical, paraclinical and clinical research units), the contingencies (situation-dependent variables) defined by Mintzberg (1979) were used.

The first research question is the most profound. The fundamental idea behind this study is, that management control is essential for success in biomedical research and pharmaceutical innovation. This idea can be transformed into the following main hypothesis, underlying all the other hypotheses about management control in chapter 5.

Hypothesis 1
A number of management control variables will be judged more positively by the research management in the more-than-average performers than in the less-than-average performers.

Exhibit 1.4 PERPENDICULAR CROSS-SECTIONS OF TECHNOLOGY FIELDS, INDUSTRIES AND ORGANIZATION TYPES



Janszen (1994) states that successful management of R&D has to be in accordance with the specific characteristics of the R&D technologies (the hardware and software tools used in the R&D process), which may differ for various technology fields and industrial sectors. The research programme of the Management of Technology Department in Rotterdam concentrates on comparing management and organization across technology fields and industries. In this study, a perpendicular cross-section is taken. The study design is concerned with only one technology field (biomedical research) and one related industry (pharmaceutics), but within three different organizational settings (universities, institutes and company laboratories), in which the contextual variation in objectives and goals, environmental and task uncertainty may be regarded as maximized. Given this large variation in (sub-)contexts (see also § 1.1.2), it is clear that if consistency in the relationships of management control and effectiveness are found, this will enhance confidence in the generalizibility of the findings to related contexts in other technology fields. The integration of the findings of such perpendicular cross-sections ('context-comparisons', see exhibit 1.4) is expected to generate new and fruitful research in-

sights into the fast-growing field of the management of technology.

Generalizibility
If replication of the study design in the three strata yields consistent results, this will enhance confidence in the generalizibility of the findings.

1.3 OVERVIEW OF PREVIOUS STUDIES

A great deal of academic papers has been published on different aspects of the management and organization of research. A proportion of the literature covers the managerial aspects of industrial R&D (for a selected overview, see Tushman and Moore eds., 1988). These studies mainly concentrate on strategic and operational aspects, such as project selection and evaluation, project planning, human resources management and staffing, and the interfaces with marketing and production. Comparably less, but still considerable, attention has been paid to the managerial aspects of research in the academic world. A number of papers focus on strategic planning (e.g. Dits 1988 and Zeldenrust 1989), on academic research management in general (e.g. Mason 1979 and Latour 1987) and on individual laboratories (e.g. Latour and Woolgar 1979 and Knorr-Cetina 1981). Gilley et al. (1986) and Birnbaum (1988) concentrate on individual leadership, and Spangenberg (1989) on management and atmosphere in relation to performance and effectiveness. In the area of the research institutes, a qualitative study by Mayntz (1985), including interviews with thirteen research Directors of the Max Planck Institute in Germany, is worthwhile mentioning. However, all these empirical studies concentrate on only one type of research organization, leaving the contextual differences out of the scope of research. Although much attention has been paid to the possible similarities and differences from a theoretical point of view (for instance Marsh and Olson 1972), up to now only two large European surveys have been conducted that include universities, institutes and companies in the study population (Andrews ed., 1979 and Franklin, 1987). However, in these studies, the large contextual differences between technology fields and industries (such as electronics, aircraft and pharmaceutics), were mostly disregarded.

1.4 CLASSIFICATION OF RESEARCH AND DEVELOPMENT

In order to provide for standardized measures, the Organization for Economic Cooperation and Development (OECD) issued the *Frascati Manual*, in which generally accepted definitions for science and technology are given. In the *Frascati Manual*, research and experimental development (R&D) is defined as follows (OECD 1981): '*Creative work undertaken on a systematic basis in order to increase the stock of knowledge . . . and the use of this stock of knowledge to devise . . . new materials, products, or devices . . . new processes, systems or services, or ... improving substantially those already produced or installed.*'

The OECD distinguishes between three types of R&D activities: basic research, applied research and experimental development. Although universities, institutes and companies all span activities covering basic and applied research as well as experimental development, generally speaking the main objective of universities is to perform basic research, that of institutes is to perform applied research, and that of companies is to perform applied research and experimental development. Basic research, applied research and experimental development are first described as performed in universities, institutes and companies, respectively. Thereafter, they are discussed as part of the industrial innovative process.

'*Basic (fundamental) research is defined as original investigation undertaken in order to gain new scientific and/or technical knowledge and understanding*' (Freeman 1982). A number of aspects of basic research can best be compared with top sports. Whereas in top sports the boundaries of the human physical potential are tested and shifted centimetre by centimetre, in basic research it is the boundaries of human knowledge and understanding that are shifted. Top scientists can be obsessed by their work and there is strong international competition, in which scientific quality is the ultimate criterion. Just as top sports people strive to eternal fame by winning the Olympic Games, so basic scientists hope to win the Nobel price. Other aspects of basic research have more in common with art. Namely, if is looked upon the talented scientist as someone who opens the window to new insights by combining existing and new scientific knowledge in an original and creative way. Basic research is often related to curiosity and the urge to discover and elucidate new and unconceived phenomena. Researchers are led by their own ideas and scientific interests or those of their direct supervisor(s). Basic research is also con-

nected with serendipidity. This means that important discoveries are often made as accidental side-products of research directed towards other subjects (*'to look for a needle in a haystack and to find the farmer's daughter'*). A famous example is the accidental discovery of penicillin by Fleming[1].

Although basic research sometimes does lead to the formulation of a new theory or even a new scientific paradigm (Kuhn, 1970), the everyday practice of experimental science is one of laborious searching for small pieces of empirical evidence using standard experimental and methodological methods. As soon as research results are obtained, they are published in specialist journals and presented at scientific congresses. Here the scientific debate takes place about their reliability and importance, and if they stand up to this critical evaluation, they are incorporated into the body of scientific knowledge.

'Applied research is undertaken to gain new scientific and/or technical knowledge, but it is directed primarily towards a specific practical aim or objective' (Freeman 1982). It is often difficult to draw the line between basic and applied research. Janszen (1994) states that, although basic and applied research use the same methodologies and heuristics, means and ends are reversed. In basic research a natural process is isolated from the system and analyzed by studying the input-output relations, by varying the relevant parameters in a systematic way under controlled conditions. For instance, starting from the observation that aspirin slows down the blood clotting process, and by systematically changing the relevant parameters, it was found that prostaglandins play an essential role in the process. In applied research this knowledge is used to synthesize aspirin-like chemical structures which can modify the blood clotting process in the desired manner. Essentially, in basic research the (physical, chemical or biological) system is disturbed and the output is studied

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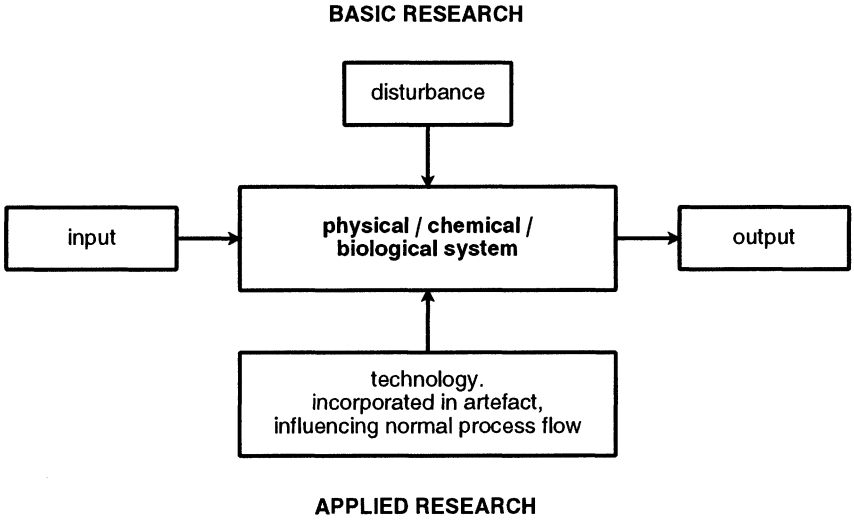
[1] In 1928 Fleming was cultivating cultures of Staphylococcus (a bacterial genus, including numerous species which can cause infections). By accident one of his cultures was infected by a fungus of the genus Penicillium. Around the fungus colony the cultures of Staphylococcus were diluted. It is the genius of Fleming that he did not ignore this unexpected phenomenon. He rightly concluded that the fungus had produced an antibacterial substance. He isolated a small amount and called it penicillin. In the Second World War, Chain and Florey continued the experiments, by order of Churchill, to find a drug which would protect the British army against gonorrhoea. They found the process to produce penicillin on an industrial scale. In 1945, Fleming, Chain and Florey together received the Nobel price for Physiology and Medicine.

systematically, while in applied research technology (basic knowledge) is incorporated into an artifact (e.g. a biological or chemical compound), consciously influencing the normal process. Exhibit 1.5 shows the difference between basic and applied research schematically.

Exhibit 1.5 BASIC VERSUS APPLIED RESEARCH



source: Janszen 1994

The Dutch Research Policy Council (RAWB 1983) gives the example of the study of the genome of pathogenic viruses. This can be studied from a fundamental standpoint, for instance as a model for certain life processes, but also from an applied angle, as the genetic basis for pathogenesis. Therefore, in recent years *application-oriented research* (also called mission-oriented research, Van Dijk et al. 1993) has also been distinguished. Application-oriented research includes basic research performed in areas of public or economic interest with a middle-term or long-term potential for application (such as biotechnology). If a possibility for application arises, further research is carried out in research institutes and company laboratories. Applied research in universities and institutes is mostly carried out on a contractual basis for governmental agencies or industry. In recent years *contact research* (van Dijk et al. 1993) has also been emerging. In contact research an industrial or governmental con-

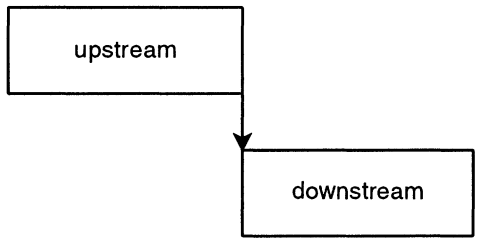
tractor is not so much interested in the possibility of the direct application of the research results, but rather uses a research group as a sound-board, or a sensor and pilot tester of new scientific and technical developments. Whereas basic and applied research concentrate on gaining abstract knowledge and understanding, experimental development (or engineering) is concerned with the activities needed to progress from abstract ideas to (industrial) products and processes. '*Experimental development is the use of existing scientific and technical knowledge to produce new or substantially improved materials, devices, systems or services*' (Freeman 1982).

1.5 INDUSTRIAL INNOVATION

Basic research, applied research and experimental development can also be classified as successive activities in industrial or technological innovation. This process can be considered as a set of activities which transform client orders, market demands and technological advancements into product and process designs (De Weerd-Nederhof et al. eds. 1994, pg. 12). It includes R&D and the succeeding production, marketing and sales activities needed for market introduction. These activities are carried out as part of the R&D function (or corporate R&D, Betz 1987). The R&D function is therefore more broadly defined than the sum of the activities of the R&D laboratories, because marketing and production are also involved.

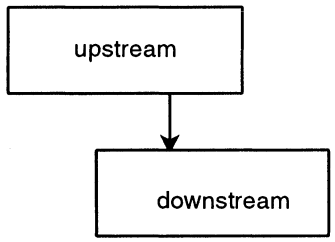
Industrial innovation starts with strategic project choices, based upon the market demand (market or demand pull), or the technological possibilities (technology push). After these choices have been made the research phase starts. This can be basic research in the research laboratories of large, often multinational, companies, or in small high-tech firms (for instance in biotechnology), or cont(r)act research carried out in conjunction with research groups in universities and institutes. Applied research is then conducted, leading to patents for products or processes, or ideas for prototypes. Subsequently, experimental development will start. Experimental development includes activities necessary to produce the final product, for instance its design (in the case of audio equipment, cars etc.), safety requirements and extra possibilities for application. At the end of this stage, the production process must be designed. Pilot plants have to be built, existing production processes must be scaled up or redesigned for the production of the new products etc. Most of the R&D

Exhibit 1.6 FROM A SEQUENTIAL TO A CONCURRENT PROCESS



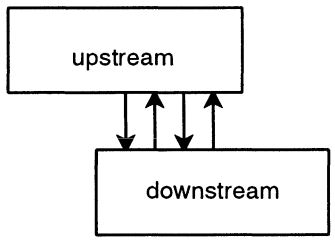
the downstream activity begins only after receiving finalized information upon completion of the upstream activity

sequential process



the coupling between upstream and downstream activities is removed resulting in a parallel process; limited communication from upstream to downstream activities

parallel process



the upstream and downstream activities are concurrent requiring frequent mutual information exchange in project teams

concurrent process

source: after Krishnan et al. 1994

budget is spent on experimental development. Therefore, the experimental development activities are increasingly conducted in a parallel and yet integrated way.

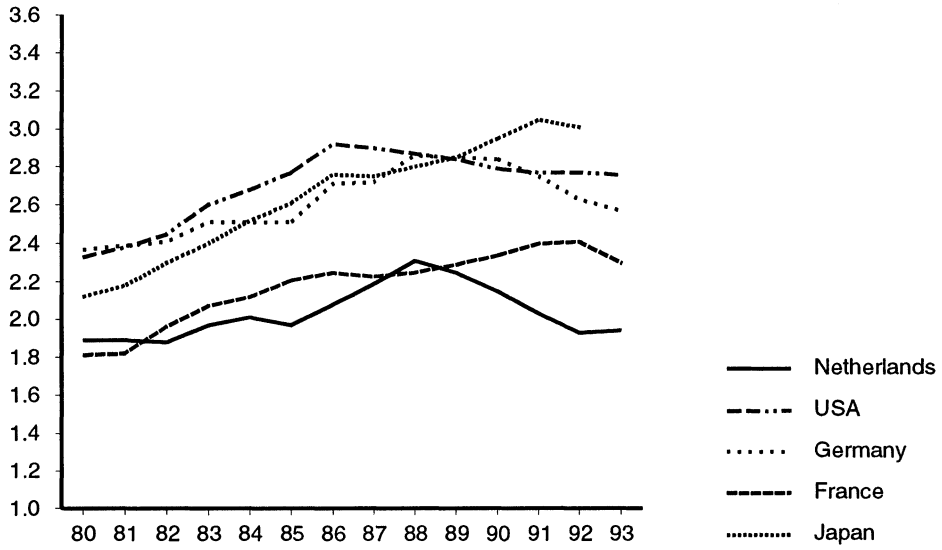
Formerly, the research laboratories working on different parts of the R&D process were sequentially dependent in a chain of R&D activities. They used the results of an upstream department, transformed it, and passed it through to a downstream department. The communication between the different departments was limited. When intensified competition forced the companies to accelerate the R&D process, the linear sequence was gradually replaced by parallel development. Now downstream activities started before having received finalized information upon completion of upstream R&D activities. However, because the communication between upstream and downstream departments did not intensify, integration problems arose. Allen (1977) found a high level of association between the flow of information between scientists in different phases of the R&D process and the performance of an industrial laboratory. Following these findings, in recent years, companies have greatly intensified the communication across the R&D process and with marketing and production (lateral and cross-functional communication), leading to concurrent development (see exhibit 1.6). In accordance with Allen's findings, both upstream and downstream activities turn out to benefit from the improved communication and integration (see for example Clark and Fujimoto 1991 and Millson et al. 1992). A functional hierarchy does not support lateral and cross-functional communication. In order to achieve that project goals can take precedence over functional goals many companies have installed lateral and cross-functional project teams, which draw members from throughout the organization (see for example Donellon 1993, and Henke et al. 1993).

1.6 RESEARCH AND DEVELOPMENT IN THE NETHERLANDS

In order to give an impression of the division of labour and resources over universities, institutes and companies, some general facts and figures about Dutch R&D will be presented, before will be turned to biomedical research in particular.

Exhibit 1.7 shows that in contrast to most industrial nations, Dutch R&D expenditure has declined in the last six years, from 2.3% in 1988 to 1.9% of the Gross Domestic Product in 1993, with this latter percentage being similar to the spending in the early 1980s. Since then the difference with the leader, Japan (3% in 1992), has become considerable. Even a fast growing 'Asian tiger', such as South Korea, spends a higher percentage on R&D (2%). This

Exhibit 1.7 TOTAL R&D EXPENDITURE AS PERCENTAGE OF GROSS DOMESTIC PRODUCT IN FIVE INDUSTRIAL COUNTRIES FROM 1980 TO 1993



source: OECD in Merit 1994 and Van Dijk et al. 1993

decline in the R&D expenditure is partly due to budget retrenchments by the Dutch government. However, 55% of Dutch R&D is paid for by industry, and dominated by the five Dutch multinationals: Philips, Shell, Unilever, AKZO and DSM[1]. Therefore, the recent budget retrenchments by Philips negatively influenced the Dutch R&D expenditure. Another factor which has caused part of the decrease of the R&D expenditure, is the relative decline in the salary level of Dutch scientists compared to those in other industrial countries. Whereas Dutch scientists were the most expensive in Europe at the start of the 1980s, nowadays this position has been taken by France and Italy (Minne 1992). From the perspective of the international competitive position of Dutch researchers, this can even be regarded as advantageous. Unfortunately, even if it is adjusted to take account of these two factors, the Dutch R&D expenditure is still lower than in most other industrial countries.

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1 Another 30% is conducted by companies with more than 1,000 workers. The remaining 15% is carried out in small and medium-sized companies (Van Dijk et al. 1993).

According to the Central Bureau of Statistics (Van Dijk et al. 1993) about 70,000 scientists and engineers are working in the Netherlands. About one quarter work in universities, another quarter in institutes and half of them in company laboratories. In total 54% of the R&D expenditure is spent in industry, compared to 22% in research institutes and 20% in universities. The R&D in industry is the least labour intensive. Whereas about 60% of the total expenditure in universities and institutes is spent on personnel, this figure is only 47% in companies. Consequently, the capital costs per scientist are clearly higher in industry (US$ 95,000 versus US$ 67,000). In the industrial R&D laboratories, the percentage of scientists out of the total R&D staff is much lower (22%) than in universities and institutes (36% and 38%, respectively). This is probably due to the fact that in development less scientists are needed than in basic and applied research.

The following figures show that not only in universities, but also in research institutes and industry, a considerable amount of basic research is carried out. In 1986 20% of the R&D in industrial laboratories was directed towards basic research, 25% to applied research and 55% to development. In research institutes, these percentage were 28% for basic research, 53% for applied research and 19% for experimental development. The expenditure in industrial laboratories was higher than in other OECD countries (3% to 5%), due to the fierce research efforts of the five Dutch multinationals. If their efforts were excluded, the percentage of basic research dropped to around 8% (Ministry of Economic Affairs 1990).

1.7 BIOMEDICAL RESEARCH AND PHARMACEUTICAL INNOVATION

Biomedical research has been chosen as the domain of the study, because:

- In all three strata, universities, institutes and companies, a large study population is available.
- It provides a good example of research in an applicational context.
- Ethical (prescription) drug pharmaceutics is the most technology driven of all industries (see § 1.7.3).

Biomedical research is defined in accordance with the Dutch Science Advisory Board (RAWB 1983) as concerned with medical biological studies, for in-

stance into cell and tissue cultures and animals. Consequently, the biological object, and not the research method used, accounts for the classification criterion. The link with patient care is much looser than in clinical medicine and the scientific interest in the biochemical and physiological background of illnesses prevails. Biomedical research in pharmaceutical companies is concerned with the study of biological and chemical compounds meant for therapeutic use. The fast progress in biomedical research has an enormous impact on medical care. The increased knowledge of the biochemical and physiological background of diseases has enabled physicians to provide the patient with a large spectrum of more effective drugs. Increasingly, research efforts are being put into more complex therapeutic areas for which no easy solution is forthcoming e.g. cancer, arthritis and multiple sclerosis. These terrains of research require a degree of sophistication in methodology and scientific knowledge that is unprecedented in medical history. With the growing impact of biomedical research, the laboratories have increased in number and size. However, the governmental budget retrenchments, and the political debate to restrict the medical costs in Europe and the United States, combined with the growing consciousness of the limitations of technological solutions in medical care, has put clear limitations on the further growth of biomedical research.

In the light of the discussions about the ever increasing costs of medical care, it is important to note that the total medical research costs (biomedical and clinical research) are relatively low. In 1994 the total cost of medical research (biomedical, paraclinical and clinical research) in medical faculties, academic hospitals and health research institutes accounted for only 1% to 2% of the total medical costs (Ministry of Health, VWS 1993). Contrary to R&D in general, most medical research is paid for by the Dutch government. About US$ 300 million is directly or indirectly (via the Netherlands Organization for Scientific Research, NWO) financed by the Dutch government, compared to US$ 50 million funded by charitable trusts for research in specific therapeutic areas (cancer, heart or kidney diseases etc.), and another US$ 50 million by funding based on public health insurance (the Counsel for Medical Research, RGO 1993 and 1994). In industry, US$ 230 million is spent on R&D, US$ 70 million on research and US$ 160 million on development. Roughly speaking US$ 330 million is spent on research conducted in medical faculties and (academic) hospitals, US$ 170 million in Health Research Institutes and only US$ 150 million in industry (Ministry for Economic Affairs, EZ 1993).

In 1987 the relative share of biomedical publications compared to other disci-

plines, amounted to 15% above the world average. The relative share of Dutch biomedical publications in the top 10% of the most cited papers equals the world average (figures from 1975 until 1982). In recent years many biomedical researchers have become 'cosmopolitans' (Gouldner 1957). Whereas in 1973 around 10% of the biomedical publications were based on international cooperation, as is indicated by foreign co-authorship, this percentage had risen to 20% in 1987. Only in traditionally internationally oriented sciences, such as astronomy, physical geophysics and mathematics, is the percentage of foreign co-authorship higher (Heeringen en Langendorf 1988).

1.7.1 Universities

Thirteen universities[1] are situated in the Netherlands, which together educate about 165,000 students. The universities can be classified as seven traditional and six specialized universities. The traditional universities teach the whole spectrum of research and the specialized ones concentrate on a limited number of research fields (for instance, agriculture, economics or technology). There are ten state universities and three (two traditional and one specialized) Christian universities. For a good understanding of the Dutch situation it must be remembered that the large variation in quality, funding and orientation which can be found in the USA does not exist in Holland. All Dutch universities are publicly financed, operate under the same conditions, and have, within boundaries, the same access to funding.

In Dutch universities, the scientific staff spends in total nearly 14,000 full-time equivalents (ftes) on research. A substantial portion of this research, more than 3,000 ftes, is carried out in medical research. In this study, only those universities in which biomedical research is carried out are analyzed: the seven traditional and one specialized university. In these universities biomedical research is carried out in medical faculties and/or academic hospitals. At the research unit level the research is carried out in preclinical, paraclinical and clinical units. In preclinical units (such as medical cell biology and medical physiology) no direct contact with patients exists. Often the research is

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[1] In addition to these 13 universities an Open University focusing on distance learning, seven theological and one private university are also situated in the Netherlands.

carried out by biologists and biochemists. In paraclinical units (advising and diagnostic testing, e.g. anthropogenetics and clinical immunology) the relationship with patients is of an advisory nature. Consequently, more physicians are working here than in preclinical units. In clinical units (such as clinical endocrinology and clinical neurology) clinical practice is the predominant task.

The percentage of university research that is financed by the Dutch government has decreased over the years. Whereas 87% of Dutch medical university research was publicly financed in 1977, this percentage gradually decreased to about 60% in 1992 (Van Dijk et al. 1993). It must be considered, however, that the 40% external funding also includes a number of research activities which are indirectly financed by the Dutch government, such as research grants and contracts conferred by governmental agencies and the European Union (EU). At the end of the 1980s the Dutch government tried to secure high-standard research from budget retrenchments by concentrating it in separate Graduate (Research) Schools. At the moment about 100 Graduate Schools in different scientific areas are found. Two of those are specifically oriented towards drug research (GUIDE, the Groningen Utrecht Institute for Drug Exploration and the Leiden/Amsterdam Center for Drug Research). In these Schools, research departments from different universities and institutes work together, under direct responsibility of their respective university boards (Advisory Board for Science and Technology Policy, AWT 1994, the former Dutch Science Advisory Board, RAWB). Another development in the 1980s was the foundation of special Expertise Centres, expensive research facilities, such as a Centre for Computer Assisted Organic Synthesis/Computer Assisted Molecular Modelling (CAOS/CAMM) or a Centre for Laboratory Animals, which are financed for a limited period of time by the Dutch Government. After this period the Expertise centres should have generated enough contract research to become independent. It must be feared that part of these institutions will show only limited survival capacity, because they are governmental initiatives, with only weak foundation in the academic world. Until recently most of the Expertise Centres have not generated enough external funding to become self-supporting (van Dijk 1993).

1.7.2 Institutes

In the course of this century a number of research institutes have been found-

ed by the Dutch government or by governmental and private agencies. These institutes have as their objective, to conduct research into specific areas of industrial or social significance. This can range from basic research in institutes closely linked to universities (para-university institutes) to contract research for government and industry.

There are 22 para-university institutes in the Netherlands, with a total budget of about US$ 100 million (Van Dijk et al. 1993). They are closely related to universities:

- they are often situated on the university campus,
- university professors are appointed to the institute,
- many graduate and PhD students work in these institutes.

Until recently some of the para-university institutes were administered by the Ministry of Education and Sciences. These days, all the para-university institutes are administered by either the Netherlands Organization for Scientific Research (NWO) or the Royal Dutch Academy of Science (KNAW). Two para-university institutes participated in this study, both falling under the governance of the Royal Dutch Academy of Science, and with a research budget of US$ 2.5 to US$ 3 million each.

There are 7 research institutes working on a not-for-profit basis in the Netherlands, with a total budget of more than US$ 700 million in 1992 (van Dijk et al. 1993). Although it is not the main objective of a not-for-profit organization to make profit, it has to prove itself on the market by gaining earnings out of contracting activities etc. This is in contrast to non-profit organizations, such as hospitals and schools (Hofstede, 1981). Most of these not-for-profit institutions work in fields of expertise which require large investments, such as a nuclear power reactor, a wind tunnel or a large water basin. The main objectives of these institutes are to maintain an infrastructure in science and technology, to increase the innovative ability, and to improve the international competitive position of the Dutch industry. The tasks of these institutes range from agricultural research to research for the aviation and spacecraft industry. One not-for-profit institute is examined, with a research budget of about US$ 30 million (RGO 1994).

There are 18 research institutes which are part of different government ministries. Although they are involved in contract research, their main task is to

prepare and support departmental policy. Because of their close links with the ministries, their independence is sometimes questioned (AWT 1991). Because it is difficult to obtain separate data the one institute which is involved in biomedical research, could not be examined in this study. In health care especially, there are independent research institutes working in certain therapeutic areas, such as cancer, which are (partly) dependent on private funding, or which rely on the distribution of and control over vital medical products, such as blood. The two medical institutes are analyzed, with a research budget of US$ 12 and US$ 22 million, respectively (RGO 1994).

1.7.3 Companies

Because the pharmaceutical laboratories in this study are situated in several countries in the EU, it would not be relevant to discuss the Dutch situation separately. Therefore, in this paragraph a global overview is given of industrial pharmaceutical R&D.

The pharmaceutical industry is exceptionally technology driven. It is very reliant on the continuous flow of new pharmaceutical products. The profitability, and, ultimately, the long-term survival of the firm depends on the maintenance of a competitive position. In turn, the competitive position is strongly influenced by the rate of innovation. High barriers for entrance of new competitors (Porter, 1985) are raised by a constant stream of new drugs, by improvement of existing drugs, and by their use for an expanded range of symptoms. A recent study by Capron (1994) comparing 135 companies in 10 high-technology industries, under which 22 branded ethical drug firms, indicates that the branded ethical drug industry attains both the highest short-term and long-term return on R&D investment. He concludes that the competitiveness of pharmaceutical enterprises, both in market share and demand from customers, depends heavily on their technological performance.

Patents are a highly significant form of resources control, and thus a very important source of market power for the companies holding them, because the active compounds of the drugs are often easy to imitate by competitors (except, for instance, for synthetic hormones). For the same reason, manufacturing equipment can often be used for the production of many different drugs. In this sense, the process aspects of the drug industry shares many facets with

non-related industries relying on the inclusion of active substances[1], such as toiletries and cosmetics (Taggart, 1993). Only the differentiation in dosage form, together with the stringent quality requirements regarding purity and lack of contamination, make the process aspects more complicated. Nevertheless, it is not surprising that pharmaceutical companies often diversify into these industries.

The ethical drugs industry can be characterized by the following features. A relatively small number of large pharmaceutical companies is surrounded by a multitude of small sellers. In 1986 only 270 larger pharmaceutical companies could be counted out of 2,757 firms. (Chew et al. in Taggart 1993). Gross (1983) estimates the number of really innovative pharmaceutical firms not higher than 30 to 35. Until recently, the ethical drug market was highly segmented. In 1988 the top-ranked company Merck & Co. had a market share of just 3.9%, and 76% of the firms had a market share below 1.9% (EZ 1993). In recent years a clear tendency towards concentration has been observed. Thirtyseven percent of the world market today is held by the top ten firms against 24.9% in 1988. It is expected that the top ten firms will control 60% to 70% of the pharmaceutical market before the end of this century. Based on 1994 figures, but assuming the completion of recently announced mergers, Glaxo Wellcome is market leader with 6%, followed by Merck & Co. with 4.9%, Hoechst/Marion Merrell with 4.7% and American Home Products with 3.8%. The precise logic of mergers and acquisitions varies from case to case. Sometimes the overriding consideration is cost rationalization, as with the mounting take-over of Wellcome Burroughs by Glaxo. Other considerations are the spreading of the ever increasing R&D costs over a larger basis, as in Roche Holding's purchase of Syntex. For other companies the desire is to step into a certain geographic market, such as Hoechst's planned purchase of Marion Merrell Dow, or to enhance a key technology, as with Ciba Geigy's stake in the biotechnological company Chiron (Tracey, 1995[2]). Pharmaceutical companies also try to lower the level of competition by joint ventures (for instance DuPont-Merck) and strategic alliances. The fierce competition has caused that the branded ethical drug companies are increasingly stepping into the markets of generic drugs, over-the-counter drugs, and diagnostics, as well.

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1 (1) compounding and dispersion of ingredients; (2) granulation and coating; (3) tableting or encapsulation; and finally (4) the packaging of the tablets or capsules

2 *Reuter*, March 20 1995.

There is a clear tendency in the whole Healthcare system to shorten the line from producer to the final consumer, for instance drug distributors are increasingly trying to bypass the pharmacies. In line with this tendency, pharmaceutical companies try to get hold of the distribution system by building up 'mega-corporations' (Jones, 1995[1]), focusing both on pharmaceutical products and wider aspects of Healthcare. The recent take-overs of the drug distributors and drug purchasers for their managed-care customers, Medco Containment Services and Diversified Pharmaceutical Services (DPS) by Merck & Co. and SmithKline Beecham are examples of this tendency. SmithKline Beecham has also announced a strategic alliance with United HealthCare (the former DPS's parent), which owns a chain of American Health Management Organizations (HMOs), firms that supply comprehensive health services to patients for a flat fee. United HealthCare's database should help SmithKline Beecham to study the medical effects and the cost effectiveness of its drugs. Pharmaceutical companies are also preparing to promote and market their drugs directly to the patients by setting up health education campaigns and health information telephone lines, because direct promotion of drugs is often forbidden. Genentech, for instance, has set up a foundation for cystic-fibrosis patients to get information about their disease in the USA[1].

The customer function of the pharmaceutical industries can be regarded as divided into three different entities: the consuming patient, the prescribing physician, and the paying agency. For this reason a huge and differentiated marketing effort is needed, bringing the brand name to the attention of the prescribing physician, convincing the patient of the quality of the product and negotiating with the health insurance companies and governmental agencies over the extent of the reimbursement. There is an indication that the authority of the prescribing physician is diminishing. Governmental regulatory agencies, insurance companies and HMOs are increasingly taking over control of prescription. The concentration of bargaining power in the hands of the insurance companies (in the Netherlands in the KLOZ) and the plans for a profound revision of the system of reimbursement of medical costs are important threats for the pharmaceutical industry (Snier 1995).

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1 *The Economist*, May 7 1994, p. 70-71 and *Time*, May 16 1994, p. 51.

1.8 CONCLUDING REMARKS

This chapter has provided the research methodology, the research questions and a broad overview at the study domain. Basic research, applied research and experimental development have been described as performed in universities, institutes and company laboratories, and as parts of the industrial innovative process. A factual overview of Dutch R&D in general, and biomedical research in universities and research institutes in particular, has been combined with a global overview at industrial pharmaceutical R&D. In the next chapter the structure and behaviour of research organizations will be described, using the concepts of systems theory.

CHAPTER 2

STRUCTURE, BEHAVIOUR AND CONTROL IN RESEARCH ORGANIZATIONS

This chapter concentrates on structure, behaviour and control in universities, institutes and companies. It starts with a short outline of the concepts of systems theory, which underly this study. The contingency theory and Mintzberg's typology of organizations, which are based on these concepts, are used to describe the structure and behaviour of the organizations. Following this, the systems theory of control is introduced, based on the paradigm of control as defined by De Leeuw (1990). In the succeeding paragraph a description of the three strata, universities, institutes and companies is given. This chapter ends with a general overview of the relative strengths of the different system variables in the strata, based on the theoretical considerations presented.

2.1 DESCRIPTION OF SYSTEMS

The starting-point of the systems theory is that reality can be viewed as a (multitude of) system(s). De Leeuw (1990) describes a system as a collection of parts (entities, elements, or objects) with certain attributes, and the relations between them. An entity may be a person, a place, a thing, or an event. A system can refer to different aggregation levels in organizations, such as a department, a project team, a research institute, or a network of cooperating universities, institutes and companies. As a consequence, the entities in a system can be diverse: e.g. the individual researchers in a university, staff members from R&D, marketing and production in an industrial project team, or the different research departments in an institute. A system can be divided into part-systems: sub-systems, aspect systems, and phase systems. Sub-systems are taken from the original system by concentrating on a sub-set of the elements. For instance, if a university is defined as the system, a university department can be a sub-system. Aspect systems concentrate on a sub-set of the relations, for instance, the information flow or the power relations between different university departments. A phase system is studied continuously or

periodically over a longer period of time, for instance for purposes of long range planning.

2.1.1 Systems and their Environment

Anything external to the system is considered to be part of the environment. Depending on the level of controllability from within the organization, the environment can be divided into the remote (or general) and the operational (or task) environment (Pearce and Robinson 1988, and Daft 1992). The remote environment consists of the economic, political, social and technological factors which affect all organizations, although not in the same way or to the same extent. Changes in the remote environment can be anticipated, but they cannot be controlled by any of the organizations individually. The operational environment, on the contrary, consists of those factors which interact directly with the organization and have a direct impact on the organization's ability to achieve its goals. Examples are suppliers, customers, and competitors in industry, or research groups in universities and institutes, competing for scientific credibility in the same research field. In recent decades, especially, universities, institutes and companies have been confronted with ever faster changing environmental conditions to which they must (reactively or proactively) respond. For instance, pharmaceutical companies are facing pervasive international competition and increasing regulatory pressure to improve the therapeutic efficacy and safety of drugs. Universities and institutes are confronted with budget retrenchments, a decreasing number of students because of demographic changes, and the pressure to improve market orientation.

Systems are separated from the environment by boundaries (see exhibit 2.3). In order to continue to adapt and to survive, organizations must be able to import people, raw materials, and information through their boundaries from the environment (inputs), and in exchange direct their finished products, services, or information back to the environment (outputs). Controlling the boundary conditions plays a very important role in systems thinking. As Koehler (in Emery, 1972, p. 9) states: '*the primary task of management is to manage the boundary conditions of the enterprise.*' System boundaries exist on a continuum from extremely permeable to almost impermeable. Open systems have permeable boundaries, interactions of many kinds with the environment occur. Open systems are dynamic, parts of the system constantly change as they

interact with themselves and with the environment, and the system evolves over time. Systems researchers use the following metaphor to reflect the dynamic character of these systems: '*It is like playing a game in which every move changes the rules*' (Birnbaum 1988, p. 35)[1]. Most research departments in universities, institutes and companies can be considered as relatively open systems. There is a continuous flow of information, both within the department and to and from the environment. For instance, PhD students present their latest results in frequent research meetings, while senior and junior researchers together try to integrate this knowledge into (new) models and theories. At international congresses and workshops, the researchers share their insights and views with the scientific community, generating new ideas for future research. At the opposite end of the continuum closed systems are found. For instance, a pharmaceutical company will try to screen off the information about a promising NCE (New Chemical Entity), for which a patent has not been submitted, yet, in order to avoid putting a competitor on the trail. The same situation can occur if a real scientific break-through is made in a highly competitive research field in universities. In the time span that it takes for the additional experiments to be conducted to get the conclusive evidence for the claim, the external communication will be reduced.

Box 2.1

Screening off strategic scientific information is sometimes difficult, even in industry, as can be shown by the following example. In 1973 Dr J. Black, Nobel Prize winner and distinguished researcher at the pharmaceutical company SmithKline & French, held a lecture for a scientific audience in Hatfield Polytechnic. In this lecture Black revealed that the research of his group had shown that histamine was a physiological controller of acid secretion, which at that time was thought to induce ulcers. A chemical compound which would inhibit histamine would thereby also block the development of ulcers. Two researchers from Glaxo, who were in the audience, now knew what to look for. They did not win the race, and in 1976 SmithKline & French launched the anti-ulcer drug Tagamet. However, guided by

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[1] By using this metaphor, the open systems theory comes close to chaos theories. These are mathematical theories about system states depending on nonlinear feedback loops or other recurrent behaviour patterns. Under certain conditions, these patterns may lead to a stable system state. Systems may circle between two or more definite system states, or even between an infinite number of system states, for more about chaotic behaviour, see Peitgen and Richter, 1986.

the information from Black, in the same year Glaxo Research discovered raditidine, the active substance of their anti-ulcer drug. In 1981 it was launched under the name Zantac. By now, Zantac has become by far the world's best selling drug, while Tagamet has dropped back (Lynn 1991).

2.1.2 Tight versus Loose Coupling

In order to understand how the various elements and sub-systems within a system interact, it must be considered how they are connected or coupled. Coupling can range from tight to loose. Conceptually, they can be differentiated by two criteria: the extent to which sub-systems have shared variables between them and the extent to which these variables are important to the sub-systems. If the sub-systems have many components in common, and if those elements are among the most important, the sub-systems are likely to be relatively tightly coupled, and changes in the one should produce clear changes in the other, the relation is deterministic (Ashby, 1956). Examples of relatively tight coupling between sub-systems can be found in industry. The R&D process can be viewed as a continuous flow of learning loops in which the information obtained by one department can be used by the next department in a concurrent way (see chapter 1). For instance, the information obtained by a pharmaceutical discovery department about a new NCE will serve as the input for a pharmaceutical development department. Clinical knowledge about the possible side-effects of new drugs obtained by clinical development can serve as input for marketing and sales, whereas the information obtained through the marketing process about population trends and therapeutic demands may serve as an input for R&D.

The relations in a loosely coupled system are uncertain, there are discontinuities in the way the sub-systems are connected. Compared to industry, research departments in universities are loosely coupled. Most researchers have only a vague knowledge about the work of their colleagues in neighbouring departments. Loose coupling has been attacked as merely a slick way to describe waste, inefficiency, or indecisive leadership and as a convenient rationale for the crawling pace of organizational change. It has been argued that if coupling were tighter, the organizations would achieve predictability, would better control their processes and by doing so, would better achieve their goals (Lutz

1982). Loosely coupled systems do have additional costs, as sub-systems may be uncoordinated and in conflict with each other. Furthermore, loose coupling makes it difficult to 'repair' defective sub-systems, and to use management processes to effect change. But loose coupling also has significant benefits. Having partially independent and specialized organizational elements increases the adaptive ability to changing environmental demands in the organization as a whole. It makes it possible to seal off ineffective departments, localizing their failures. For instance, university departments whose research fields have become obsolete, and in which student interest has diminished over time, can be decreased in size, whereas adjacent departments in new research fields with substantial student interest (like immunology or molecular biology) can grow rapidly. To withstand environmental disturbances, Galbraith (1973) suggests introducing 'slack' into the strict organization.

2.2 CONTINGENCIES

The basic idea of the contingency theory is that the internal structure of an organization is mainly dependent (contingent) on the following dimensions (De Leeuw, 1990):

- the environment,
- the technology or task,
- the strategy and goals.

The first two dimensions are thought to pose the greatest degree of uncertainty for an organization. These uncertainties may concern the choice of the goals to be pursued, the alternative actions to achieve these goals, and the predictability of the outcomes. Burns and Stalker (1961) observed that organizations adapt to their tasks and environment, which may be more stable or more turbulent. Some organizations may live in a rather homogeneous world, while others are constantly confronted with new and unexpected problems. Resources may be scarce, scattered and difficult to grasp for some organizations, or clustered and easy to obtain for others. A more turbulent environment requires a system with higher adaptive ability. So a more loosely coupled system would probably give the best results in this situation. While, in contrast, in a stable environment a more tightly coupled system, with a high level of control, would probably perform better. In the terms of Burns and

Stalker (1961): unpredictable environments, that require innovation-oriented production, need organic organizations, while stable markets, requiring efficient production of standard products, need mechanistic forms of organization. In the classical contingency theory, organizations merely react on disturbances in the environment, leaving no room for proactive management[1]. Child (1973, 1974) meets this problem by introducing a degree of choice regarding the environment, technology and internal structure (constrained choice).

In order to be effective also sub-systems within the organization should adapt to the characteristics of their specific sub-environment (Lawrence and Lorsch 1967). That is, simple sub-environments call for simple uniform internal processes and structures, while complex sub-environments call for complex processes and structures. This may not only lead to a differentiation in tasks between sub-systems, but also to a differentiation in goals. With the introduction of the sub-system idea, two new variables are introduced: differentiation in the organization as a whole, and integration which is needed as a result of this differentiation. Woodward (1965) found that organizational structure is also dependent on the production technology, and that the effectiveness of the organization depends on the 'goodness of fit'[2] between technology and structure, which in a broader sense is depicted as the technological partsystem. Understanding the technological partsystem is critical, because it describes the characteristic way in which inputs are transformed into outputs. It can differ in terms of complexity (the number of elements an organization must simultaneously deal with), uncertainty or unpredictability (the uniformity of elements on which work is carried out and the ability to predict the outcomes of work), and the interdependency (whether work processes are interrelated). Daft (1992) integrates these findings in the following contingency model for environmental uncertainty in relation to organizational structure

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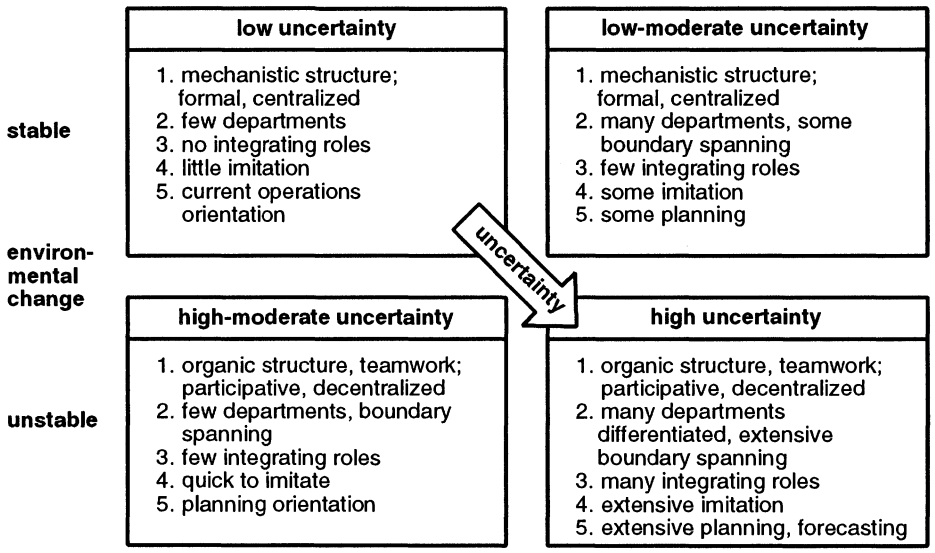
1 Maturana and Varela (1984) use the term autopoiesis to refer to the fact that organisms proactively select and create their own environment. In analogy to autopoiesis in organisms, Varela suggests the term autonomy for use in organizations. Autonomous organizations are geared to maintaining their own identity by ignoring or proactively counteracting fluctuations in the environment.

2 Note that the concept of 'fit' is based on the same powerful, but circular, reasoning on which the famous adage in evolutionary biology 'survival of the fittest' is based. Who survives? The fittest. How do we know that they are the fittest? Because they survived.

and behaviour (see exhibit 2.1).

Exhibit 2.1 THE CONTINGENCY MODEL FOR ENVIRONMENTAL UNCERTAINTY AND ORGANIZATIONAL BEHAVIOUR AND STRUCTURE



source: Daft 1992

2.3 MINTZBERG'S TYPOLOGY OF ORGANIZATIONS

In 'The structuring of organizations' Mintzberg (1979) has attempted to synthesize the concepts of the systems theory concerning behaviour and functioning of organizations. He made a useful classification of organizations on the basis of their structure. In accordance with the systems theory he defines structure in a broad sense as: '*the sum total of the ways in which an organization divides its labour into distinct tasks and then achieves coordination among them.*' In this definition, organizational structure refers to the structure of individual positions, patterns of communication, planning procedures, systems of information flow and control systems. Mintzberg defines the structure of an organization as composed of five coordinating principles, five basic organizational parts, and four sets of design parameters and contingencies. The elements of structure together can be clustered into six structural configurations

(Mintzberg 1983):

- the simple structure,
- the machine bureaucracy,
- the professional bureaucracy,
- the divisionalized form,
- the adhocracy,
- the missionary form.

Because these configurations are so well-known, they are not discussed in the scope of this book. In § 2.5 they are used to describe the structural differences between universities, institutes and company laboratories.

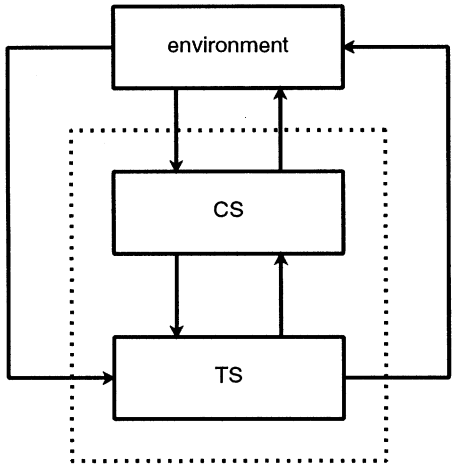
Bresser and Dunbar (1986) have shown that the contingencies defined by Mintzberg are useful tools in relating organizational structure to performance and effectiveness in research environments. Therefore the following contingencies are chosen to analyse the differences between the organizations in each stratum:

- the history related variables (organizational age and size),
- the technical system characteristics (regulation and sophistication),
- the environmental variables (stability, complexity, diversity and hostility),
- the power (human interest) variables (ownership, external power, power needs of individuals etc. and fashions).

2.4 THE SYSTEMS THEORY OF CONTROL

The systems theory of control starts from the assumption that a system can be described as a network of different control situations in which the elements (participants, departments etc.) can take different positions depending on the level of aggregation. It enables the analysis of organizational phenomena from several contrasting or sometimes even conflicting points of view. A control situation in its most elementary form is presented by a controlling system (CS) that exerts goal oriented influence on a target system (TS), while the environment affects both partsystems (see exhibit 2.2).

Exhibit 2.2 A CONTROL SITUATION



CS = controlling system
TS = target system

source: De Leeuw 1990

In management practice, control is often narrowly defined, embracing only monitoring and correcting (often used in financial terms to mean budget control). However, the systems theory of control originates from a much broader paradigm: *'any way of (goal)-directed influence'* (De Leeuw, 1990). The paradigm of control enables its application to a variety of forms of directed influence, such as power processes, teaching, convincing, organizational learning, and changing the organizational structure. It also implies that the process of management cannot be equated with the activities of the manager. Although in most situations managers do dominate this process, in principle all organizational members participate. In the case of extrinsic control, control is exerted almost exclusively by management. In the case of intrinsic control, in contrast, for instance in participative project groups, the control consists of the self-regulating activities of group members. According to Weick (1979), much mismanagement in organizations emerges from the failure to acknowledge these sources of self-control, leading to managerial interventions which disrupt the self-regulating capacity.

This broader view of control enables two, formerly separated, approaches to be combined, the system-technical and the socio-dynamic approach. While the

system-technical approach mainly concentrates on the information and communication aspects of control (such as phasing and structuring of research projects, setting of targets in terms of time, money and specifications, e.g. Twiss 1993), the socio-dynamic approach regards control primarily as a problem of leading and organizing people to achieve the objectives of the organization. Researchers, studying human behaviour in organizations, have repeatedly pointed to the lack of effectiveness because social and/or human factors had not been taken into consideration when designing the system (Benders et al. 1994). Fisscher (1991) emphasises that for management control to be effective system-technical and socio-dynamic approaches (such as informal exchange of information, and leadership aimed at motivation and commitment) should be combined. In this study the attention will be directed towards control exerted by the management, in short management control. It aims at the establishment of an optimum mix of system-technical and socio-dynamic factors for effective control in research organizations.

The distinction, first made by Etzioni (1964), between administrative and professional authority is also important in this study. Whilst administrative authority is based on control and coordination of activities by superiors, professional authority is based on autonomy, individual specialized knowledge and judgement in one or more professional areas. Researchers are among the best examples of experts relying on professional authority.

2.4.1 The Requirements for Effective Control

The attributes the controlling system should possess to achieve effective control are condensed in the following requirements for effective control (De Leeuw 1982):

- The controlling system should specify goals for the target system, which may or may not be constant in time or stated explicitly. The minimum requirement is that there exists some mechanism for evaluating the structural changes introduced by the controlling system.
- The controlling system should have a model to predict the possible effects of the control measures, or should at least have a good understanding of the target system.
- The controlling system should have sufficient information about the

state of the system and the environmental influences, and embrace the means for acquiring and updating this information[1].

- The controlling system should have enough measures of control at its disposal or the system must encompass enough degrees of freedom to cope with possible environmental and system disturbances. As stated in Ashby's law of requisite variety: '*only variety can destroy variety*' (Ashby, 1956).

However, effective control does not solely depend on the controlling system, but equally on the target system. Only if there is a good balance between the control capacity of the controlling system and the controllability of the target system can effective control be achieved. To use the analogy of the car and the driver, if the brakes are broken, even a perfect driver may have an accident. A bad driver may have an accident, even if the car is in perfect condition. Therefore, it is stressed that the requirements for effective control are necessary but not sufficient to achieve effective control. An additional point to be considered is that the different requirements for effective control do not counterbalance each other. For instance, a shortage of information handling capacity is not compensated by a greater number of control measures. In chapter 5 the requirements for effective control will be used as a check-list for the completeness of the variables used in this study.

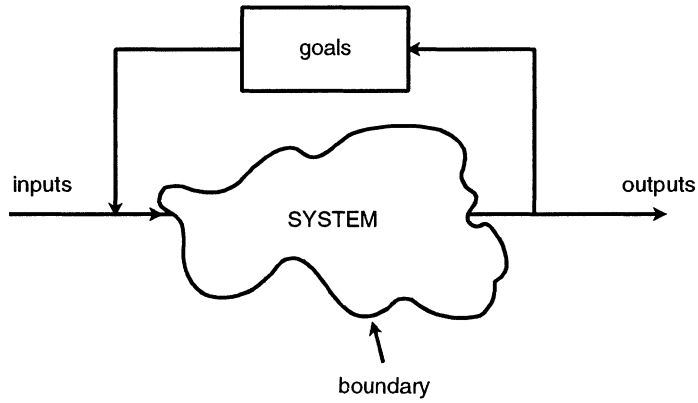
2.4.2 Feedback and Feedforward Control

Feedback and feedforward control are both forms of system control. Exhibit 2.3 shows how system outputs are used as feedback to compare actual performance to goals. This in turn helps to reformulate the input. For instance, if a pharmaceutical company discovers that relatively few drugs of their brand are prescribed in a certain region, it can intensify the number of face-to-face contacts of the sales force with the physicians in that region. However, the ideal system is one that, to a certain extent, self-corrects or self-regulates, so reactive decisions are not required. In feedforward control the management monitors possible disturbances in the system or the environment, and tries to anticipate the problem before the disturbances actually occur. It requires the re-

[1] In a later publication De Leeuw (1990) enlarged on this point by adding the requirement of sufficient information processing capacity.

placing of thinking in terms of linear chains of cause-effect relationships, with one of interactive and reciprocal loops. These loops can either be amplifying and reinforcing or self-correcting and stabilizing (buffering). The interaction of two or more amplifying and stabilizing loops can be described as a 'cause map' (Weick 1979). In box 3.1 (pg. 76) an example of such a cause map is given for university research.

Exhibit 2.3 SYSTEM OUTPUTS SERVE AS FEEDBACK THAT COMPARES PERFORMANCE TO GOALS



source: Kendall and Kendall 1988

Of course, cause maps oversimplify the complicated relationships between the elements in the circles of interaction, but are more accurate than showing either loop alone. Cause maps can aid the identification of the relevant variables, the looseness or tightness of their coupling, and their relative importance. But even when the critical variables are simple and the relationships are clear, predictions of organizational outcomes can never be certain. Even if the model is complete and correct, the fact that dynamic systems are always changing and never look exactly alike still make it impossible to accurately predict the consequences of changing any single element. Therefore, thinking in loops of interaction is a way of developing a model of management thought. Such models may help to suggest that things may be more complex than they appear and prevent us from expecting simplistic solutions to be effective. Thinking in circles can make management more effective by considering the possible side-effects of management measures in advance. In addition,

the results presented in this study must be considered in the light of the interactive and reciprocal character of cause-effect relationships. The point at which we break into the cause-effect loop and separate one from the other is often arbitrary. Therefore, no cause-effect relationships can be identified with certainty in a cross-sectional design.

2.5 UNIVERSITIES AND INSTITUTES

In this paragraph the structure and control situation in universities, institutes and companies, and the environmental and organizational constraints in these organizations will be discussed on the basis of the contingency theory, Mintzberg's typology of organizations and De Leeuw's paradigm of control. In the next paragraph the pharmaceutical companies will be described.

2.5.1 Mintzberg's Typology

Mintzberg (1979) classifies universities, research institutes and hospitals, together with law and accounting firms, as professional bureaucracies, for the following reasons:

- ***Standardization through training***: university and institute researchers obtain their knowledge and skills through extensive training during their graduate and PhD studies.
- ***Degree of task specialization***: in universities and institutes an unusually high degree of task specialization exists. It is often difficult for researchers to fully understand the research of colleagues in other departments.
- ***Horizontal decentralization***: because of the high degree of task specialization, especially in universities, the operating core is divided into relatively small and independent research units of professionals. Therefore, academic research can be considered as relatively small scale research, in general (Jain and Triandlis, 1990).
- ***Vertical decentralization***: in universities the power over many decisions, both operating, tactic and strategic, has flowed to the professionals at the operating core.

- ***Relatively small technostructure and large support staff***: Because planning, organizing and training are carried out in the operating core, a technostructure is hardly present. The administrative support staff (for instance the legal, personnel, and economic departments) is rather large in order to back up the professionals. In academic hospitals the horizontal decentralization has gone so far that a hospital can be looked upon as a holding company: a federation of quasi autonomous units of medical specialists. Furthermore, academic hospitals are more complex in their bureaucratic features than other parts of universities, because of the extra logistic problems of patient care. Therefore, a larger technostructure is generally found in academic hospitals than in other parts of university.

Contrary to universities, institutes are much more vertically integrated. The strategic apex (the Directorate of the Institute) has much more directive power than the university board. Because of this higher vertical centralization, in principle larger research projects, integrating more disciplines, can be carried out in institutes. Some very large institutes with a number of subsidiaries, often in different cities, can be regarded as divisionalized forms of professional bureaucracies. In this kind of institute the head office conducts output control over the subsidiaries.

2.5.2 Environmental and Organizational Constraints

Many factors have increased the pressure on universities and institutes. Some of these factors have arisen from the interaction with the environment and others from factors within the institutions themselves. Environmental constraints include increasing governmental control combined with budget retrenchments. Universities also suffer from the declining birth rate in industrial countries, which leads to fewer applicants. Consequently, universities show greater responsiveness to the student market. After a period of tremendous growth in the late 1960s and the 1970s, when the number of students increased rapidly and the university budgets went up accordingly, the situation changed dramatically in the 1980s. Rising governmental deficits, due to an over-ambitious task package, led to large budget retrenchments. Student numbers ceased to expand and university budgets were reduced. Under the rationale of the need for public accountability, governmental control in-

creased tremendously, incorporating central procedures for budgeting, planning and administrative operations. The primary tasks of universities were also evaluated. Strong pressure was put on universities to increase the research output in terms of papers and improve the educational programme. Far-reaching decisions were taken regarding the closing down of research departments or even whole areas of research and education.

In contrast with the general opinion in management literature (e.g. Cohen and March 1974), Mayntz (1985) considers the external environment of research institutes as more hostile than that of universities. Contractors want measurable results for their invested money. Therefore, the pressure for centralization and account formalization is stronger than in universities. The directors of such institutes, when asked, indicated that they spend, on average three quarters of their time outside the institute. A large part is spent on formal and informal contacts with (potential) contractors and funding agencies. Mayntz concludes that institutes which mainly rely on contract research, are particularly unstable. Because the projects have to be finished in a limited time span, continuity, both thematically (programmatic homogeneity) and in relation to work load, is often difficult to achieve. Therefore, when in the 1960s and the 1970s their structural budgets increased, many institutes gradually cut down their contract research activities. In the 1980s, and especially in the 1990s, the economic and political pressure increased for them to become more financially independent, more commercial in operation, more accountable, and to adopt more business-like principles and practices (Hill and Turpin 1994). Because the differences between a publicly funded and a market-oriented research institute are substantial (for instance the scientists have to give up part of their autonomy for a more commercial orientation) it is not surprising that this re-orientation is difficult and therefore proceeds slowly.

2.5.3 Management Control

Several authors have stressed that university monitoring devices are extremely underdeveloped. Cohen and March (1974) describe universities as 'organized anarchies' characterized by ambiguity of goals and fuzzy ('garbage can') decision-making. Keller (1983, p.5) describes the management control situation in universities as follows: '*they constitute one of the largest industries in the nation but are among the least businesslike and well managed of all organizations.*' The

main reasons for this observed lack of control can be found in:

- the democratic decision structure,
- the friction between administrative and professional control,
- the difficulty of measuring university performance.

A democratic structure was introduced into Dutch universities at the end of the 1960s, replacing a more hierarchical structure in which only professors had formal authority. In the new set up all staff members and students could send representatives to the boards and councils of the university down to and including the department level. The mixed composition of the boards and councils caused a lot of friction, based on real or putative conflict of interests. This, together with the frictions between the boards and councils at the different organizational levels, has diminished the decision-power in universities. A sign of a tendency to improve the governing structure may be the measure taken by one of the universities to reduce the number of university board members and appoint full-time managers instead. Only the councillor is a professor, while the chairman and the other members of the board are professional managers. It is possible that, due to the above-mentioned friction between professional and administrative authority, the over-representation of managers in the university board could become problematic in the case of conflicts. This may partly be anticipated by appointing managers with a strong scientific background.

The increased complexity of universities has led to a vigorous growth of the administrative staff. The administrative staff grew even further, both in size and importance, when the universities responded to the governmental pressure with increased administrative centralization. This was due to requirements to rationalize budget formats, implement procedures that will pass judicial tests of equitable treatment, and speak with a single voice to powerful external agencies. The increasing number and importance of administrators lead to the 'administered university' (Lunsford first used this term in 1970, p. 91). Because the administrative tasks are relatively simple and easy to monitor, compared to the professional tasks, a parallel hierarchy emerged, one conventional top-down hierarchy for the support staff and a bottom-up one for the professionals. This 'living apart together' of two different control systems, an administrative alongside a professional control system (dual control system, Birnbaum 1988), is potentially frictious. As the governmental pressure increased, the two hierarchies became alienated from each other. In the mind

of the professionals, the administration became identified with 'red tape', constraints, and outside (governmental) pressure, far removed from central academic values. In the words of Thomas (1983 pp. 169, 172) '*The function of the administration is solely to see that the funds are adequate for its purposes and not overspent, that the air is right, that the grounds are tidy- and then to stay out of its way . . . A good university doesn't need to be headed as much as to be given its head, and it is the administrator's task -not at all an easy one- to see that this happens. The temptations to intervene from the top, to reach in and try and change the way the place works, to arrive on one's desk each morning with one's mind filled with exhilarating ideas for revitalizing the whole institution, are temptations of the devil and need resisting with all the strength of the administrator's character.*' In the mind of administrators, on the contrary, faculty members are self-interested, unconcerned with control and unwilling to respond to legitimate accountability requests. The budget retrenchments themselves forced the faculty members to look around for additional funding. If they were successful this resulted in a decrease of dependency on the faculty administration.

Another problem is the difficulty encountered in measuring performance in universities. Graduate education is conducted in a classroom alone with the students. The results of research are only visible after several years, when the first papers and reports are published, and the long-term impact is unknown for even longer. These time-lag problems are also significant for this study. Therefore, several indices, covering different aspects of research performance, are used. By converging these separately imperfect measures, a more valid assessment of research performance is reached.

Especially in contract research institutes, where the performance is more measurable than in universities, administrative authority may be dominant over professional authority. Many authors prefer clear and straightforward administrative authority over unclear and fuzzy professional authority, and therefore the control situation of institutes is often referred to as a model for universities. Puts's (in de Bie et al. 1983) advice to Dutch university administrators, to learn from the 'goal oriented management' in institutes, is also based on this idea. Nevertheless, he observed a number of problems, most of them emanating from the absence of a market orientation. The continuous reorganizations occurring in most of the research institutes indicate how severe these problems are. He mentions:

- the absence of competitor relations,
- competitive forgery, because the indirect costs are not calculated,
- no clear performance measures.

2.6 COMPANIES

2.6.1 Mintzberg's Typology

Science-based industries are difficult to classify in terms of Mintzberg's typology. The production of drugs is executed in the organizational environment of the machine bureaucracy, with its emphasis on:

- *Standardization of work processes.*
- *A large technostructure*, which is needed to design and maintain the elaborate production processes. A hierarchy emerges to oversee the specialized work, leading to
- *Vertical centralization*. In the typology of the machine bureaucracy the R&D function is positioned in the support staff. However, science-based industries are exceptionally dependent on a continuous flow of new products, which are results of R&D endeavours. Therefore, the R&D function can be considered as part of the primary process of the company, and should be placed in the operating core.

R&D and production alone are not enough to attain long-term profitability for a pharmaceutical company. It is obvious that without an adequate marketing and sales force a new drug will never reach its full profit potential. Ethical drugs differ from almost all other consumer goods in that the buying decision is not made by the final consumer, but by the prescribing physicians. To influence them, frequent face-to-face contact with a highly knowledgable sales force, combined with direct mail and advertisements in medical journals, and the organization of medical congresses and other meetings, are necessary. This implies that the marketing and sales force has also many professional features. A proportion of them are MD's, or graduates in biology or chemistry, and work independently.

The large pharmaceutical companies are multinationals, having production plants and marketing and sales departments throughout the world. The differ-

ent steps in the R&D process are often carried out in a number of laboratories located in different countries. In Mintzberg's typology, the large pharmaceutical companies can therefore be regarded as divisionalized forms. But contrary to the characteristics of the divisionalized form, where the divisions are rather independent entities joined by a loose administrative overlay, in a great number of pharmaceutical companies the administrative control by the head office is rather tight, because the different phases of the R&D process must work closely together. From looking at the evidence presented above, it can be concluded that pharmaceutical companies can best be regarded as divisionalized forms of machine bureaucracies with built-in professional bureaucracies, namely the R&D, marketing and sales departments.

2.6.2 Environmental and Organizational Constraints

For obvious reasons of public health, the authorization of new branded ethical drugs on the market is subject to strict governmental and supergovernmental regulations regarding efficacy and safety. However, in the last thirty years, branded ethical drug pharmaceutics faced such a steady increase of legislation, that it has considerably reduced the time available to recoup past research expenditure. Nowadays, over 400 different EU documents (such as directives, regulations, communications and notes for guidance) have to be taken into account when applying for authorization for a medicinal product. It is expected that the further increase in the number of EU member states, and the further harmonization and integration as foreseen in the Maastricht Treaty, will further increase the legislative load.

In the 1960s, the period between the finding of the lead compound (a chemical compound with assumed therapeutic efficacy), and the introduction of a new product to the prescription drug market, was about five years. Nowadays, it often takes more than ten years to introduce the resulting product of a lead compound to the market. Whilst earnings may only start ten years after the submission of a patent for a lead compound, the effective patent protection time fell back from an average of thirteen years in around 1965, to eight to ten years in the middle of the 1980s (e.g. Redwood 1987 and De Wolf 1987). However, the future is not that bleak. In recent years a number of measures have been taken to improve the situation. First, the EU provides via the 'Supplementary Protection Certificate' the possibility to lengthen the patent pro-

tection time. Furthermore, the new European Medicines Evaluation Agency (EMEA) plans to roll the 12 regulatory bodies of the European Union (EU) into one, which ideally will lead to uniform and faster approval procedures.

In a number of industrial countries (such as the US, Canada, Germany and the Netherlands) the governments are planning to change the structure of medical care. The Health Care Plan of the US administration and the Dutch 'Stelselherziening Gezondheidszorg' are two examples of this tendency. These plans have the following general features:

- an obligatory insurance for a basic package of medical costs,
- voluntary insurance for additional care,
- a reduction in medical costs by the introduction of managed competition.

Managed competition means that hospitals, pharmacists, medical specialists, general practitioners and the pharmaceutical industry negotiate with insurance companies over the price and quality of the different packages of medical care. After the first presentation of the Health Care Plan in the USA, the drug and biotechnology stocks fell by a total of US$ 120 billion, because brokers at the New York Stock Exchange expected the innovative capacity of the industry to be at risk (De Kruijff 1993). When it became apparent that the Health Care Plan as such would not be passed, pharmaceutical stocks went up again. The measures of the different governments to reduce drug spending has reduced the growth of pharmaceutical sales from an average of 11% between 1987 and 1991 to an estimated 5% in 1994 (Ekberg 1995[1]). Pharmaceutical companies have developed different strategies to challenge these problems. This has led to large changes in the industrial structure, especially at the level of concentration and diversification (e.g. Elfferich 1992, see § 1.4.3 for examples).

2.6.3 Management Control

Business organizations are presumed to be most effective when the strategic apex specializes in coping with uncertainty, and the operating core specializes

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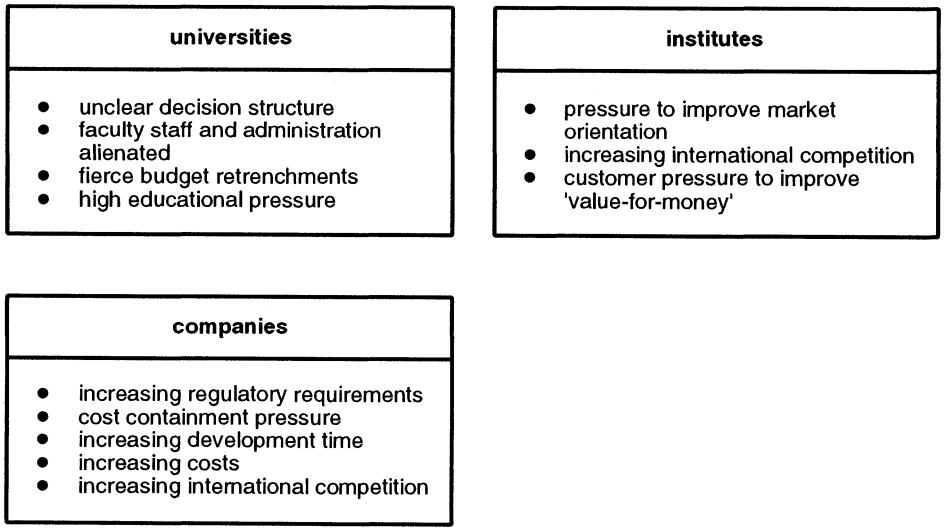
[1] *Reuter*, March 20 1995.

in functioning effectively in conditions of certainty. In most companies, the Board of Directors monitors the environment (Katz and Kahn, 1978). This is also apparent in pharmaceutical companies. 'Values and Visions: A Merck Century' (Merck & Co. 1991) is a good example of a long-term vision presented by the Board of Directors, based on the close monitoring of the scientific possibilities and the possible social values influencing the drug market in the decades to come. As in most business organizations, administrative authority is predominant in pharmaceutical companies. In the R&D laboratories themselves, however, professional authority is predominant.

Exhibit 2.4 CHALLENGES FACING UNIVERSITIES, INSTITUTES AND INNOVATIVE PHARMACEUTICAL COMPANIES



2.7 CONCLUDING REMARKS

Exhibit 2.4 outlines the challenges which faces universities, institutes and innovative pharmaceutical companies in the decades to come. In universities these include the improvement of the unclear decision structure and the withdrawal of the alienation of the faculty staff and the administration. This has to be achieved in a situation of fierce budget retrenchments, while at the same time increasing numbers of students has to be educated. In institutes

the main challenge is to improve the market orientation, to give the customer value-for-money in a situation of increasing international competition. In pharmaceutical companies, the increasing regulatory demands have led to a large increase of the development time (especially of clinical development) and thus to increasing costs of drug innovation. The cost containment pressure of the government has not only lowered the drug prices, but has increased the time-lag between drug approval and admission to the reimbursement system, as well. Combined with the increased international competition this has led to a further decrease of the opportunities to recoup past R&D investments. Together these challenges force the innovative pharmaceutical industry to reduce the time-to-market by shortening the total R&D process and the time-span between drug approval and market introduction.

Exhibit 2.5 RELATIVE STRENGTH OF THE DIFFERENT SYSTEM VARIABLES IN THE STRATA UNIVERSITIES, INSTITUTES AND COMPANIES

system variables	universities	institutes	companies	
			research	development
coupling	loose	loose-mod.	tight-mod.	tight
system control	weak	weak-mod.	strong-mod.	strong
task uncertainty	high	high-mod.	low-mod.	low
vertical centralization	low	low-mod.	high-mod.	high
horizontal centralization	low	low-mod.	high-mod.	high
accountability	low	low-mod.	high-mod.	high
authority	professional	professional	professional	administrative

mod. = moderate

Exhibit 2.5 outlines the expected strength of the different system variables in the three strata, based on the concepts of systems theory as introduced in this chapter. At one end of the scale the universities are situated. Here the task uncertainty is relatively high, the coupling between departments is relatively loose, the accountability is low and there is considerable horizontal and vertical decentralization. The strength of system control will be relatively weak and professional authority will be dominant over administrative authority. At the other end of the scale the experimental development laboratories in industry are found. Here the task uncertainty is relatively low, the coupling between departments is tight and there is a high level of horizontal and ver-

tical integration. The strength of system control will be strong and administrative authority will be dominant over professional authority.

In this chapter the structure, behaviour and control situation in research organizations has been described, by use of the contingency theory and Mintzberg's typology of organizations. In the next chapter the attention will be directed to the research unit level in universities and institutes, and to the system of research units which together form the R&D process in industry.

CHAPTER 3

STRUCTURE, BEHAVIOUR AND CONTROL IN RESEARCH UNITS

This chapter concentrates on structure, behaviour and control in research units. After a general discussion of the concept of organizational learning, the trajectories of theory construction and theory application are described in terms of value adding learning loops. Following the trajectory of theory construction the attention is focused on the managerial tasks and the questions which has to be answered by the controlling system, in the different steps of the empirical cycle. Thereafter, the trajectory of theory application is described in terms of a learning loop for structured organizational change. In § 3.2.4 industrial innovation is described in terms of a system of value adding learning loops, combining succeeding phases of theory construction (in basic research) and theory application (in applied research and experimental development). In § 3.3 the conceptual model of the double unity cell (DUC, Van Engelen 1989) is introduced. It is used to describe the entities and relations in a research unit, combining the concept of value adding learning with that of the control situation. At the end of this chapter the model of the double unity cell is integrated into the different contexts of the three strata.

3.1 ORGANIZATIONAL LEARNING

Learning is essentially a circular process in which a pattern of several small and reinforcing cycles may have a stronger learning impact than a large but occasional one. The advantage of circular learning is the possibility of leverage. Relatively small strategically chosen actions and changes can lead, through amplification, to significant and enduring improvements. Two main types of learning can be distinguished: single-loop and double-loop learning. Single-loop or adaptive learning is focused on error detection and correction to stabilize and maintain existing systems. Single-loop learning is by far the most common in organizations today. Double-loop learning, in contrast, involves questioning the system itself and the reasons why errors happen in the

first place. Double-loop learning looks at the deeper organizational norms and structures, and raises questions about their effectiveness. Related to the concept of double-loop learning are anticipatory and deutero learning. Anticipatory learning is a vision-reflection-action approach that seeks to identify the knowledge and skills needed to take advantage of future opportunities. This *planning for learning* approach is greatly advocated by global companies like Royal Dutch Shell (scenario planning). A recent example of this approach is the analysis of the possible position of drugs in different scenarios concerning the political and economic development of Dutch medical care in the decades to come (Leufkens et al. 1993). Deutero learning occurs when the organization learns from critically reflecting upon its taken-for-granted assumptions. Its members learn about previous contexts, they discover what they did that eased or inhibited learning, and invent, evaluate and generalize new strategies for learning. Argyris and Schon (1978) call this *learning about learning* (meta-knowledge in terms of Russo and Schoemaker 1989). Double-loop, anticipatory and deutero learning can be seen as more creative types of learning. Not merely reacting to negative events, but proactively bringing about changes in the organization is central in these concepts

3.2 RESEARCH AS A VALUE ADDING LEARNING LOOP

Boer (1990) describes an organization as a purposeful system of people and resources which, using multiple technologies, together perform certain activities or processes which transform inputs into outputs (the value adding chain, Porter 1985). The value adding chain includes the activities needed:

- to feed information and materials into the transformation system,
- to transform this information and material into modified information and/or finished output,
- to turn this information and/or finished output over to the (operational or task) environment.

Because of the essentially circular process of research it is preferred to use the terms value adding learning loop to describe the primary process of individual research projects and a system of value adding learning loops, for industrial innovation.

3.2.1 The Empirical Cycle

Scientific research has many facets. One is the discovery and recording of facts (descriptive science). The construction and testing of hypotheses and theories is called empirical science. The objectives of an empirical science may be identified as:

- *Explanation* why a certain phenomenon occurred. Typically, this is accomplished by representing cause-and-effect, lawlike generalizations, in a deductive or inductive model, or some other explanatory framework.
- *Prediction* of a phenomenon, either deduced from known and unknown events in a conceptually static system, or to make assertions about future outcomes based on the observation of regularities among sequences of events in the past.
- *Control* of a phenomenon, the systematic manipulation of some element related to or contained within a system so as to effect a change in one or more elements in that system (Bagozzi 1983).

In achieving the above goals, the following cycle of activities are traversed[1] (between brackets are the corresponding phases in the trajectory of theory construction, see § 1.3.1):

- ***Research objectives (exploration and description)***
  According to Rudner (1966), '*A theory is a systematically related set of statements, including some lawlike generalizations, that is empirically testable. The purpose of theory is to increase scientific understanding through a systematized structure capable of both explaining and predicting phenomena.*' Or, simply state, '*A theory is an explanation how things might work in reality*' (Van Engelen and Van der Zwaan 1994). The objective of an empirical study is to validate the lawlike generalizations in the empirical world. Typically, this involves the development of concepts and the application of rules of logic and standards for determining the internal consistency of one's theoretical frame-

[1] This is an obvious simplification. The scientific research process is more complex and contains many interactions and feedback and feedforward loops between activities.

work and a determination of construct validity. Throughout the first stage and into the second and third, the process can be described as a deductive one. That is, the progression is one from general assertions to relatively particular or specific instances.

- *Design (explanation and interpretation)*
  In this phase the research questions and hypotheses are formulated and the design of the study is chosen (for instance, case study or experiment, a longitudinal or cross-sectional design). The variables relevant to answering the research questions and testing the hypotheses are operationalized in measurable entities, and conceptual and operational connections between concepts and observations are made. The study population is selected and the size and nature of the sample (randomized or clustered sample etc.) is established. In addition, the methods to provide for reliability and validity and the instruments of data collection (for example, questionnaires, interviews, observations or desk research) and the methods of data analysis are chosen.
- *Data collection (testing)*
  Then the acquisition of significant data starts. This means, that the data should be internally consistent (e.g. have a high reliability) and be logically or causally tied to the concepts and constructs in one's theory.
- *Data analysis (testing)*
  Then comes the organizing and analysis of data in relation to the hypotheses stated in the beginning. This might entail the application of mathematical models or statistical procedures, following the analysis scheme. Through the process of interpretation, one evaluates the findings, learns from the results, and, in general, gains an understanding of the phenomenon which is to be explained.
- *Reporting and documentation (testing)*
  The scientific process comes to an end through the sub-process of induction, in which the learning attained through earlier stages is incorporated into one's theoretical framework. Induction involves taking the argument from particular instances to more general conclusions. Unlike the valid deductive argument that guarantees the truth of its conclusion given true premises, the valid inductive argument provides 'good', though not conclusive, grounds for accepting its conclusion. The scientific process is thus a continuous one, reflecting the tentativeness and uncertainty of our knowledge of the world. The researchers present the results in terms of verification or falsification of

theoretical judgements, measures, estimates and recommendations concerning the object of study, and suggestions for further research. They also render an account of the study methodology (the objectives, design, presumptions, selection criteria, sample choice, and methods of data analysis), providing the possibility for replication.

3.2.2 Management Control in the Different Phases of the Empirical Cycle

Mason (1979) has summarized the managerial tasks of the controlling system in the different phases of the empirical cycle. In chapter 3 the list of the managerial tasks will be used as an additional check on the completeness of the management control variables, as defined in this study. Mason uses a slightly different classification than the one presented above, because of the management control perspective. For instance, resource acquisition is added as a separate phase in the process. In the following pages, the terminology of Mason is followed (the corresponding phase in the empirical cycle is mentioned between brackets). The choices which have to be taken and the questions which have to be answered by the research management in the different phases are indicated by *italics*.

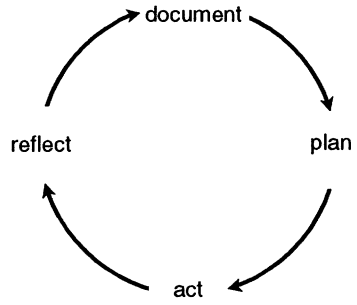
- ***Idea generation (research objectives)***
  Formulation of the basic ideas and the general objectives of the research project. The motivation to choose a project can be personal curiosity, but it can also be professional status or award expectation. Basic questions are: *What constitutes a 'good' idea, one worth pursuing? And how are the priorities set?*
- ***Planning and Design (design)***
  Formulation of hypotheses or research questions and the specification of a series of tasks necessary to complete the research project. The controlling system may face the following problems. Some theoretically attractive concepts may be too difficult to operationalize, require too much effort, or may take too long for the results to be completed. Decisions have to be taken as to which variables to estimate, what data to use, and where and how much to collect. Given the elements of cost and constraints, the controlling system must choose, for instance, between breadth compared to depth of coverage, and the number of observations versus the degree of reliability. Basic ques-

tions are: *What concepts and theories are to be used? How will the data be collected? What resources are required?*

- ***Resource Acquisition (design)***
  Obtaining of the human and capital resources. 'Big Science', such as medicine, chemistry and physics (Spiegel-Rösing and De Solla Price eds. 1977), often requires high investment in technology. The financier can be the institution itself, a contractor or a funding agency. In the latter cases, large 'marketing efforts' have to be undertaken to 'sell' the research proposal. The basic question is: *Who supplies or finances the resources?*
- ***Organizing (design)***
  In this phase the controlling system must define the tasks to be accomplished, select the people to complete the tasks, arrange for an adequate communication system among participants (for instance regular research meetings), schedule the use of facilities, and set up feedback loops to ensure that the research design is followed (supervision schedule). Basic questions are: *How are research tasks assigned to the people? How are task objectives set? Which communication channels are to be used? How are the research activities related to the organizational and external environment, and the funding agencies?*
- ***Producing (data collection and analysis)***
  Applying the resources to the research tasks according to plan. This involves integration of resources and coordination of interdependencies, use of incentives and quality control over the output. The controlling system must see to it, that (1) the work is done, (2) that it is completed according to quality standards, and (3) that it is completed within the budget and deadline limitations. Basic questions are: *How is the work carried out and supervised?*
- ***Output Dissemination, Utilization, and Evaluation (reporting and documentation)***
  In this phase the scientific conclusions are related to the original intentions (goals and plans), and communicated to the outside world. In this phase the controlling system should be concentrated on the marketing of its product. Output dissemination is the process of notifying potentially interested parties of the existence of the results and making the results available to them. Utilization is the process by which other parties (scientists, direct users, policy makers and industries) make use of the results. Evaluation involves the difficult weighing up of the long-run benefits for the scientific community or society,

against the resources used for the research project. Or, in case of contract research, the short term benefits for the contractor. Basic questions are: *Who are the potential users? How are the results communicated? And how are the results evaluated?*

Exhibit 3.1 THE LEARNING LOOP OF ORGANIZATIONAL CHANGE



source: Marquardt and Reynolds 1994

3.2.3 The Learning Loop as a Model for Organizational Change

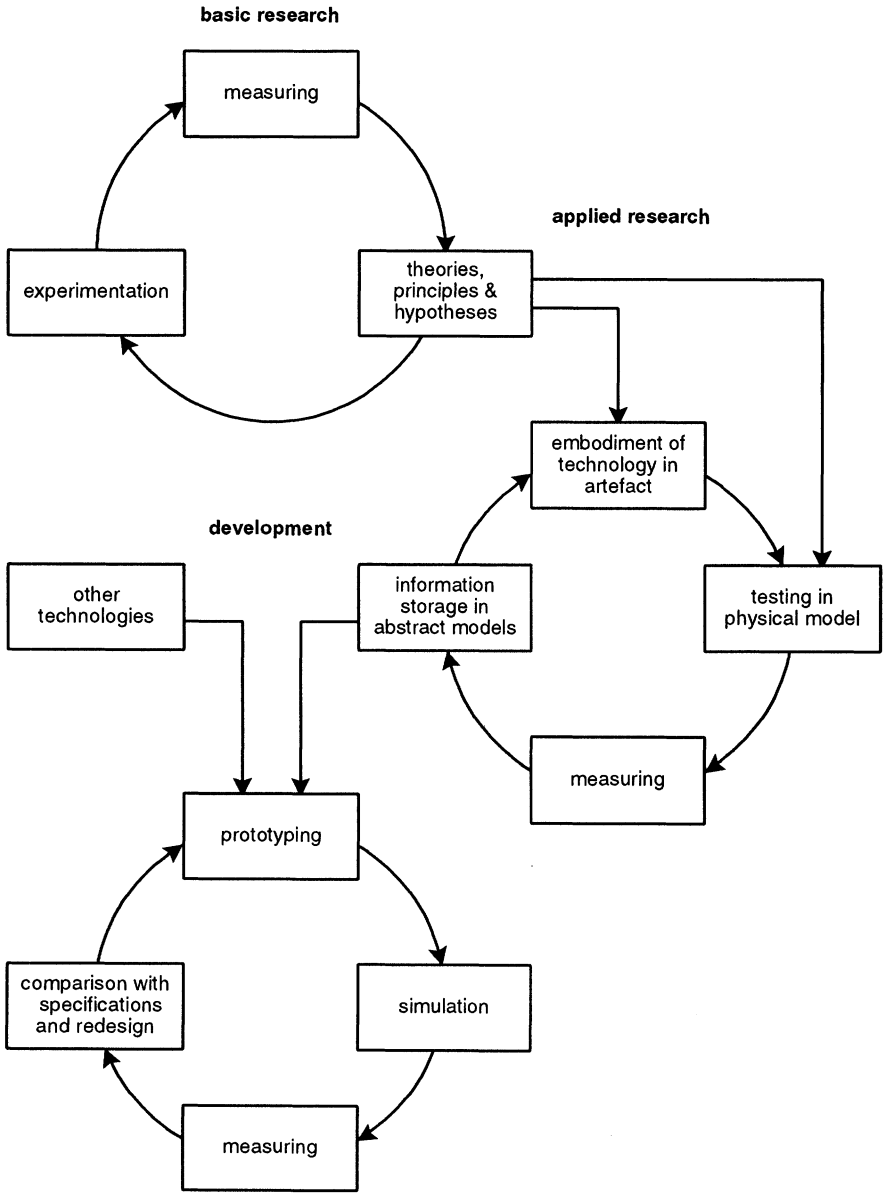
Following the trajectory of theory application Marquardt and Reynolds (1994) advocate the following cycle of activities as a learning loop for structured organizational change: (1) document, (2) plan, (3) act, (4) reflect, (5) document again (the corresponding phases in the trajectory of theory application are mentioned between brackets) to replace the satisficing and trial and error processes commonly observed in organizations (eg. Daft 1992). The learning loop for structured organizational change comes close to Deming's (1982) famous 'plan, do, check and act' cycle, or the less specific phase model of Lewin (1958) 'unfreezing, moving, refreezing'. In contrast with the general trajectory of theory application, here the phases reflect and document are added. To compensate for the contextual difficulties and unexpected side-effects encountered in the process of organizational change (a number of them are mentioned in § 1.3), Marquardt and Reynolds pay much attention to reflection on and documentation of knowledge (see exhibit 3.1).

1 *Document (diagnosis and construction)*
Description of current processes and structures or specific problems, and identification of which need improvement. Restructuring of processes and structures by incorporating different perspectives, and framing and reframing problems by looking at them in a variety of ways.
2 *Plan*
The planning of the steps which have to be taken in order to reach the improved situation.
3 *Act (implement)*
The implementation of improvements. If the changes are complex, and may have far-reaching and unexpected side-effects, the improvements may be implemented on a small scale, at first.
4 *Reflect*
The obtaining and using of feedback information. Identification of the outcomes and side-effects which were not anticipated.
5 *Document*
The documentation of the learning aspects, so that they can become part of the organization's experience. Organizations do not have memories as such, but they do have libraries, databases, procedures, drawings and other storing mechanisms for information and knowledge. If the information is not stored, there is a high risk of reinventing the wheel.

3.2.4 Industrial Innovation as a System of Value Adding Learning Loops

Exhibit 3.2 shows the industrial innovative process as a system of value adding learning loops. After general management has decided on the product market combination and the technology profile of the new product, the innovative process starts. The basic research cycle starts with the drafting of a project proposal and evaluation of the literature on the topic (*theories, principles and hypotheses*). Based on the literature, additional experiments may be conducted to fill in gaps in fundamental knowledge (*experimentation and measuring*). If sufficient knowledge is gained the applied research cycle starts with the *embodiment of technology in an artifact* (see also the explanation of exhibit 1.5) and a testing programme is set up (*testing in physical model*). In the next step the different parameters are measured (*measuring*). The information obtained

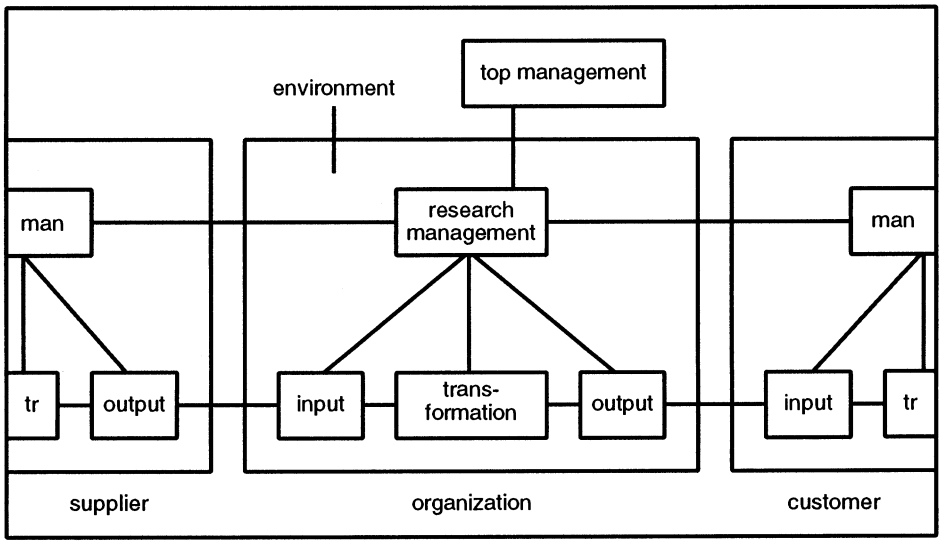
Exhibit 3.2 INDUSTRIAL INNOVATION AS A SYSTEM OF VALUE ADDING LEARNING LOOPS



source: Janszen 1994

is analyzed and stored (*information storage in abstract models*) and can be used to further improve the product in additional learning loops. The applied research phase ends with one or more prototypes, products with characteristics which sufficiently cover the product profile (*prototyping*). In experimental development, different parameters of the prototype(s) are tested in situations which more or less reflect the situation in which the product is intended to be used (*simulation and measuring*). The data are compared with the product specifications. When the specifications are not met, the design of the prototype is re-adapted and tested in additional learning loops until it works according to the set of specifications (*comparison with specifications and redesign*).

Exhibit 3.3 THE DOUBLE UNITY CELL



man = management tr = transformation *source: Van Engelen 1989*

3.3 THE DOUBLE UNITY CELL

The object of study is the research unit in universities and institutes and the system of research units which together form the R&D process in industry. The conceptual model of the double unity cell (DUC) has been used to des-

cribe a research unit as an aspect system (see § 2). The basic assumption has been that biomedical research and pharmaceutical innovation can be considered as a (system of) value adding learning loop(s), through which research input is converted into output, while control over the transformation process is conducted by the research management. Exhibit 3.3 shows a simplified model of a research unit, for the complete model the reader is referred to Van Engelen 1989, p. 38, figure III.3.1. The following entities, objects and relations can be distinguished.

Research management
The research management is the controlling system. It communicates with the supplier and customer function, the top management and the environment. It includes the professors in universities, and the heads of different research departments in institutes and companies, assisted by their senior scientific staff.
Research process (input, transformation, output)
The research process is considered to be a (system of) value adding learning loop(s) through which research input (information and chemical compounds) is converted into output (publications for universities and institutes, and patents or registered drugs for pharmaceutical companies).
Supplier function
The input for the research process stems from the supplier function. In universities and institutes the supplier function includes (1) the suppliers of the information on which the research questions are based (for instance the scientific community or the community of physicians and patients), (2) the suppliers of the resources to carry out the research process (laboratory equipment, chemicals etc.), and (3) the suppliers of the financial resources.
Customer function
The output of the research process is directed towards the customer function. Hazeu and Spangenberg (1991) divide the research output into direct and effective output. Direct output refers to the research output as reported in scientific papers, reports, congress contributions and books, whereas, effective output refers to the output used as input by the customer function.
Top management
This consists of the faculty or university board, or the board of directors in institutes and companies.
Environment
The environment includes both the general and the task environment. The general environment includes, for instance, the increased governmental regulations regarding the safety of drugs, influencing pharmaceutical R&D. The

task environment includes, for instance the other units in the faculty, with which the research unit cooperates or has to compete for resources.

The model of the double unity cell was originally elaborated in solid-state physics to describe the macroscopic properties of materials by analysing the microscopic behaviour of the atoms and their interaction in the atomic structure. In terms of systems theory, it was used to explain some aspects of the system by concentrating on the constituting elements or part-systems. In a linear atomic structure, the double unity cell turned out to be the smallest part-system that still contained all characteristics of the system as a whole. In many management studies on research (e.g. Spangenberg 1989), a traditional input-output model has been used. In such a model the research unit is described as the place where the primary process (research) takes place, independent of the operational environment. In the model of the double unity cell, however, the supplier and customer function are incorporated into the system. If we consider the fact, that over the years former external relationships are increasingly integrated into the organization (see for instance, the fast increase of strategic R&D alliances or supplier-customer partnerships in joint development teams and cooperative networks of universities, institutes, and companies, i.e. Biemans 1992 and Morgan 1994), it is obvious that the shift of the system boundaries has clear support in the real-life situation.

3.3.1 Universities and Institutes

Research units in universities and institutes may be considered as rather independent sub-systems. Spangenberg (1989) uses Ouchi's (1980) typology of the clan to describe them. They also show a number of the characteristics of the simple structure in Mintzberg's typology (Mayntz 1985). Mintzberg describes simple structures as highly flexible and innovative organizations. They are relatively small project organizations, under the supervision of an autocratic leader who participates in the primary process and monitors the environment. The span of control of the leader limits the size of a simple structure. The similarities of a research unit and a simple structure are remarkable. University research units (at least, the excellent ones):

- are innovative,
- show a flexible organization consisting of a number of small, and rela-

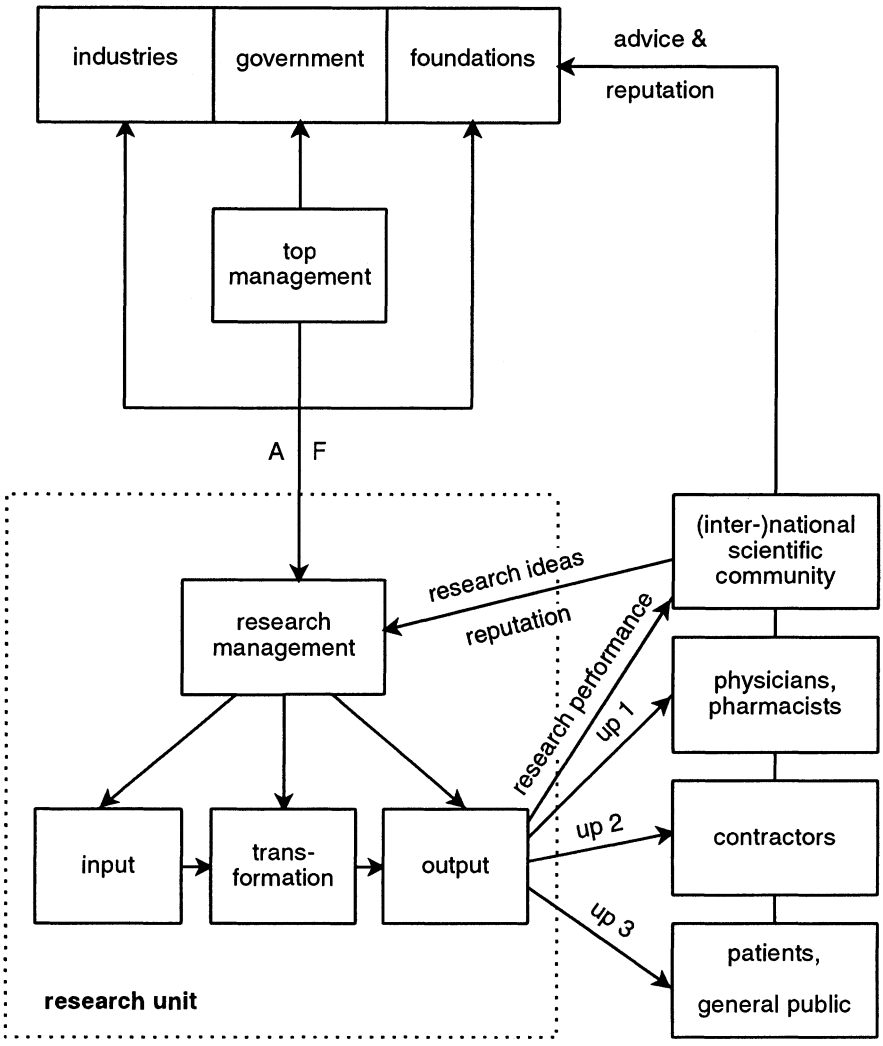
tively independent research projects, which constantly shift in composition and size,

- are supervised by professors, who participate in the primary processes (research and education) and monitor the scientific environment, and who try to dominate it by participating in international scientific forums and editorial boards,
- unlike the model of the simple structure, the scientific staff has a relatively large decision power,
- the size of the research unit is limited by the span of control of the head of the unit. Based on the span of control of the head of the unit, Mayntz (1985) predicted that the maximum size of a research unit will be roughly 7 research projects of 1 to 5 scientists each, in total 20 to 30 scientists. One of the objectives of this study is to check this figure against the empirical data.

Exhibit 3.4 depicts the financial and information flow in the biomedical research units in universities and institutes. The output of the research process can be directed towards the following customer functions:

- ***The (inter)national scientific community***
  The scientific community is reached by publishing in international scientific journals and by presenting papers at congresses and in workshops. In this study the performance directed to the scientific community will be referred to as *research performance*. The leading scientists in a certain research field (the 'Scientific Forum', De Groot 1984) exercise quality control over the scientific output. They evaluate the scientific output of the research units in that field, for instance as referees for scientific journals (professional control, Hardy et al. 1984). In some disciplines the methodologies and concepts are generally accepted and clear, such as in physics (disciplines with a high level of paradigm development, Kuhn 1970 and Bresser and Dunbar 1986), but in others much confusion exists. Different Science Forums ('Schools') with different methodologies and conceptual frameworks oppose each other, such as in sociology and psychology (disciplines with a low level of paradigm development). The field of biomedical research consists of a number of high paradigm (sub-)disciplines, each of them having their own Scientific Forum. As a consequence, the re

Exhibit 3.4 THE DOUBLE UNITY CELL MODEL IN UNIVERSITIES AND INSTITUTES



A = accounting of performance in annual reports, in reports for governmental and industrial contractors, in reports of granted projects and in periodical evaluations by peer groups. F = governmental financing of regular tasks and financing of governmental or industrial contract research and financing of granted research projects. Top management = faculty and university board in universities and directorate in institutes.

up = user performance

search units in this study are confronted with quite different situations, for instance regarding the access to scientific journals. The citation patterns can also differ across (sub-)disciplines. In the discussion of the different performance and effectiveness measures in the next chapter will be returned to this point.

- ***The community of users***
  In this study, the community of users consists of:
  - The *physicians* who can use the research concepts and results as the basis for new therapies or therapeutic agents. They are reached by publishing in journals for physicians (*user performance 1*[1]).
  - The *industrial and governmental contractors*, for instance pharmaceutical industries, which can use the concepts elaborated by the research units as the basis for new drug development (*user performance 2*).
  - The *patients and general public,* to be reached via popularized articles in periodicals (*user performance 3*).

The scientific community and the community of users are also important supplier functions. For instance, the (inter)national scientific community or the community of users can act as a source of ideas for new research projects and concepts, as a source of resources (for instance as scientific advisers for the government or funding agencies or in peer review committees, see box 3.1), and as a source of competition. The overlap between the supplier and customer function implies that producing interesting results for the scientific community or the community of users can lead to an increase in the size of a research unit. But if Mayntz (1985) is right in her qualitative observation that the span of control of the research unit leader sets clear limitations on the size of a research unit, then the growth of the unit will be limited through coordination problems (see box 3.1).

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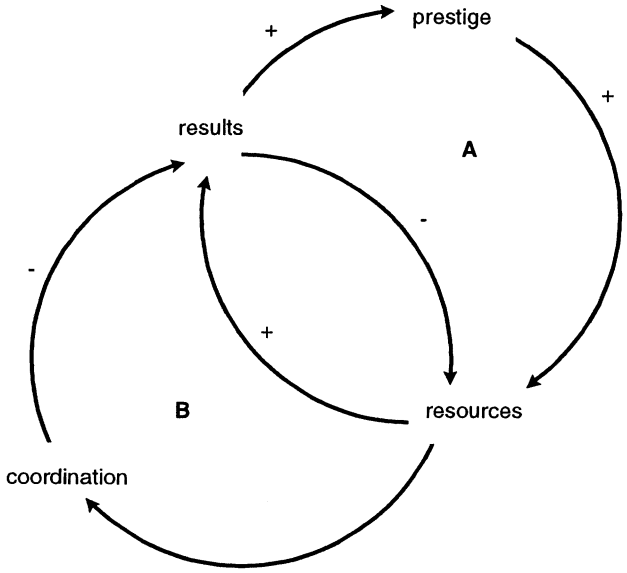
[1] The reach of national journals for physicians is larger than most people realize. For instance, the number of subscribers to the largest Dutch journal *'Het Nederlands Tijdschrift voor de Geneeskunde'* is larger than that to *'The Lancet'*.

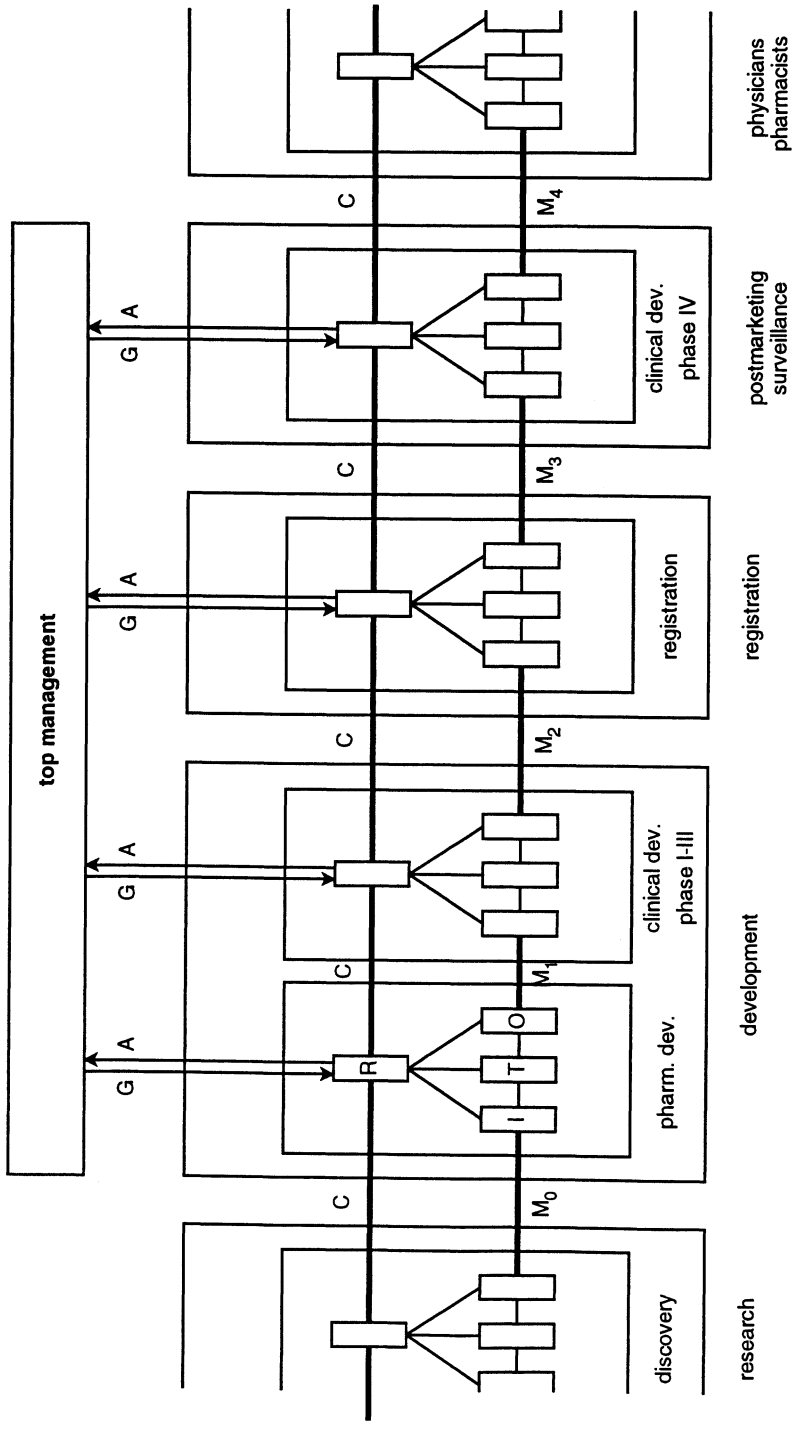
Exhibit 3.5 CAUSE MAP OF RESEARCH RESULTS, PRESTIGE, RESOURCES AND COORDINATION



Box 3.1

When a research unit in an university or institute has obtained interesting research results, it gains prestige in the scientific community or in the community of users (for instance physicians). As a consequence it is likely to get extra financial support: foundations, advised by scientists or physicians are more likely to supply grants for new project proposals, the faculty may award extra personnel and material means on the basis of a positive evaluation of a peer review committee, or governmental and industrial contractors may grant more contract research. This can lead to the amplifying loop A. However, above a certain level, when the span of control of the head of the research unit has been reached, the increase of the resources may cause coordination problems within the unit or in relations with other units, resulting in a lower quality of the research process. As a consequence the research results, and therefore the research unit resources, decline again, resulting in the stabilizing loop B.

Exhibit 3.6 DOUBLE UNITY CELL MODEL OF PHARMACEUTICAL INNOVATION



3.3.2 Companies

The research units in universities and institutes can be considered as relatively independent sub-systems, and therefore the double unity cell as such can be used as the unit for the analysis. The input and output of an individual research unit can be distinguished, so, within boundaries, the effectiveness of the use of the resources can be accounted for that unit. In companies, in contrast, the output is not attributable to a single unit, but to a number of units working together in the innovative process. Therefore, in exhibit 3.6 pharmaceutical innovation is presented as a system of double unity cells. Each cell depicts a clearly distinguishable phase in this process concluded by a milestone (M_0 - M_4), such as a patent at the end of the discovery (M_0) or a marketable drug at the end of the development phase (M_2).

Top management includes the general management, the Board of Directors, assisted by the R&D Management, the (sub)-Directors of R&D (for instance, the Directors of Discovery, Pharmaceutical Development, and Clinical Development), and the general R&D planning departments. The Board of Directors monitors the general environment (Katz and Kahn 1978) and sets the goals and objectives (G) which the research management has to meet. The research management (R) monitors the task environment and renders account of the progress of the different R&D projects to the top management (A). In the discovery phase, monitoring of the task environment includes the scanning of the international scientific network (Biemans 1992) on new and innovative ideas. The network includes, for instance, the biomedical departments in universities, health research institutes, biotechnological and other pharmaceutical companies (research network communication RNC, not depicted in exhibit 3.6). Gambardella (1992) concludes, in an extensive study of the relations between in-house scientific research and external scientific knowledge in the US pharmaceutical industry, that: '*To be part of a network, and to be able to effectively exploit the information that circulates in the network, has become even more valuable than being able to generate new knowledge autonomously.*' Monitoring of the task environment is also essential in the development phase. But here the primary goal is to broaden the contacts with physicians (the clients of the companies and the conductors of the clinical trials) and with other pharmaceutical companies, in order to provide a learning curve for the eventual marketing of the new product.

The pharmaceutical innovative process starts with strategic choices regarding

new drug development, based upon the market demand of patient populations and the therapeutic significance (market or demand pull), together with the scientific attainability (technology push). After general management has decided upon the indication area (product market combination) and has agreed upon the desired efficacy and side-effect profile of the new product, the innovative process starts. The research in the *discovery phase* starts with the drafting of a project proposal, evaluating the existing literature on the topic and selecting the theories which explain the possible working mechanisms of existing drugs or compounds and their effects on human tissue. Following the existing literature, compounds are synthesized with assumed therapeutic efficacy and tested for therapeutic activity (see also exhibit 3.2, embodiment of technology in artifact). A screening programme is set up, which consists of different tests to clarify the characteristics of the compounds. These tests use analytical and biological measures (for instance, antibody or specific enzyme reactions), and can be conducted in a pharmacological (for instance, blood platelets) or animal model of the human body or tissue. In recent years the screening and testing methods have improved tremendously. High capacity screening equipment has been elaborated, in which a large variety of structural variations of a molecule can be tested on therapeutic activity in a relatively short period of time. The use of high capacity screening equipment has made it possible to start a screening programme even if only very low activity was measured in the original compound. On the other hand, biomolecular modelling, supported by Nuclear Magnetic Resonance (NMR) and Mass Spectronomy to check for the structure identity and purity of the active compound, has made a more targeted approach possible. The structure of the active molecule is designed by computers to specifically attack the target (for instance an enzyme, a receptor, or a virus). In this rational drug design approach, smaller quantities of compounds have to be screened and tested. However, it is often impossible to design the attacking molecules beforehand, because insufficient information about the target is available. Therefore, this technique is often used to optimalize the active molecules, found by high capacity screening (lead optimalization). The discovery phase ends with the finding of the lead compound(s), which is in fact the prototype(s) which will be developed further in the development phase.

Although the use of new techniques has made the searching for the lead compound less fortuitous, the research work in the discovery phase is still highly unpredictable. In contrary to this, the toxicity and clinical testing in *pharmaceutical* and *clinical development* can be planned according to strict schedules.

Whereas the research work in pharmaceutical development is largely carried out in-house, the clinical testing is carried out in hospitals. After *registration and launch* onto the branded ethical drugs market, the *postmarketing surveillance* starts, aiming to improve the product (e.g. search for side-effects with low and moderate incidence, and improvements in drug delivery). If a new indication area is found, a learning loop occurs and specific clinical trials are conducted to get them registered. In box 3.2 an outline is given of the research activities in the different phases of the pharmaceutical R&D process.

Box 3.2

1 ***Discovery phase***
Before the discovery phase starts, strategic choices are made regarding the research projects which will be conducted, based upon an evaluation of therapeutic and commercial significance and scientific attainability. Typically, more than 10,000 chemical compounds in the high capacity screening approach and 1,000 in the rational drug design approach have to be synthesized and tested for therapeutic activity in pharmacological or animal models for a single 'hit'. The discovery phase ends with the finding of the lead compound.

2 ***Pharmaceutical development phase***
The pharmaceutical development phase starts with further pharmacological screening and characterization of the active substance. Pharmacokinetical research into degradation speed and acute and subacute toxicity along with mutagenicity tests are done, and the synthesis of the active substance for clinical testing is performed. Also a patent dossier is submitted to the authorities.

3 ***Clinical development phase***
In the clinical development phase I, dose-effect relationships, and duration of effects and side-effects, are tested in 20 to 30 healthy volunteers. In phase II the first controlled clinical trials are carried out on patients (about 100 to 200). In phase III the double blind randomized clinical trials are executed on a great number of patients (about 1,000 to 3,000) in hospitals in different countries, to demonstrate therapeutic efficacy and to establish contra-indications, side-effects with a relatively high incidence and optimal dosage. The phase IV surveillance to trace side-effects of drugs with low and moderate incidence also starts. This phase ends with the presentation of the registration dossiers to the authorities.

4 ***Registration and launch phase***
In this phase the test dossiers are examined by the authorities for approval for the drug to be launched onto the market. During the registration period the designing and building of the production

facilities and manufacturing process continues, the marketing plan is formulated and the training of the sales force starts. In recent years the period of time between registration and launch has increased, because of the increased requirements for admission into the governmental or private security reimbursement systems.

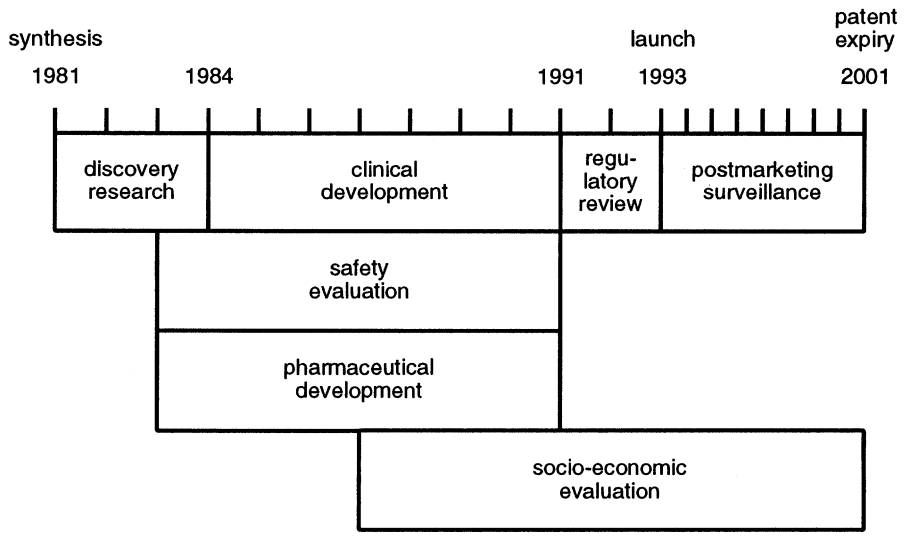
5 ***Postmarketing surveillance***
After the launch the postmarketing surveillance starts to trace the side-effects of drugs with low and moderate incidence, and to investigate the possibilities of broadening the indication area.

Sources: Ballance et al. 1992, Fitzgerald 1992, Taggart and Blaxter 1992, and this study.

The research units in the different phases of the research process differ considerably, depending on their tasks. The research units in the discovery phase show the largest resemblance to those in universities and institutes. With increasing frequency, research projects are not being aimed at the production of a new or modified drug, but at understanding the cause of a particular disease and towards the specific actions and side-effects of drugs on the human body and its individual tissues and organs. Driven in large part by scientific and technological advances that make basic biomedical research a key element in drug discovery and drug design, many pharmaceutical companies are increasing their funding of scientific research in universities and research institutes, a trend that is likely to expand in the coming years (Abbott et al. 1993). Taylor (1994) calculates the innovative pharmaceutical industry to spend 10% to 20% of the total R&D budget on academic collaboration and sponsoring. The departments in pharmaceutical development can be rather large in size (100 to 150 staff members). In clinical development, the designing and monitoring (case record control) of the clinical trials conducted in hospitals and in general practices, is the predominant task.

DiMasi et al. (1991) estimate the average total R&D cost per approved NCE as high as US$ 230 million. Therefore, it is not surprising that since the start of the 1980s pharmaceutical companies have increasingly used parallel development to reduce the time-to-market. At the same time that the clinical trials are executed, the long term biological testing for chronic and subchronic toxicity continues and the up-scaling for production starts. In order to limit the integration problems, lateral and cross-functional communication within project teams is intensified enormously. Researchers of different phases of the R&D process, and staff members of marketing and production, discuss the ongoing research projects on a regular basis (see exhibit 3.7).

Exhibit 3.7 PARALLEL PHARMACEUTICAL R&D PROCESS



source: Centre for Medicines Research 1993

Allen (in Bowers 1994) raised the question of whether the 'users' role in biomedical innovation is as important as in other forms of innovation. As a reply Bowers pointed at the charitable involvement in biomedical research, providing seed funding for innovative projects and plugging gaps left by the public sector. However, apparently Bowers is generalizing about the UK situation, where patient groups and their families are predominant in charities. In contrast, in Holland, for instance, only a few charities are dominated by 'users'.

3.4 CONCLUDING REMARKS

The theoretical foundation for this study has been laid in this Section. In the last two chapters the structure, behaviour and control situation in research organizations has been described, at first at the level of the institution as a whole, and then at the research unit level. The next Section focuses on the study design, relating management control to performance and effectiveness in the specific context of the three strata.

SECTION 2

STUDY DESIGN

CHAPTER 4

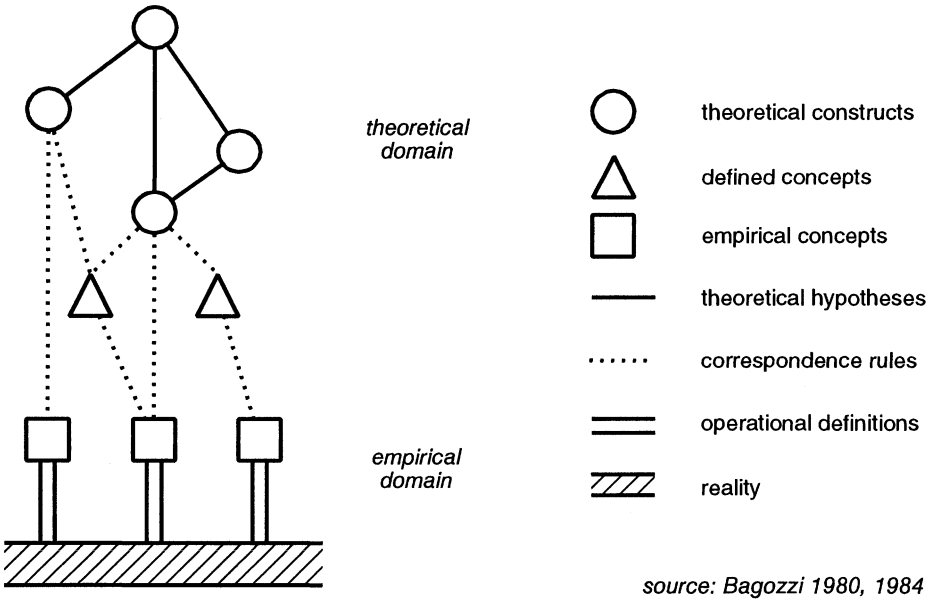
THEORY CONSTRUCTION

This Section focuses on the study design. In chapter 4 the principles of theory construction, as advocated by Bagozzi (1980, 1984), are used to present the theoretical concepts, hypotheses and operationalizations in one meaningful system, the triangular model. The defined and empirical concepts are deduced from the model of the double unity cell and are matched with the requirements for effective control to check for complete coverage of the relevant entities, objects and relations. Chapter 5 discusses the hypotheses deduced from the triangular model, relating different aspects of management control and the contingencies to performance and effectiveness. Chapter 6 concentrates on the methods used to relate the theoretical constructs to the observations in the empirical world. The attention is focused on the instruments of data collection, the sampling procedures, the inclusion criteria, the measures taken to provide for validity and the methods of data analysis.

4.1 THE STRUCTURE OF THEORY

As was depicted in § 1.3, the empirical study basically follows the (formal and informal) process of theory construction. According to Bagozzi (1980, 1984), the overriding objective in theory construction is to represent one's concepts, operationalizations, and propositions in one meaningful system that is both internally consistent and testable. In general, theory construction can be viewed from two different angles: as a process and as a structure. The process of theory construction involves the application of the principles of logic, the implementation of methods and procedures (e.g. the experimental method) and the observance of standards of conduct and evaluation. To these more formal processes such informal processes as creativity and decision-making must be added: these include conflict, debate and give-and-take between researchers, and social and political processes among groups and institutions.

Exhibit 4.1 THE STRUCTURE OF THEORY



source: Bagozzi 1980, 1984

Theory structure is taken to mean the concepts in a theory, the hypotheses made by the theory, the observations and measurements included in the theory, and the formal organization of all these elements in an overall representation (see exhibit 4.1). The theoretical constructs are related to each other through hypotheses (i.e., non-observational postulates or propositions). Theoretical constructs are not directly defined nor do they contain observational terms. Rather, theoretical constructs are implicitly defined by their relationships with other theoretical constructs, defined (derived) concepts, and/or empirical concepts. Defined or derived concepts obtain their meaning from empirical concepts. Empirical (also called observational or operational) concepts refer to events, or things recognizable in the world of experience. Empirical concepts obtain their meaning from operational definitions that specify procedures for measuring observations in the world of experience. The relationships connecting theoretical constructs to either defined or empirical concepts are called correspondence rules. Below, the structure of theory, as depicted in exhibit 4.1, will be used to link the theoretical constructs and the relationships of constructs to observations in this study.

4.2 THEORETICAL CONSTRUCTS AND HYPOTHESES

Equation 4.1 shows, in a mathematical form, the assumption, made in § 1.1, that performance and effectiveness can be considered as a function of management control and contingencies.

Equation 4.1 $$PE = f(MC, Cn) + \mu$$

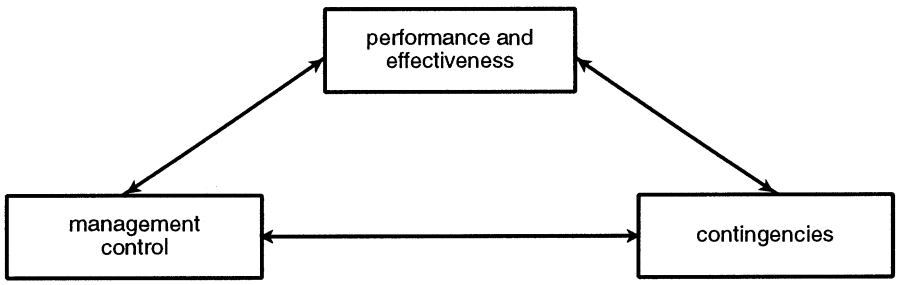
PE = Performance and Effectiveness, MC = Management Control, Cn = Contingencies, μ = residual variation

For clarity of presentation, no distinction is made between performance and effectiveness. Performance refers to the total output, such as the number of scientific papers of a research unit in universities or institutes, or the number of patents at the end of the discovery phase in industry. Effectiveness relates the output to the invested input (such as the number of papers or patents per researcher) and the apparent use of the output by the customer function (measured, for instance, by the number of citations per scientific paper). Management control is expected to have the largest impact on effectiveness, and the contingency size on performance (ten researchers can do more than one). The other contingencies are incorporated in the model to fine-tune for differences at the research unit level (see § 2.3). Other contingencies, such as the level of autonomy, the innovative strategy and the cultural background of the head office are used as bases for different cross-sections through the industrial study sample. The parameter μ reflects the residual variation, for instance that caused by the omission of certain parameters influencing performance and effectiveness, the natural response variability in the study sample, or errors in the measurements as a result of the imperfect correspondence between constructs and operationalizations.

Exhibit 4.2 shows the interdependency of the contingencies, management control and performance and effectiveness in a triangular model. Many examples of these interdependencies are given in the first three chapters. For instance, elements of system control, process control and external control, together with unit size and power, are related with performance and effectiveness in a simplified cause map of an amplifying and a stabilizing loop (see box 3.1, pg. 76). As was already stated in chapter 2, a cross-sectional design breaks into an ongoing process at a certain point in time. If the empirical results suggest, for example, that higher effectiveness of personnel policy affects performance

positively, it is possible - and even plausible - that the actual relationship might have a reverse or (more likely) a two-sided causality, with higher performance leading to a more positive assessment of the personnel policy situation and vice-versa. However, the triangular model does enable us to confirm or falsify the propositions made in this study. In addition, the model enables a comparison of the relative contribution of each independent variable in 'explaining' (in a strictly statistical sense) the variance in performance and effectiveness. Consequently, answers can be given to such questions as whether system control is more important than process control in relation to performance and effectiveness.

Exhibit 4.2 THE TRIANGULAR MODEL, RELATING MANAGEMENT CONTROL AND THE CONTINGENCIES WITH PERFORMANCE AND EFFECTIVENESS



4.3 THE DEFINED AND EMPIRICAL CONCEPTS

4.3.1 Management Control

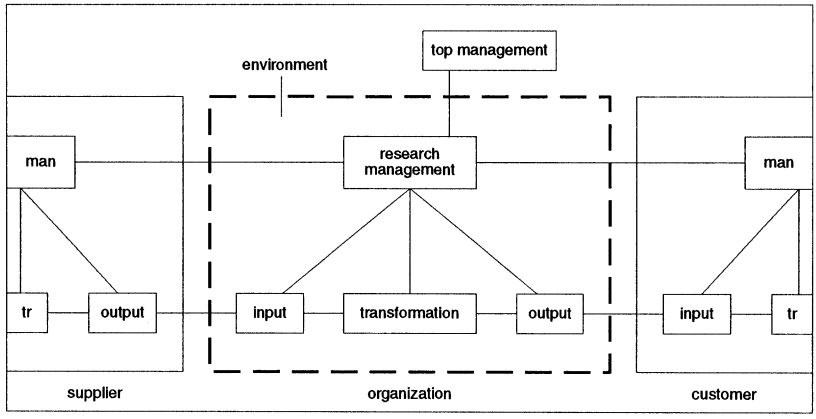
According to Volberda (1992), management control (MC) can be considered to be a function of organizational flexibility (OF) and control capacity (CC, see equation 4.2).

Equation 4.2 $MC = f(OF, CC) + \mu_1$

MC = Management control; OF = Organizational Flexibility; CC = Control Capacity; μ_1 = residual variation

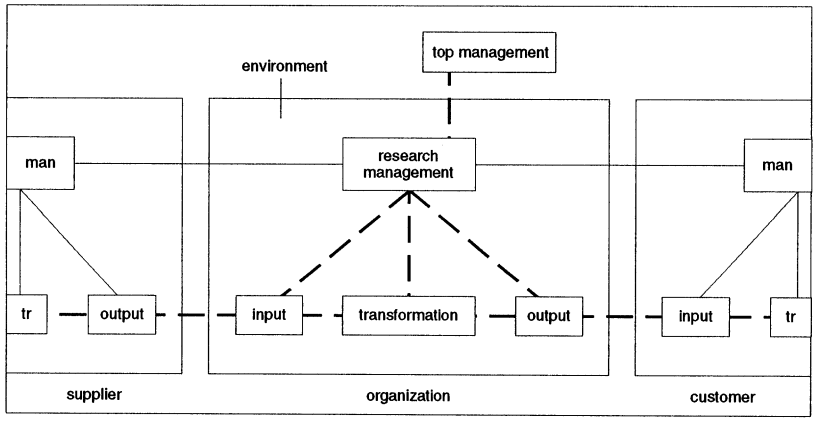
Exhibit 4.3 THE DOUBLE UNITY CELL IN RESEARCH ORGANIZATIONS

4.3a



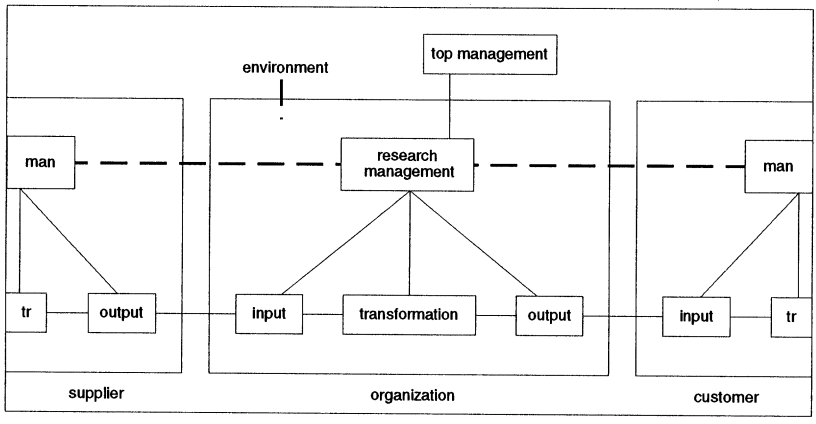
— · = system control

4.3b



— · = process control

4.3c



— · = external control

Organizational flexibility refers to the ability of the organization to adapt to changing situations at strategic, tactic and operational level, reflected, for instance, in the level of rigidity of the administrative rules. Operational flexibility refers to routine adaptations to changes in the environment, tactical flexibility to adaptive changes, and strategic flexibility to non-routine proactive changes of the organization. The extremes are to some extent comparable to a mechanistic versus an organic organization (Burns and Stalker 1961), or a bureaucratic versus a normative culture (Hofstede 1980). The control capacity refers to the quality and competence of the research management to achieve adaptations given the level of organizational flexibility. A highly competent research management may reach a high adaptation level, even if the organization is relatively inflexible, whereas a less competent research management may fail, even if the organization is highly flexible. In this study, 'subjective' views and judgements of the research management about items of organizational flexibility and control capacity have been combined with 'objective' measures, such as the number and scope of the existing incentives.

In order to assure complete coverage, the defined concepts of management control are deduced from the model of the double unity cell. Exhibit 4.3 shows that the defined concepts of management control (system, process and external control) together include all the relevant entities, objects and relations distinguished in the double unity cell model.

System control refers to the control over the personnel and material resources of the research unit (see exhibit 4.3[a]). Personnel control embraces the 'objective' quality of the reward system (organizational flexibility, number of material and immaterial incentives, career policy etc.), and the competence of the research management to react to changing situations (control capacity, e.g. pace and manner of conducting reorganizations). The challenge of research management is to create the conditions conducive to meeting the corporate goals of scientific performance as well as the scientist's need for satisfaction and motivation. Several examples of effective reward systems for researchers have been reported (e.g. Badawy 1988 and Kanter 1989). They all point at the importance of recognition, individual rewards, open communication, self-development and growth in enhancing the motivation and performance of R&D personnel. However, a study done by Gerpott (cited in Krüger 1994) pointed at the importance of pecuniary rewards in the German pharmaceutical industry. In this study the material and immaterial incentives as distinguished by Jauch (1976) are used to operationalize the 'objective' quality of

the reward system. Resources control refers to the level of control over the resources in the double unity cells. It is assessed by the subjective assessment of the adequacy of personnel and material resources, laboratory equipment, devices and space. In addition, administrative control is assessed, including the estimated pace of administrative procedures for appointments and procurement of equipment and the reallocation of a large part of the personnel and material resources to a new research line. In fact this is a reflection of the results of organizational flexibility and control capacity at the operational level.

Process control is divided into planning and research process communication (see exhibit 4.3[b]). The assessment of the importance of strategic, tactical and operational planning by the top management for everyday research work relates to the goal setting/accounting relationship between the research management and the top management (O and A in exhibit 3.7). Research process communication, in contrast, relates to the control capacity of the research management; the gradual transition from 'hands on' to 'hands off' control (relatively close to relatively loose monitoring). It is divided into the frequency of research (project team) meetings and the attendancy mix. The attendancy mix refers to the question of who, in general, is attending the research meetings: the head of the unit, the (senior) scientific staff, the support staff, as well as researchers from adjacent laboratories or staff members from other R&D phases and/or marketing and production in industry (lateral and cross-functional communication, the communication relationships C in exhibit 3.7).

External control refers to the communication with the R&D environment and with the supplier and customer function and is assessed by international and contractor communication (see exhibit 4.3[c]). International communication refers to the position of the research unit in the international scientific network. Science is sometimes referred to as competitive cooperation (Hull 1988). Cooperation among scientists has always occurred, either initiated spontaneously by researchers, or encouraged by research organizations who believe that collaborative work is more productive than individual research. International communication is measured by the frequency of international contacts with scientists, physicians and, in the case of industry, also colleagues from other companies, for instance at congresses and workshops. Contractor communication is measured by the frequency of contacts with industrial and governmental contractors (universities and institutes only). Exhibit 4.4 outlines the defined and empirical concepts of management control.

Exhibit 4.4 THE DEFINED AND EMPIRICAL CONCEPTS TOGETHER CONSTITUTING THE THEORETICAL CONSTRUCT OF MANAGEMENT CONTROL

defined concepts level 1	defined concepts level 2	empirical concepts
system control	*personnel control*	• effectiveness personnel policy
	resources control	• adequacy of resources • administrative control
process control	*planning*	• planning
	research process communication	• frequency • attendancy mix
external control	*international communication*	• international communication
	contractor communication	• contractor communication

4.3.2 Contingencies

Bresser and Dunbar (1986) have shown that the contingencies, as distinguished by Mintzberg (1979, see also § 2.3), supply sufficient coverage and decomposing ability to study the similarities and differences between high and low paradigm disciplines in academia. Because it can be assumed that the research environment in institutes is not so different from that in academia, Mintzberg's contingencies are used to study the situation-dependent factors in universities and institutes. Namely, the history-related variables of organizational age and size, the technical system characteristics (technology) and the power balance between the environment and the administration (power). The environmental contingencies (such as uncertainty, complexity and dynamics),

and the structural power relations (such as public or private ownership) are used as a framework for the comparison of the strata. In universities, time-allocation has been added as a contingency, being specifically relevant for distinguishing between preclinical and paraclinical units with clinical units.

The concept of attaining a positive power balance is very similar to the concept of attaining system control. In both concepts the controlling system tries to avoid dependency (Pfeffer and Salancik 1978) or tries to dominate the environment by gaining competitive advantage (Porter 1985). Companies encounter their main threats in the environment. A company will try to get a competitive advantage in order to keep up with or to dominate its competitors. In universities especially, the power balance 'in-house' is equally important. Possible ways of attaining a positive power balance will be assessed under the contingency 'power'. The internal power balance is of comparably less importance in industry. Therefore, power is only assessed under system control. Organizational age is not measured in industry, because the innovative process is conducted in a number of laboratories with quite different histories. Other contingencies, as the cultural background of the head office (Anglo-American or continental European), autonomy or dependency (the 'pure play pharmaceuticals' or the pharmaceutical divisions of large chemical conglomerates) and the R&D orientation (radical or incremental), are used as bases for different cross-sections of the industrial study sample. Exhibit 4.5 outlines the defined and empirical concepts of the contingencies.

4.3.3 Performance and Effectiveness

For control to be effective it is important to have an insight into the performance and effectiveness parameters. In production they are normally clear (plant A produces more products than plant B). In professional bureaucracies this is often more difficult. The results of scientific research can only be measured after some time, and the long-term impact is extremely difficult to ascertain. In pharmaceutical industry too, the results of the efforts of a discovery department can only be judged after a decade or more. Therefore, intermediate indicators are used, for instance publication counts in universities, and separate measures for discovery and development in industry. When the associations of management control and the contingencies with the different performance and effectiveness measures point in the same direction,

Exhibit 4.5 DEFINED AND EMPIRICAL CONCEPTS TOGETHER CONSTITUTING THE THEORETICAL CONSTRUCT OF THE CONTINGENCIES

defined concepts	empirical concepts
size	• sales • R&D expenditure • total staff • research staff • project size
time-allocation	• research • education • management and acquisition • clinical practice • other
organizational age	• research experience • management experience
technology	• technological support capacity • material resources • percentage discovery
power	• signatory authorization capacity • external funding • junior to senior scientist rate

this enhances confidence in the reliability of the results. This method of converging a number of imperfect indicators (Irvine and Martin 1985), reflecting different aspects of performance and effectiveness, is called 'triangulation' (after Webb et al. 1966, this was an additional reason to call the theoretical model used in this study, the triangular model). It is comparable with the concept of 'convergent validity' in Campbell and Fiske's (1959) multitrait-multimethod approach.

In universities and institutes a division is made between research and user

performance. Research performance refers to the output directed to the scientific community. It is measured by the number of papers published in international scientific journals, and the number of PhD theses produced (both achievement indicators). This is combined with the credibility the research unit wins from the scientific community, as measured by the number of papers received from scientific journals for peer review, and the participation on Editorial Boards by the senior scientific staff (reputational and/or personal indicators). The user performance refers to the output directed to users, measured by the number of papers in journals for physicians and reports for governmental or industrial contractors (in institutes especially). Effectiveness is assessed by the number of papers published per full-time equivalent scientific staff member and by the apparent use of the research results by the scientific audience (effective scientific output, Hazeu 1989, see § 3.3), as measured by the citation score.

In industry performance and effectiveness are measured at the level of the research process (innovative performance and effectiveness), and at the level of the company as a whole (industrial performance and effectiveness). Innovative performance and effectiveness primarily relates to the control capacity of the research management, and industrial performance and effectiveness to organizational flexibility. The number of patents per investment in discovery is used as a measure for innovative performance and effectiveness in the discovery phase and the length of the developmental process as a measure for the development phase. Because drugs are often relatively easily imitated by competitors, patents are a highly significant form of resources control, and thus a very important source of market power for the companies holding them. However, there are a number of problems involved in the use of patent statistics, for instance the possible difference in patenting policy (timing and scope) between companies (Basberg 1987 and Pavitt 1988), the difference between leading (real innovative), defensive and follow on (me-too) patenting, as well as the increased importance of licensing-in and licensing-out in order to attain a complete patent portfolio (to buy the right to use a patent from or to sell this right to a competitor, Fitzgerald 1992, Gambardella 1992 and Valle and Gambardella 1993). Paragraph 6.2.3 addresses these problems. As was shown in § 3.3.2, the developmental process takes many years. The companies which succeed in reducing the development time will considerably improve their time-to-market and therefore their profitability and competitive position (e.g. Redwood 1987 and Taggart 1993).

Exhibit 4.6 DEFINED AND EMPIRICAL CONCEPTS TOGETHER CONSTITUTING THE THEORETICAL CONSTRUCT OF PERFORMANCE AND EFFECTIVENESS

defined concepts	empirical concepts
research performance and effectiveness	• scientific publications • number of PhDs • citation score • scientific credibility
user performance and effectiveness	• physician papers • contractor papers • user papers
innovative performance and effectiveness	• number of patents • length of development
industrial performance and effectiveness	• operating profit margin
general performance and effectiveness	• annual growth rate

Innovation, although essential, is not enough to reach the goal of attaining long-term profitability. It is obvious that without an adequate marketing and sales force an innovative drug will never reach its full profit potential. Vos (1989) analyzed two companies which jointly developed a drug. The successive marketing effort was separately done. The firm with the best R&D-marketing interface clearly got the highest return on investment. Therefore, the industrial indicators (measures of industrial efficiency), the annual growth rate and the operating profit margin, are used in this study. Exhibit 4.6 outlines the defined and empirical concepts of performance and effectiveness.

4.4 CHECK ON COMPLETENESS

International literature and information obtained from experts in the field of biomedical research yielded 38 factors which are related to performance and effectiveness. Exhibit 4.7 shows that most of these factors are covered by the empirical concepts of management control and the contingencies. Elements related to research culture are implicitly referred to under personnel control.

Exhibit 4.7 LINKAGE OF THE EMPIRICAL CONCEPTS OF MANAGEMENT CONTROL AND THE CONTIGENCIES TO THE RELEVANT LITERATURE

contingencies	literature
size, project size	s,p,g,j
time-allocation	s,p,g
organizational age	s,a
technology	g,j
power	j

management control	literature
system control	
personnel control	v,j
resources control	s,a
process control	
planning	a
research process comm.	s,a
external control	
international comm.	s,a
contractor comm.	-

s = Spangenberg 1989
p = Pelz and Andrews 1976
a = Andrews 1979
v = van der Ven and Ferry 1980
g = Graves, Marchand and Thompson 1982
j = Johnes 1988

comm. = communication

In order to check whether the defined and empirical concepts of management control provide sufficient descriptive coverage, they are compared with the requirements for effective control (see § 2.4.2)

- ***Goal formulation capacity*** is assessed under planning, the strategic, tactical and operational goal formulation and the division of the personnel and material means over the different research projects.
- The variables which give insight into the ***model*** all have reference to the structure and behaviour of the target system (Kramer and de

Exhibit 4.8 CONFRONTATION OF THE CHOICES AND TASKS OF THE RESEARCH MANAGEMENT WITH THE VARIABLES OF MANAGEMENT CONTROL

phase 1: idea generation	
1	choice of research field (process control: planning)
phase 2: planning and design	
2	choice of research questions (process control: planning)
3	choice of variables and number of data (process control: planning)
phase 3: acquisition	
4	resources acquisition (system control: adequacy of resources)
phase 4: organization	
5	definition of tasks (process control: planning)
6	select people to tasks (process control: planning)
7	draw up supervision schedule (learning loops; process control: research process communication)
8	communication of research activities to outside agencies (external control)
phase 5: production	
9	control of quality standards (supervision: research process control)
10	within budget and time (system control: administrative control)
phase 6: output dissemination	
11	dissemination (external control)
12	utilization (external control)
13	evaluation (research process control: double loop learning)

Smit 1982). The empirical concepts measuring the degree of administrative control give an indication of the level of flexibility, and thereby

the structure and behaviour, of the target system.

- Attaining ***information*** about the research process and the task environment is essential. These two elements are thought to pose the greatest degree of uncertainty for an organization. Information about the scientific community and the contractors is obtained by international and contractor communication. Information about the (system of) value adding learning loop(s) is obtained by research process communication.
- ***The measures of control*** regarding the personnel and resources of the research unit can be found under system control (the effectiveness of personnel policy, the adequacy of the resources, and the pace of resource allocation). The measures of control of the (system of) value adding loop(s) can be found under research process communication and the intensity of international and contractor communication. Each measure of control also relates to one of the other requirements for effective control, because the structure and behaviour determining characters of the model also sets limits on the number and nature of the available measures of control,

Exhibit 4.8 confronts the empirical concepts of management control with the tasks of and choices to be taken by the research management (Mason 1979). Most of these are related to process control, the choices and tasks 1, 2, 3, 5, and 6 refer to different aspects of the planning of the research process; 7, 9, and 13 refer to research process communication, the building of a supervision structure to enhance single-loop and double-loop learning; and 8, 11, and 12 refer to external control, the communication of research activities and results to outside agencies (e.g. funding agencies, the scientific community and the community of users). Finally, the choices and tasks 4, and 10 refer to elements of system control, the acquisition and allocation of resources and administrative control, respectively.

4.5 CONCLUDING REMARKS

In this chapter the triangular model is introduced, which relates the empirical concepts of the contingencies and management control with performance and effectiveness. Based on the evidence presented in this chapter, it can be concluded that the contingencies and management control sufficiently cover the

relevant entities, objects and relations to achieve effective control. In the next chapter the hypotheses based on the triangular model are formulated. They predict the expected differences in the management control situation between high and low performers on the one hand, and between the strata on the other. Following this, the hypotheses regarding the contingencies are drawn up and different cross-sections of the industrial study sample are made.

CHAPTER 5

HYPOTHESES

This chapter concentrates on the hypotheses concerning the relationships between management control and the contingencies on the one hand, and performance and effectiveness on the other. In § 5.1 the main hypothesis will be elaborated for the three strata, taking into account their specific goals and objectives, the profit or not-for-profit background of the organizations and the level of task uncertainty. Paragraph 5.2 concentrates on the hypotheses concerning the contingencies, and § 5.3 examines different cross-sections of the industrial study sample. Companies with a more radical R&D orientation are compared with those with those with a more incremental orientation, autonomous pharmaceutical companies (the pure play pharmaceuticals) are compared with 'dependent' pharmaceutical divisions of chemical conglomerates, and Anglo-American companies are compared with continental European ones. This chapter ends with an overview over the different hypotheses.

5.1 MANAGEMENT CONTROL

As was already stated in § 1.2, the following three research questions relate management control to R&D performance and effectiveness:

1 *Do certain aspects of management control affect R&D performance and effectiveness in a positive way?*
2 *If so, to what extent do these aspects affect R&D performance and effectiveness, and which instruments should be used to increase R&D performance and effectiveness?*
3 *What is the impact of the organizational setting (universities, institutes and company laboratories) on this relationship?*

The basic idea behind this study is that management control, being the resultant of organizational flexibility and control capacity, is fundamental for success in biomedical research and pharmaceutical innovation. Hypothesis 1 (the

main hypothesis and generalization, see § 1.2) is underlying all the other hypotheses concerning management control, and supposes the following answer to *research question 1*:

Hypothesis 1
A number of management control variables will be judged more positively by the research management in the more-than-average performers than in the less-than-average performers. If replication of the study design in the three strata yields consistent results, this enhances confidence in the generalizibility of the findings.

Not all factors of management control will be equally important. One of the objectives of this study is to indicate which are the most critical for success in biomedical research (*research question 2*). In chapter 2, three important sources of differentiation between the three strata were distinguished. There are differences originating from:

- the objectives and goals,
- the profit or not-for-profit background of the organizations,
- the environmental and task uncertainty.

In this paragraph these sources of differentiation and their expected influence on the relative strength of management control in the three strata will be discussed (*research question 3*).

5.1.1 The Objectives and Goals

In Bresser and Dunbar's (1986) study the objectives and goals of the different research units were more or less the same, all belonging to the academic world. The objectives and goals in the three strata, however, are quite different. The main objective of universities is to produce and disseminate scientific and technical knowledge. This objective is met by doing fundamental research and by teaching at graduate and post graduate level. In addition, public services are performed (university museums, botanic gardens etc.). One of the most important of these services is patient care in academic hospitals. Research, education and patient care are equally important. One can rightly argue that a professor, by writing a university textbook, which inspires hundreds

of students, has contributed more to the advancement of his/her discipline than his/her colleague who writes an article for a scientific audience. Patient are also more interested in the medical skills of the physician than in his/her scientific prestige. The reader should keep in mind that a department which performs poorly in research might well be one of the leading surgery or education departments in the Netherlands. The main objective of institutes is to produce research services for governmental or industrial contractors, or for user groups, such as physicians and patients. The main reason for the existence of the R&D function in a company is to produce '*marketable knowledge*' (Veblen 1957 [1918] first used this term for universities). An industrial R&D laboratory has to direct itself to the commercial objectives of a company. For the company it does not matter whether the research on which it is based is of a high standard or not. In exhibit 5.1 the different objectives of universities, institutes and companies are summarized.

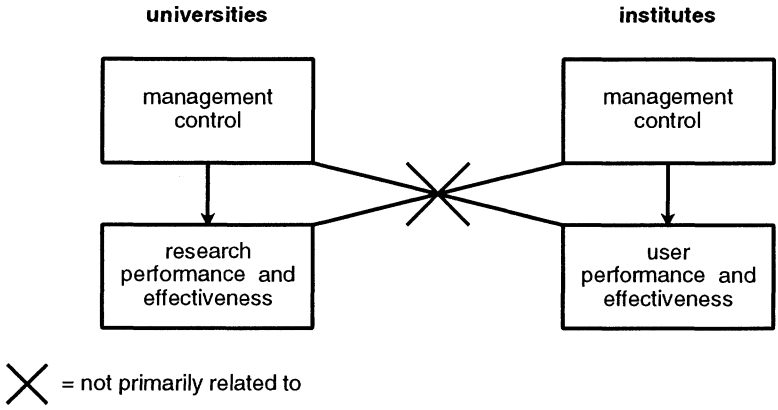
Exhibit 5.1 DIFFERENCES IN THE OBJECTIVES OF UNIVERSITIES, INSTITUTES AND COMPANIES

	universities		institutes	companies
	pre/para-clinical units	clinical units		
research	x	x	-	-
education	x	x	-	-
public services	-	x	x	-
marketable knowledge	-	-	-	x

In this study the performance and effectiveness measures are chosen in such a way that they can be regarded as reflecting the primary goals and objectives of the organizations (research performance and effectiveness in universities, user performance and effectiveness in institutes, and innovative and industrial performance and effectiveness in companies). Due to the fact that in both universities and institutes the same set of performance and effectiveness measures are used, performance and effectiveness measures are also applied, which can be considered as reflecting secondary goals and objectives, such as user performance and effectiveness in universities and research performance and effectiveness in institutes. It is expected that the performance and effectiveness measures which reflect the primary goals and objectives of the orga-

nization will be strongly and similarly related to management control across the strata, whereas the performance and effectiveness variables which reflect the secondary goals and objectives will be weakly, and not uniformly, related to management control. These expectations can be transformed into the following sub-hypothesis of hypothesis 1. Exhibit 5.2 depicts hypothesis 1.1 in terms of relationships between theoretical constructs.

Exhibit 5.2 THE SUPPOSED RELATIONSHIPS OF MANAGEMENT CONTROL WITH PERFORMANCE AND EFFECTIVENESS IN UNIVERSITIES AND INSTITUTES



Hypothesis 1.1
As regards the performance and effectiveness measures which reflect the primary (secondary) goals and objectives of the organization, strong and similar (weak and different) relationships with management control will be found across the strata.

It is possible that the management control situation in some of the organizations is 'objectively' better than in others. Perhaps there are universities or institutes which really get the best out of their scientific staff by increasing their organizational flexibility, by limiting the bureaucratic constraints and improving the human resources situation. Such universities or institutes are likely to attract the best researchers. If this is the case, it would be expected to find an uneven distribution of high-quality research units among the different universities and institutes. Therefore, the results are analyzed at the level of the organization as a whole. Because of the high level of aggregation only a

qualitative analysis was carried out (see § 9.6).

Hypothesis 1.2
An uneven distribution of high-quality research units over the different universities and institutes may indicate a difference in organizational flexibility.

In contrast to universities and (although to a lesser extent) institutes, the variables of system control in the more vertically integrated pharmaceutical companies are expected to be more directly related to the objectives and goals of the top management, and thus to organizational flexibility, than to the control capacity of the research management. It is therefore expected that these variables will be primarily associated with the industrial performance and effectiveness variables, which reflect the performance and effectiveness of the organization as a whole. Most variables of process and external control, however, are expected to reflect the control capacity of the research management. They are therefore expected to be primarily associated with innovative performance and effectiveness.

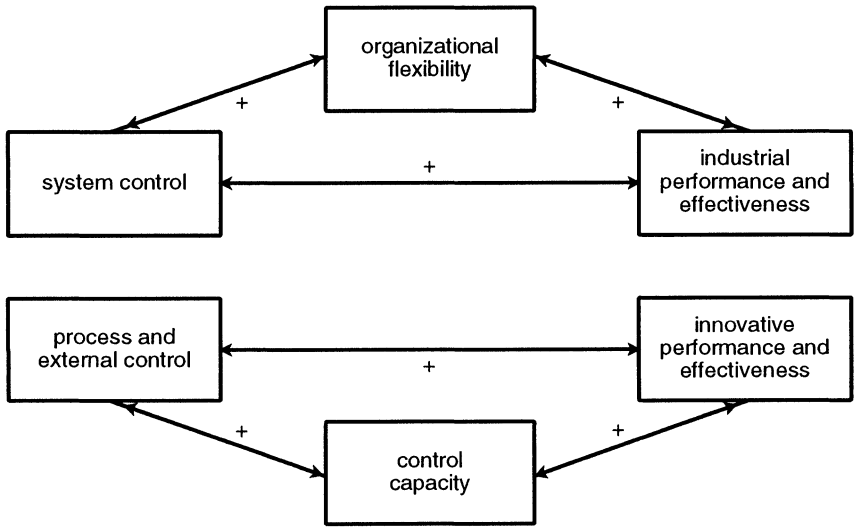
Hypothesis 1.3
System control is expected to be more closely associated with industrial performance and effectiveness, and process and external control with innovative performance and effectiveness (see exhibit 5.3).

5.1.2 Profit versus Not-For-Profit

All universities and most institutes are part of the public sector, and therefore subject to state (e.g. personnel, purchasing, and construction) regulations and budget management restrictions. The personnel complement is largely fixed through tenure and contractual provisions. Life-time appointment, combined with a strong legal status, limits the possibilities of decisive intervention in situations of conflict. As was shown in chapter 2, additional problems arise in universities because of the large horizontal and vertical decentralization and the resulting loose coupling. Short-term reallocation of resources is constrained by conflicting interests within the faculty or between the different organizational levels. The yearly planning begins with the largest share of the budget precommitted, so that even when resources are available certain expenditures are impossible. In the more centralized institutes the different de-

partments have fewer possibilities to delay short-term reallocations. Furthermore, the great task specialization in universities makes it difficult to reallocate scientific personnel to another specialist area. Therefore, management instruments such as job rotation often cannot be used. Also, with the average salary level in universities and institutes being significantly lower than in industry, it is more difficult to build up a competent staff, from the earnings point of view. Therefore, work-intrinsic motivation ('spiritual income') is especially important in universities. Seen from the angle of income it is interesting that Spangenberg (1989) discovered that the researchers in the outstanding research units in clinical medicine earned considerably lower than their colleagues in the less performing ones, spending their 'after-office hours' on research instead of on more profitable private clinical practice.

Exhibit 5.3 THE SUPPOSED RELATIONSHIPS OF MANAGEMENT CONTROL WITH PERFORMANCE AND EFFECTIVENESS IN INDUSTRY



+ = positive relationship

The accountability, the relationship between objectives and performance, is most clear in companies. As Besse (1973, p. 110) states: '*In a business organization there is always one quantitative measure of performance ... the rate of earnings on the capital invested. Because dollar profits are both the objective of the activity and the measure of performance, the operation of the company is*

keyed to accountability for the profit achieved.' Although it is too simple to say that the main objective of a business enterprise is to make money for long-term survival on the market, this assertion contains an underlying truth that to a great extent provides a clarity of purpose and an integration of management that are absent in universities and institutes. The feedback on a reduction in results is very direct. The operating profit margin is very compelling, because of the permanent threat of being overreached by a competitor. In companies, administration and professionals have corresponding interests: maintaining the profitability and thereby the competitive position of the company. The convergent goals, together with the interdependency, prevents competition between units getting out of control. The above considerations lead us to expect that the relative strength of system control will be highest in pharmaceutical companies and lowest in universities, with the institutes taking up an intermediate position (see also exhibit 2.5, pg. 58).

Hypothesis 1.4
The assessment of system control will be most positive in industry, and least positive in universities, with the institutes taking up an intermediate position.

Comparing different companies in industry, the knowledge about and the degree to which the laboratory management can meet the needs and wishes of the scientific staff may be one of the factors determining the level of system control. In § 5.3.2 which compares autonomy and dependency will be returned to this point.

5.1.3 Environmental and Task Uncertainty

Environmental and task uncertainty is generally assumed to decrease as activities pass through the sequence basic research, applied research and experimental development (Cohen and March 1974, Zeldenrust, 1989). The research activities are thought to be rather uncertain, especially in basic research, in the sense that task outcomes are not repetitive and predictable. Therefore, scientific research is said to be conducted in a sea of unforseen contingencies. To lower the level of environmental and task uncertainty, university researchers must keep in constant communication with colleagues, not only in-house but also national and, especially, with international colleagues, to keep up with the state-of-the-art in their research field. It is expected that

the scientific staff in the best research units in our sample will be fully integrated in the international scientific network and will show the highest frequency of international communication (the 'cosmopolitans' in terms of Gouldner 1957, see § 5.2.5).

But contrary to this dominant view, the high environmental and task uncertainty may not be such a disadvantage. This is because, in academic research negative results are also important in theory building (falsification principle), and may lead to new theoretical constructs or sometimes even to new paradigms. Furthermore, in institutes and in the discovery phase in industry, environmental and task uncertainty are also relatively high. Mayntz (1985) considers the external environment of institutes even as more hostile than that of universities (see § 2.5.2). The fact that outside contractors expect value for money in terms of applicable concepts and artifacts, can put a lot of pressure on the institute's management. It is therefore expected that contractor communication is of great importance in institutes. Mayntz indicated that the research directors in her sample used most of their time outside the institute negotiating with contractors and funding agencies. Therefore, it is expected that much emphasis is placed at contractor communication in the best performing research units in institutes.

Although the use of new techniques has made the searching for the lead compound less fortuitous, the research activities in the discovery phase are still highly unpredictable (see § 3.2.2). The scientific staff may try to reduce the environmental and task uncertainty by intensive in-house and R&D network communication. It is expected that especially the researchers in the best performing discovery departments will put a lot of effort into R&D network communication, being most eager to attain innovative ideas. A survey of general and R&D managers of 39 companies in different industries in Holland revealed that twice as many innovative ideas came from the external network (designers, innovators, universities and research institutes) than from the internal organization (Smak 1990). An interesting example of the opportunities for scientists in the discovery phase to obtain new and innovative ideas by R&D network communication was also given in box 2.1 (see pg. 39). In-house communication must also be intensive to get the best alignment of the different projects in the discovery phase. International communication is also important in clinical development. But here the primary goal is to broaden the contacts with physicians, the customers of the companies and the gatekeepers for the clinical trials, and also to broaden the communication network

with other pharmaceutical companies, to provide a learning curve for the eventual marketing of a new product.

In contrast to the discovery phase, the research activities in pharmaceutical and clinical development are of a more repetitive and predictable nature, and can be planned according to strict schedules. There is always a certain tension between the rigidity of planning and the creativity of the researcher. It is therefore expected that in the most successful development departments the scientific staff is more committed to the necessities of planning and will therefore react more positively to planning directives. Especially in late pharmaceutical and clinical development, intensive cross-functional communication with marketing and production is thought to be essential to improve the time-to-market. It is therefore expected that cross-functional communication will be most intensive in the best performing development departments. This leads to the following hypotheses:

Hypothesis 1.5
High performers will show a higher level of external control than low performers. In universities and in pharmaceutical innovation this will be made apparent through more frequent international communication, and in institutes in more frequent contractor communication as well.

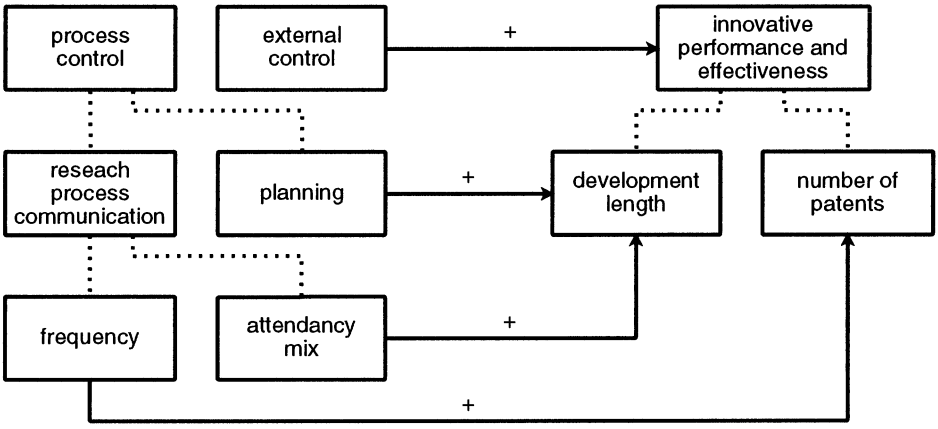
Hypothesis 1.6
In the best performing development departments, (1) the scientific staff will put more emphasis on the importance of planning, (2) the level of cross-functional communication with marketing and production (measured as the attendancy mix) will be higher, and (3) the international communication will be more frequent (see exhibit 5.4).

5.2 THE CONTINGENCIES

5.2.1 Size, Economies of Scale and Threshold Level

Size can be considered to be by far the most important contingency in relation to performance. But does larger size also lead to higher effectiveness? In other words, can 'economies of scale' be observed in biomedical research and pharmaceutical innovation?

Exhibit 5.4 THE SUPPOSED RELATIONSHIPS OF EXTERNAL CONTROL WITH INNOVATIVE PERFORMANCE AND EFFECTIVENESS



+ = positive relationship

Economies of scale are common in industrial production. Scale economies permit relatively large producers to manufacture and market their products at lower average cost per unit than relatively small producers. The principal basis of scale economics is specialization or the division of labour. Special machinery can be designed to perform special tasks with considerable savings in time and labour. Another benefit derives from reserves. A firm which is anxious to maintain continuity, must hold equipment in reserve against machine breakdown or to meet fluctuations in demand. A larger firm can hold a relatively smaller portion of its capacity in reserve than a smaller one, and can spread the overhead costs over a larger range of products. From a dynamic point of view, the 'economies of scale' principle is related to the phenomenon of the learning curve. When a new product is introduced the cost per unit is initially high, probably too high for the small producer, but as cumulative output increases, the cost per unit output falls. Of course, the decline in costs per unit cannot continue indefinitely. In nearly all production and distribution operations, the realization of scale economics is subject to diminishing returns. For instance, difficulties in controlling large scale production with frequent breakdowns or careless work might overwhelm the savings due to high volume.

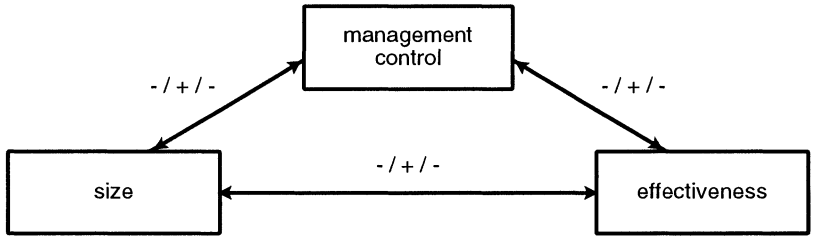
Taggart (1993) concludes, on the basis of different studies, that a minimum investment in pharmaceutical R&D is needed, beneath which it is difficult to achieve satisfactory returns on investment. Above this level the picture is not quite so clear. A number of researchers (e.g. Angilley, 1973 and Shrieves, 1978) conclude that above this threshold increasing returns on investment are obtained through pharmaceutical innovation. Contrary to this, Soete (1979), on the basis of a more detailed database, points at a tendency towards decreasing returns on investment. In a recent paper, Graves and Langowitz (1993) also showed diminishing returns to increasing size of R&D expenditures. In their study, however, biotechnological firms were compared with pharmaceutical firms. The large differences in size and markets (mostly diagnostics in biotechnology) make it difficult to compare them. As was shown in chapter 1, large mergers have occurred in the pharmaceutical industry in recent years in order to attain cost leadership and 'economies of scale' in marketing and production. This book will analyze whether this tendency towards concentration is also valuable from the perspective of effectiveness in pharmaceutical innovation.

A number of researchers (e.g. Spangenberg 1989 for clinical medicine and economics) claim to have found 'economies of scale' in academic organizations. However, larger size has been criticized for creating a poor research environment (e.g. Stroup 1966). In addition, a number of studies have actually shown a negative association between size and effectiveness (e.g. Bresser and Dunbar 1986). The much greater horizontal and vertical integration of units in institutes when compared to universities means that the size of the unit in institutes can only to a small extent be attributed to the work of the research unit management itself. Therefore, the hypotheses formulated below can only be tested in universities.

There is some literature about the optimum size of a research unit, but no information exists concerning the minimum size. Still, it is an important factor in system design. In this study it is hypothesized that a threshold level exists, below which the primary tasks of the research management (research, education and clinical practice) take so much time that time for acquisition is lacking. It is therefore expected to find a lower annual growth rate (or even a negative one) in smaller research units than in larger ones. Smaller unit size can also be the result of poor quality, or the result of the professor's policy of keeping the unit 'small but beautiful'. Therefore, no hypothesis can be made about the research effectiveness of these small units compared to larger ones.

Above this threshold level, larger size may improve the number and range of management tools and thereby enlarge the control capacity of the research management. Until a certain optimum level, larger size may positively influence personnel control (the number of incentives is larger and the possibilities of separating staff members in case of conflict is greater); resources control (there are fewer conflicts over limited resources), planning (it is easier to reallocate personnel means between research projects, or to start a new research line), research process communication (there is a larger variation in expertise, know-how etc.) and external control (there is a larger budget to send researchers to congresses abroad and there is relatively more time available for contractor communication) leading to higher performance and effectiveness and accelerated growth (the amplifying loop A in box 3.1 on pg. 39). Above this optimum level, 'economies of scale' may turn into 'dis-economies of scale' because the span of control of the head of the unit may put limits on the size of the unit because of coordination problems due to weaker control capacity (the stabilizing loop B in box 3.1, Mayntz 1985, see § 3.3.1).

Exhibit 5.5 THE SUPPOSED RELATIONSHIP BETWEEN SIZE, MANAGEMENT CONTROL AND PERFORMANCE AND EFFECTIVENESS



- / + / - = below threshold level a negative relationship, between threshold and optimum level a positive relationship and above optimum level a negative relationship

Hypothesis 2.1

A certain threshold level will exist, beneath which pharmaceutical innovation will be difficult to maintain, and university research units will be less viable. Above this level economies of scale will appear, with increasing research and innovative performance and effectiveness. This will continue until an optimum level is reached, above which the effectiveness will decline.

5.2.2 Project Size, Programmatic Homogeneity

Mayntz (1985) indicates that one of the most difficult tasks of the head of a research unit is to maintain programmatic homogeneity. Programmatic homogeneity refers to the question of whether the scientific staff is working on a coherent research programme, which consists of a limited number of more general themes, or whether the research programme is split up into many relatively small research projects. A unit with a high number of relatively small projects has the advantage of spreading of risk. Some of the research lines may lead to interesting break-throughs, which otherwise would never have been found. The disadvantages, however, are obvious. Such a unit cannot profit from 'economies of scale', both in terms of research equipment and in terms of organizational learning. Building up expertise within the unit, where the one researcher or research group profits from the insights obtained by others, is more problematic. However, above a certain level the disadvantage of insufficient risk-spreading may counteract the 'economies of scale'.

In this study, the relative size of the largest research project is used as a measure for programmatic homogeneity. One should realize, that different demarcations between research projects are possible. One can demarcate according to individual PhD curricula, according to research lines (a number of more or less integrated research projects under the supervision of one or more senior scientists) or according to funding. Because of the aim to assess programmatic homogeneity, the demarcation according to research lines has been chosen.

Sub-hypothesis, size 2.1.1
The projects in the research units will show an optimum size, above which the effectiveness will decline.

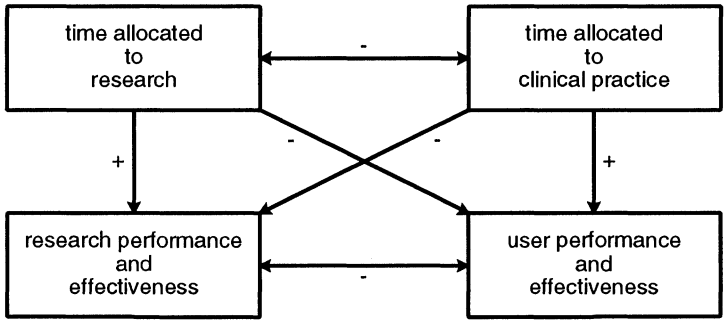
5.2.3 Time-Allocation, Research versus Clinical Practice

It is possible that the performance and effectiveness of a research unit is largely determined by the non-research tasks, the most important of these being patient care in clinical units. It is expected that researchers working in a clinical setting will present more papers of interest for physicians. Spangenberg (1989) found a positive relationship between research performance and

the time spent on research, and a negative one between research performance and the time spent on clinical practice outside the hospital. Therefore it can be expected, that:

Hypothesis 2.2
The time allocated to research and clinical practice will show an inverse relationship. A positive association will be found between the time allocated to research and research effectiveness and between the time allocated to clinical practice and user effectiveness.

Exhibit 5.6 THE SUPPOSED RELATIONSHIPS OF TIME-ALLOCATION WITH PERFORMANCE AND EFFECTIVENESS



+ = positive relationship
- = negative relationship

5.2.4 Age, The Life Cycle Concept

The analogy of the life cycle of organisms (birth, growth, maturity and decay) is often used to describe the development and decay of organizations, products or markets in management literature. Confirming evidence that the life cycle concept can be applied to research has been provided by Allen (1977) for industrial innovation, who found the highest effectiveness in the first years after the appointment of a research director. If the life cycle concept is applied to academic research (see box 5.1) it can be postulated that in the years following the appointment of a professor the research unit will grow vigorously, both in size and performance, reaching a mature level, and will decline

again in the time gap between superannuation and the appointment of a successor. Based on the life cycle concept it is expected that the more successful research units will employ a relatively younger research and support staff. This is operationalized by the percentage of staff in the different ranks under the age of 40 years.

Hypothesis 2.3
On the basis of the life cycle concept, a positive relationship between organizational age and research and user performance, and negative ones between organizational age and research and user effectiveness and annual growth rate, are postulated. The more effective research units will employ a relatively younger staff than the lower performing units.

Box 5.1

The life cycle of a professor can be described through the analogy to the life cycle of organisms. After the appointment of a young professor an ***incubation*** period starts. In this period the research unit has to be built up. Frictions may arise with the existing scientific staff. Career expectations may be frustrated, and it often takes time to get acquainted with the research techniques or way of working of the newly appointed professor. This switching of research interest can be especially problematic in fast changing research fields. In times of budget retrenchments it may be difficult to build up a research unit on faculty resources. Therefore, a young professor will have to look around for additional resources. He/she may attend international congresses more frequently to gather ideas for new research lines, to look for niches (areas of research which are not occupied by (too many) other research groups) and to present the new group to the scientific community. After about four years the young professor can start to harvest. The first PhD students defend their theses, and the results of the first externally financed projects can be presented. The group starts to find a niche and becomes accepted by the scientific community or/and the community of users. A period of ***rapid growth*** can start. The newly appointed assistant and associate professors give a further stimulus to the research programme. More research projects can be presented to the scientific community, leading to the amplifying loop A (see box 3.1, pg. 39). A large variety of different projects are started, and the research programme branches out to related research fields. The unit is externally oriented, many congresses are attended and more and more colleagues visit the unit. Many articles are received for peer review and the professor may be asked to attend the editorial board of a scientific journal. This rapid growth phase may take 10 years.

Then the unit reaches ***maturity***. The growth has slowed down or may even have stopped. The professor has a strong position within the faculty, he/she has become a member of the faculty board or chairman of the research committee etc. Consequently, the unit becomes more internally oriented. However, the position within the scientific community is secure, the group is distinguished. This period of maturity may last for 10 to 15 years. At the end of this period the ***decay*** starts. The unit is not very innovative any more, not many new and interesting papers are sent to scientific journals. The position in the faculty is strong. The professor is Dean of Faculty and has many contacts on the university level. This period ends with the superannuation of the professor.

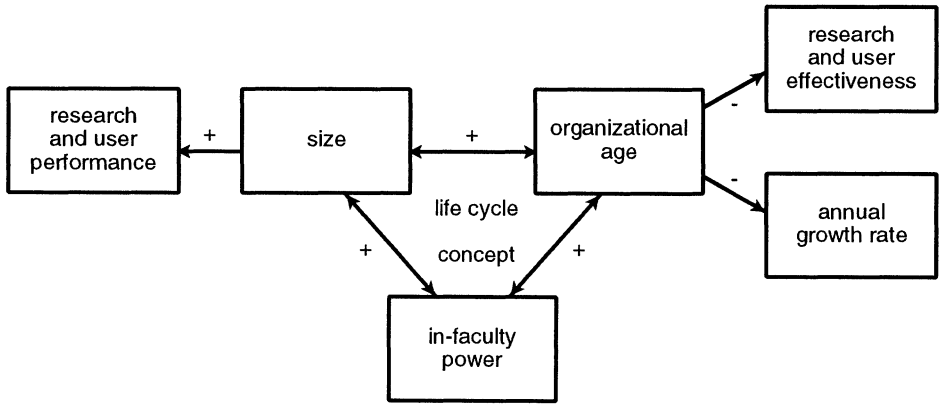
5.2.5 Power, Internal versus External Orientation

Two main strategies can be distinguished for attaining a positive *power* balance. A head of a research unit can either build up a strong position within the faculty or institute (*internal orientation*, assessed by *signatory authorization capacity*), and/or increase the number of financial resources by obtaining additional *external funding* (*external orientation*). External funding lowers the dependency on governmental funding and therefore on the faculty administration. Due to the non-structural character of external funding, junior scientists will generally be appointed to externally financed projects. Therefore, it is expected that external funding is positively associated with a high junior to senior scientist rate. It is hypothesized that the head of the research unit in the maturity phase of the life cycle will have a larger research unit, and more authority within the faculty than a starting professor.

The contrast between internal and external orientation can also be referred to as the two polar types of scientists, cosmopolitans versus locals, as first distinguished by Gouldner (1957). Cosmopolitans are faculty peers, whose colleagues are across the world and share their specialized scholarly interest. They tend to conduct research and publish, to find their rewards and satisfaction in their disciplinary activities, and to use their institutions as a basis for their external activities. Cosmopolitans are less likely to be concerned with faculty issues. Contrary to this, locals are primarily faculty members, heavily involved in faculty activities and politics, and only secondarily externally oriented scholars. If these polar types still exist, an external orientation is expected to be positively related to a cosmopolitan attitude.

Hypothesis 2.4
Positive associations of organizational age and size with internal orientation and negative ones with external orientation are expected. Via organizational age and size, internal orientation will be positively associated with research and user performance and negatively associated with research and user effectiveness and annual growth rate, while external orientation will show the inverse relationships.

Exhibit 5.7 THE SUPPOSED RELATIONSHIPS OF SIZE, ORGANIZATIONAL AGE AND IN-FACULTY POWER WITH PERFORMANCE AND EFFECTIVENESS



+ = positive relationship
- = negative relationship

5.3 DIFFERENT CROSS-SECTIONS IN INDUSTRY

Different cross-sections of the industrial study sample have been made in order to answer questions regarding the innovative strategy, dependency or autonomy, and the cultural background of the head office of the company. In the coming paragraphs the respective hypotheses will be discussed.

5.3.1 Radical versus Incremental Orientation

Although the companies in our study were selected on the basis of a considerable 'in-house' innovative capacity, the primarily orientation may differ. As Roussel et al. (1991) state, the amount and the advancement of the technology a company needs also depends on the orientation of the company, towards research (radical strategy) or development (incremental strategy). A company conducting a radical strategy emphasizes discovery, whereas a company conducting an incremental strategy is primarily directed towards speeding up product development in order to introduce drugs with small improvements on a regular basis (Taggart 1993). The importance of such incremental improvements is sometimes neglected. As Gross (1983, p. V) states: '*Developmental operations may also contribute substantially to progress and may serve in various respects to improve medicines and expand therapeutic possibilities better than the results of many original research efforts.*' For example, the way a drug is administered, whether it has to be injected or can be taken orally, can make a large difference to the patients concerned.

No large differences are expected between more radical and incremental companies in building and maintaining an extensive R&D network. More radical pharmaceutical companies will put considerable effort into gathering innovative ideas, and implementing joint research projects with universities, institutes or biotechnological or other pharmaceutical companies. More incremental companies have to maintain a high level of basic biomedical knowledge as well, to judge the merits of the patents licensed-in and of joint research projects with external R&D partners. In recent years, innovative pharmaceutical companies have moved gradually from a more radical to a more incremental strategy. This has been done in order to increase the life cycle of their products, by implementing smaller improvements (for instance in drug delivery) on a regular basis (Taggart, 1993). These recent changes and their influence on effectiveness in innovation will be analyzed in this study. It is expected that the innovative strategy chosen by the company is reflected in the following technology parameters.

Hypothesis 3.1
Companies conducting a more radical strategy will spend a larger part of the R&D expenditure on the discovery phase. They are expected to employee a higher percentage of scientists in R&D and their scientists will pay more attention to international communication, being more eager to gain new inno-

vative idea's. In contrast, companies conducting a more incremental strategy will pay more attention to the planning and organization of the developmental process, and thus are expected to show more frequent lateral and cross-functional communication.

5.3.2 Pure Play Pharmaceuticals versus Conglomerates

In order to study the possible influence of dependency versus autonomy, the industrial study sample was divided into pharmaceutical divisions of chemical conglomerates and autonomous pharmaceutical companies (the 'pure play pharmaceuticals'). Pharmaceutical companies have gradually diversified into related and non-related markets, such as over-the-counter drugs, diagnostics, veterinary products, specialized chemicals, and cosmetics and toiletries. In addition, conglomerate diversification has occurred, such as in the case of pharmaceutical companies entering consumer products and services. On the other hand, large, mostly chemical, corporations have obtained interests in pharmaceutical companies. Taggart (1993) predicts from the cost perspective that only the large chemical conglomerates will have the financial strength to survive, and will acquire more autonomous pharmaceutical companies in the years to come. Contrary to this is the observation that autonomous companies are generally better adapted to their specific markets (e.g. Allen 1977). The recent divestments of non-drug interests by some pharmaceutical companies, and the demerger of a pharmaceutical division by a chemical conglomerate, seem to support this observation.

Hypothesis 3.2
Autonomous 'pure play pharmaceuticals' will perform better than the dependent pharmaceutical divisions of conglomerates, due to their better adaptation to the pharmaceutical market.

5.3.3 Anglo-American versus Continental European Companies

The conglomerates in the study sample have a predominantly continental European background, while the pure play pharmaceuticals generally have an Anglo-American origin. Larger differences in organization, management and

work-related values, influencing the innovative climate of a company, have been observed between Anglo-American and continental European companies (e.g. Hofstede 1980). In order to get an idea of these differences, this study compares subsidiaries and companies with an Anglo-American to those with a continental European head office.

5.4 CONCLUDING REMARKS

In the following the main hypothesis and the derived hypotheses to be tested in the empirical study are summarized in the exhibits 5.8a and b.
The world of deductive reasoning is not similar to the empirical world. It is quite different to demonstrate that there is a rationale for a positive relationship between aspects of management control and research performance and effectiveness, and to demonstrate that there is evidence which confirms this relation in the empirical world. Valid instruments are needed to measure management control and performance and effectiveness, and a selection has to be made of the organizational units to be included in the study population. The next chapter concentrates on the instruments of data collection and the methods of data analysis.

Exhibit 5.8a OUTLINE OF THE HYPOTHESES

1 **management control**	1.1	The more-than-average performers will more positive scores from the research management than the less-than-average performers on a number of management control variables. When replication of the study design in the three strata yields consistent results, this enhances confidence in the generalizibility of the findings.
	1.2	For those performance and effectiveness measures which reflect the primary (secondary) goals and objectives of the organization, strong and similar (weak and different) relationships with management control will be found.
	1.3	An uneven distribution of high-quality research units over the different universities and institutes may indicate a difference in organizational flexibility.
	1.4	System control is expected to be more closely associated to industrial performance and effectiveness, and process and external control to innovative performance and effectiveness.
	1.5	The assessment of system control will be most positive in industry, and least positive in universities, with the institutes taking up an intermediate position.
	1.6	High performers will show a higher level of external control than low performers. In universities and in pharmaceutical innovation this will be apparant through more frequent international communication, and in institutes in more frequent contractor communication, too.
	1.7	In the best performing development departments: (1) the scientific staff will put more emphasis on the importance of planning; (2) the level of cross-functional communication with marketing and production (measured as the attendancy mix) will be higher; (3) the international communication will be more frequent.

Exhibit 5.8b OUTLINE OF THE HYPOTHESES

2 **the contingencies**	2.1	Certain threshold level will be found, beneath which pharmaceutical innovation will be difficult to maintain and university research units will be less viable. Above this level economies of scale will appear with increasing research and innovative effectiveness. This will continue until an optimum level is reached, above which effectiveness will decline again. • The projects in the research units will show an optimal size.
	2.2	The time allocated to research and clinical practice will show an inverse relationship. A positive association will be found between the relative time allocated to research and research effectiveness and the relative time allocated to clinical practice and user effectiveness.
	2.3	On the basis of the life cycle concept, a positive relationship between organizational age and performance, and a negative one between effectiveness and annual growth rate, is postulated. The more effective research units will employ a relatively younger staff than the lower performing units.
	2.4	Positive associations of age and size with internal orientation and negative ones with external orientation are expected. Via age and size, internal orientation will be positively associated with performance and negatively associated with effectiveness and annual growth rate, while external orientation will show the inverse relationships.
3 **different cross-sections in industry**	3.1	Companies conducting a more radical strategy will spend a larger part of the R&D expenditure on the discovery phase. They are expected to employ a higher percentage of scientists in R&D and their scientists will pay more attention to international communication, being more eager to get new and innovative ideas. In contrast, companies conducting a more incremental strategy will pay more attention to the planning and organization of the developmental process, and thus are expected to show more frequent lateral and cross-functional communication.
	3.2	Autonomous 'pure play pharmaceuticals' will perform better than dependent pharmaceutical divisions of conglomerates, due to their better adaptation to the pharmaceutical market.

CHAPTER 6

METHODS OF DATA COLLECTION AND DATA ANALYSIS

This chapter concentrates on the instruments of data collection and the methods of data analysis. The first two paragraphs focus on the linkage of the empirical concepts through the instruments of data collection (questionnaires, public reports and bibliometric methods) to the empirical world and to the relevant literature. Following this, the measures taken to guarantee the reliability of the methods of data analysis are discussed. This chapter ends with describing the selection criteria and approach of the study population.

6.1 INSTRUMENTS OF DATA COLLECTION

The study consisted of structured interviews with professors and research directors. In addition, two questionnaires were sent to the research management, regarding quantitative and qualitative aspects of management control and contingencies. In order to warrant objectivity, the performance and effectiveness measures were obtained from public reports and bibliometric measures.

6.1.1 Structured Interviews and Research Questionnaires

Structured interviews were held about management control of biomedical research in particular and research organizations in general with a selected sample of experienced professors and with one or two of the Research Directors of each Health Research Institute. In each pharmaceutical company, one or two of the Directors of the Research, Development and Clinical Research Divisions (mostly members of the Board) was/were interviewed. To avoid misinterpretation, the structured interviews were tape recorded. The results of the interviews were sent to the respondents for approval, mistakes were corrected and confidential information excluded. In addition, two questionnaires

were sent, ReQuest 1 and 2 (Research Questionnaire 1 and 2, see appendix A). In order to ensure uniform interpretation, definitions of the variables were included in the questionnaires.

ReQuest 1 consisted of quantitative questions about the personnel and material resources as input measures, and publications, congresses, patents and licences as output measures. If the output data obtained from public sources did not correspond with the answers on ReQuest 1, this was checked by the management concerned. In universities and institutes, one respondent per research unit was asked to fill in ReQuest 1. Because only a few questions in ReQuest 1 regarded the company situation, these were included in the structured interviews (see appendix B). The output data obtained from public sources were checked with the answers in ReQuest 1. If discordance was found, this was checked by the research management concerned. In institutes and industry only limited discordance was found. In universities, however, in a number of cases the public reports proved to contain incomplete or obsolete information (see § 7.3.1).

ReQuest 2 was submitted to those members of the scientific staff who were directly or indirectly in charge of research management, the heads of the research units and their senior scientific staff in universities and institutes. In the much larger company laboratories the questionnaires were submitted to the heads of the different research departments. In ReQuest 2, the scientific staff was asked to give qualitative judgements regarding personnel policy, pace of administrative procedures and the adequacy of laboratory equipment, facilities and space. For most of the items Likert 5-point response format was used, and a limited number of items were assessed with 2 and 3-point response formats. Before the data sampling started the questionnaires were tested on a sample of 12 biomedical researchers from the Faculty of Science, and 4 retired staff members of pharmaceutical and chemical industry. Their comments were incorporated into the questionnaires. Exhibit 6.1 shows which questions in the research questionnaires link the theoretical constructs of management control and the contingencies to the empirical world. The exhibits C.1 and C.2 in appendix C outline the operational definitions of management control and the contingencies.

Exhibit 6.1 LINKAGE OF THE THEORETICAL CONSTRUCTS OF MANAGEMENT CONTROL AND THE CONTINGENCIES TO THE QUESTIONS IN REQUEST 1 AND 2

contingencies	ReQuest 1	ReQuest 2
size, project size	1, 3, 7	-
time allocation	2	-
organizational age	-	1, 2, 3
technology	1, 7	-
power	7	17

management control	ReQuest 1	ReQuest 2
system control		
personnel control	-	11, 12, 19 to 27
resources control	-	10, 15, 16, 18
process control		
planning	-	4, 5
research process commun.	-	6, 7, 13
external control		
international communication	8 to 13	14
contractor communication	-	14

6.1.2 Operational Measures for Performance and Effectiveness

UNIVERSITIES AND INSTITUTES

Sixteen different performance and effectiveness measures for universities and institutes were mentioned in the relevant literature. They can be divided into two broad groups: quantitative measures (as number of scientific publications,

PhDs, memberships of Editorial Boards etc.) and qualitative judgements by national and international peers. In order to assess the relative importance of the different measures, Franklin (1988) asked the respondents in his European survey to select the 3 to 4 most important indicators for evaluating research performance out of a list of 12 (see exhibit 6.2). The indicators were divided into achievement indicators (number of articles, books, conferences participated in, but also number of awards), reputational indicators (memberships of organizations with national or international scientific credibility, and honorary doctorates), and personal indicators (personal communication with peers and peer review). In contrast to the expectation of Fisscher (1986), that scientists will prefer personal indicators (especially peer review), nearly all scientists mentioned at least two achievement indicators. The most important achievement indicator was the number of articles; 91% of the scientists mentioned articles in refereed scientific journals, compared to 38% who mentioned one of the personal indicators, which is even lower than active conference participation. Citation indices were perceived as comparatively unimportant achievement indicators, and a number of criticisms concerning this measure will be addressed in the next paragraph. Also the relatively low perceived importance of international awards and honorary doctorates as measures for performance and effectiveness is intriguing. In this study the achievement indicators 'articles in refereed scientific journals' and 'citation index' are used, combined with the reputational indicator 'elective office in international organizations' (elective office on Editorial Boards). An account is given below of the different performance and effectiveness measures, and the steps taken to provide for the reliability of the measures.

Publication counts

The performance and effectiveness of the research units was measured by the Centre for Science and Technology Studies (CWTS) in Leiden. For a thorough description of the methodology used is the reader referred to Moed et al. (1992). A computer search was done to count the number of publications attributed to different authors, using the database of the Institute for Scientific Information (ISI) in Philadelphia (USA). The computer search started with an updated list of the last names of the heads of the units and the senior scientific staff, provided by the author of this book. This list was matched with the author index of the ISI database. To avoid mis-interpretation, the selection of the authors was made using the family name, taking into account possible variations in the family name due to mistakes at data entry, and the first initial of the author, combined with the name of the city where

Exhibit 6.2 THE PERCENTAGE OF SCIENTISTS STRESSING A PARTICULAR ITEM AS BEING ONE OF THE THREE MOST IMPORTANT INDICATORS FOR EVALUTING SCIENTIFIC PERFORMANCE

achievement indicators	percentage %
1 articles in referred scientific journals	91
2 active conference participation	44
3 books and chapters in books	30
4 citation index and other indices	17
5 international awards and distinctions	15
reputational indicators	**percentage %**
6 elective office in international organizations	34
7 memberships in academic associations	19
8 elective office in national organizations	16
9 honourary doctorates and other honours	11
10 entries in 'who's who' etc.	3
personal indicators	**percentage %**
11 personal scholarly communications	38
12 reports from colleagues (peer review)	38

source: Franklin 1988

the research unit was located. Manually, those articles were eliminated of which the author, although complying with the above three criteria, worked in a different laboratory (for instance there could be a brother or sister with the same first initial). The number of papers (normal articles, letters to the editor, notes, and reviews) was measured:

- in which one (or more) of the scientists of the research unit was a (co-)author,

- which were published in international scientific journals from 1985 to 1990,
- which were entered in the Science Citation Index (SCI), the Social Science Citation Index (SSCI) or the Arts and the Humanities Citation Index(A&HCI).

In case of a considerable difference the reason for this was checked by the research management concerned. A problem of publication counts is that each publication does not equally contribute to the body of scientific knowledge. To overcome this problem the citation score was measured. A second problem is that publication traditions vary enormously among disciplines. Whereas in disciplines with a high level of paradigm development the scientific paper was the most commonly used vehicle for transfer of scientific knowledge, in low paradigm disciplines this was more often a textbook. This is one reason why comparisons can only be made between units operating in one technology field, using similar research facilities, and publishing in the same body of literature, subject to comparable refereeing procedures. As has already been stated in § 3.2.1, biomedical research can be considered a high paradigm discipline. One should realize, however, that for each (sub-)discipline a different 'scientific forum' exists. As a consequence, research units can be confronted with differing access to scientific journals. Also the citation patterns can differ considerably across (sub-)disciplines. The following discussion of the citation score will address this aspect further.

Citation score

The number of citations was assessed by the average number of citations per paper entered in the SCI, the SSCI and the A&HCI in the first three years after publication, starting with the year of publication. The number of citations per paper was related to the impact factor, i.e. the average number of citations in the journal in which the unit has published, taking into account the year of publication and the type of paper (e.g. normal article, review, and so on[1]). Because a research unit publishes in several journals rather than one, an average was calculated, with the weights determined by the number of papers published in each journal, separately. By using this procedure, one is

[1] To give a particular example, the number of citations received during 1987-1989 by a 'letter to the editor' published in 1987 is compared to the average number of citations received during the same period by all 'letters' published in the same journal in the same year.

able to assess whether the articles of a research unit are cited relatively frequently or not. If the articles are cited more c.q. less-than-average, the citation score weighed for journal is more c.q. less than one. It should be noted that the comparison of the journal weighed citation score has been criticized on the fact that the scientific stature of the journals was ignored. As one of the critics stated: '*this analysis does not at all encourage groups to publish in the most prestigious journals*' (Moed et al., 1992). To overcome this problem the citation rate was compared with the 'world' average citation rate of all papers published in the subfields in which the research unit was active. To assess the 'world average' citation rate, the scientific journals were classified into subfields using the subject category listing of ISI[1]. If a journal was assigned to more than one category a fractional counting scheme was applied: part of the journal's papers was assigned to the first category and the other part to the second. To calculate the citation score weighed for each (sub-)discipline the same procedure was used as the one applied for the journal weighed citation score, replacing journals by (sub-)discipline.

The use of citation analysis presents a number of technical problems (Garfield 1979):

- Incomplete coverage of journals by the SCI, the SSCI and A&HCI.
- A paper containing results subsequently found to be wrong may be heavily cited, at least until the error is clearly revealed. Here one should distinguish between the intrinsic quality of a paper and its impact at the research front. Only for the latter does citation frequency provide a reasonable indicator.
- The variation in citation rates among (sub-)disciplines. Moed et al. (1989) found high short-term citation rates (based on three-year citation-countings) in biochemistry and medium and low citation rates in physics and inorganic solid-state chemistry, respectively.
- In addition, self-citation or citation by other authors of the research unit is a notable problem. Because most research groups proceed on

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[1] The validity of the classification into (sub-)disciplines by the ISI is often criticized. For instance, biochemical and molecular biology research is published in journals with different citation patterns. The classification of the ISI does not in all cases reflect this diversity. However, up to now it has been the best method available. Recently, the CWTS started creating a database for journal-to-journal citation. An improved classification will be made by use of cluster analysis.

earlier results, many (co-)authors cite their earlier work.

Because most of the research results in biomedical research are communicated in the English language, the first point can be considered as a minor problem. Together the Indices cover most of the Anglo-American scientific literature. The second problem was overcome in universities, by checking high citation scores (more than twice the world average) with independent experts outside the study sample. The third problem was overcome by weighing for the average number of citations in the journals in which the paper was published and for the average number of citations in the journals of the (sub-)discipline(s) involved. The fourth problem has been met by excluding citations of researchers from within the research unit.

Another question is whether the citation score can be considered as a valid measure for the quality of the research output. Cole and Cole (1973) found a relatively high citation score for Nobel Prize laureates (about ten times above average), even before they had won the prize (cf. Nederhof and Van Raan 1987). Narin (1987) also pointed out that citation analyses are often in concordance with the opinion of 'peers'. On the other hand, Moed et al. (1992) revealed a lack of agreement of citation analysis and peer review judgment. However, this lack of agreement may not only be due to shortcomings in the citation analysis. To amplify this statement, peer reviewing will be discussed below.

Peer review
A peer review of a research unit typically includes:

- a site-visit of the laboratory,
- written and oral presentations by the researchers,
- interviews with the research unit management and junior and senior researchers.

Peer reviewing has clear merits for the evaluation of research units. If carried out in an optimal way, it is the only methodology which can give some insight into possible future performance. However, peer reviewing was not included in this study, and not only for practical reasons (the high costs involved). If peer reviewing is done in the Netherlands, objectivity can be at risk, because the leaders of the groups to be evaluated are often closely connected (for instance, former PhD students) to the reviewing peers. If international peers

are consulted, problems arise concerning time, costs and the threat that peers may replicate the best research ideas in their own laboratory.

Annual growth rate
The only data which provide a longitudinal picture of the development of the research units over a longer period of time are the annual growth rates. Data were gathered about the personnel and material means, and the relative weight of basic versus external funding in 1980, 1985 and 1990 (ReQuest 1, question 7).

INDUSTRY

As has already been stated in § 4.1.3, the percentage income from sales spent on R&D, the number of patents granted per R&D investment, the length of the developmental process, and the number of new products launched, were used as measures for innovative performance and effectiveness in industry. In addition, the industrial indicators of industrial efficiency, the annual growth rate and the operating profit margin, were used in this study. The operational definitions of the innovative performance and effectiveness measures will be discussed below.

Number of patents
A patent search was conducted by the Centre for Information and Documentation of the Dutch Organization for Applied Scientific Research (CID/TNO). The number of patents for new synthetic chemical pharmaca[1] with first priority date submitted world-wide between 1986 and 1991 was obtained by using the Pharmdoc Section of the World Patents Index Database of DERWENT Publications. Only compound patents (patents for NCEs), and no process or formulation patents have been considered. A compound patent gives protection for a specific chemical compound and its derivates (a group of closely related biochemical compounds). In order to assess whether the patents were submitted for NCEs and not for minor variations of drugs of other companies ('me too patents') or pharmaceutical or therapeutical extensions of existing

[1] The Derwent categories $B_{1,2,3 \text{ and } 5}$ include the steroids, the heterocyclic carbons, aromats, aliphats and organo-metals. The number of patents in the categories B_4 (the 'biotechnology' patents: the oligo- and polipeptides, the immunodiagnostics, and the DNA- and RNA-sequences); and B_7 (new formularities, for instance tablet, capsule or catheter) were also measured, but not used (see the text).

drugs (for instance an improved version or a new indication area), the CAS registration numbers (Chemical Abstract registration of new chemical compounds) were checked. Only those compounds were selected of which the CAS number indicated that they were new at the time of patenting.

The primary interest of this monograph was to get a better understanding of the work of the proprietary innovative efforts of a company. Therefore, the results of the R&D network of a pharmaceutical company, with universities, institutes and biotechnological and other pharmaceutical companies, has not been studied. For instance, the joint development of a drug by two or more companies, licensing-in and licensing-out, and 'biotechnological' patents have not been taken into consideration. A computer search revealed that the 'inventors' of most of the biotechnological patents were not working in the pharmaceutical companies submitting the patent, but in biotechnological companies, research institutes or universities. For a discussion of the R&D network the reader is referred to Gambardella (1992) for US pharmaceutical companies; della Valle and Gambardella (1993) and Albertini and Butler (1994) for European companies and Sapienza (1993) for Japanese firms. Fitzgerald (1992) provides a recent description of the possible licensing strategies of pharmaceutical companies.

A notable problem is the possible difference in patenting policy (timing and scope) between companies. Basberg (1987) and Pavitt (1988) indicate that some companies play for safety and apply for a patent at an early stage of the innovative process, while others wait longer. The first strategy will decrease the risk that a competitor will submit a patent for a similar compound, but increases the patents fees and translation costs and can put a competitor on the track. The second strategy has complementary (dis)advantages. In § 11.2 will be returned to this point.

Length of the Development Phase

In order to obtain comparable data about the average length of the developmental process, the Research Directors were asked to give an estimation of the average time span between the patenting of the lead compound and the introduction of the registrated drug on the prescription drug market. Anti-hypertensive and anti-ulcer drugs were chosen because the developmental process was neither relatively short (as with antibiotics) nor very long (as with anti-psychotics). The reported length of the process was checked for ten drugs which were launched after 1987 distributed over five companies. In all cases

the findings proved to correspond; the period between patent submission and launch being one to two years shorter than the reported maximum length of the developmental process. The finding of the lead precedes patent submission, therefore the time-span between patent submission and launch will always be shorter. The exhibits C.3 and C.4 in appendix C outline the operational definitions of the performance and effectiveness measures.

6.2 RELIABILITY OF INSTRUMENTS

Most questionnaires were filled in completely, so the number of missing values was relatively low. No questionnaires had to be excluded because of too many missing values. In some cases respondents had filled in two adjacent scores or between two scores on the Likert 5-point scale. In such cases the score towards the 5-end of the scale was included in the data matrix. To assure the reliability of the data matrix automatic out of range checks were used during data entry. Afterwards, all data were visually checked. In addition, the frequency tables were checked for inconsistencies. At the end of data processing, 10% of the data were checked again. Only 13 out of 2,904 items had to be corrected. This is well below the 5% reliability limit of Gadourek (1976). All the bivariate relationships were plotted to check for outliers. If an outlier was found it was omitted from the analysis.

6.3 METHODS OF DATA ANALYSIS

Different statistical methods were used to analyze the data. The bivariate procedures included t-test, one-way ANOVA, Kruskal-Wallis test, Pearson product-moment correlation and Spearman rank correlation. The multivariate procedures included factor analysis, canonical correlation, multiple regression and neural network modelling. The items, measured at ordinal and interval level were analyzed by non-parametric statistics or by parametric statistics on the ranking numbers. Whenever possible, more than one technique was used. In general, substantive conclusions were supported by all statistical techniques. For clarity of presentation, all bivariate relationships are presented using Spearman rank correlation and one-way ANOVA. Non-parametric analysis of group means, using the Kruskal-Wallis test, did not alter the conclu-

sions.

The bivariate curvi-linear relationships on ratio level and all the multivariate associations were assessed by 4Thought, a multilayer feedforward neural network. It may be considered as a large analogue computer comprising of different layers of processing elements (called nodes), in sequence linked by a large number of individually weighed interconnections. Inside a node the inputs are added and an algorithm (in 4Thought an exponential sum formula based upon series expansion) is used to calculate the node's output value. In every step of the 'unsupervised learning' process a neural network compares numerous pairs of input and output values in parallel. For the next step of the learning process that model is chosen, in which the sum-of-squares error between the current and the desired mapping performance is most rapidly reduced (Hoptroff et al. 1991). Up to now neural networks have seldom been used in empirical management studies. Nevertheless it is the only multi-variate technique available which enables the comparison of empirical concepts which are operationalized at different measurement levels (such as at ordinal and ratio level in this study). Because of their general use in multivariate analyses, the term 'explained variance' is used, which, strictly speaking, only relate to predicted (mostly linear or transformed to linear) relationships. In neural network modelling, however, no preliminary assumptions are made. This is its strength and its weakness at the same time. On the one hand, it provides the opportunity to recognize underlying patterns in situations of complex multi-causality. On the other hand, there is a threat of 'over-fitting'. An 'over-fit' model fits too perfectly to the data set, ignoring the natural variability (the 'noise') in the data. The neural network 4Thought is specially designed to avoid this problem. It divides the data into two groups: a 'training' set of 80% and a 'test' set of the remaining 20% of the data. The neural network builds a model on the training data and tests this model on the data of the test set, simultaneously. The 'learning' process is only allowed to proceed as long as the errors in the training set and the test set are both dropping. Initially, both the errors for the training and the test set fall. When the noise in the data begins to dominate the learning process, the error for the test set starts to rise while the error in the training set continues to fall. At this point the learning process is stopped and the resulting model is presented. Statistically it means the selection of a biased fit to the training set data based on the optimum fit to the test set data. The designers of 4Thought call the technique the concurrent iterative steepest decent technique, because of the simultaneous dropping of the training and the test set error (Hoptroff et al.

1991). The choice of the test set can influence the results, because of the relatively small study population. Therefore, four independent runs of the neural network were conducted, using different training and test sets, plus an additional run without a test set, to obtain maximum statistical power. The five independent runs gave similar results, in general. Only for industry were different models found. However, in all cases at least three of the five models used the same variables to 'explain' (in strictly statistical terms) performance and effectiveness. In the other one or two models only one variable differed. The model which gave the best approximation of the different runs is presented.

A factor analysis (ANOVA followed by Varimax rotation) was performed on the empirical concepts measured at ratio level, to reduce the number of items and to examine whether they loaded on the empirical concepts defined. Cronbach's α (1970) was calculated for the items measured at ordinal and interval level, to find out whether they corresponded with the empirical concepts defined, and to check the internal consistency of the items, which are supposed to measure a single concept. In order to prevent eventual co-variation of size with the other contingencies and management control, size was entered first in the multivariate analysis. In institutes, the data concerning material resources and external funding could only be obtained for the institute as a whole. Due to the small number on which they are based, the correlations of these variables with performance and effectiveness are only given for the sake of completeness. For the same reason these variables were not used in the multivariate analysis.

6.4 STUDY POPULATION

The International Standard Nomenclature (ISN) of research fields was used to demarcate biomedical research. A unit was included in the study population if it carried out research in one of the following fields of the life and medical sciences (see exhibit 6.3).

The 1989 and 1990 year reports of the universities were studied to judge which research units should be included. In the case of doubt (for instance, about internal medicine) only those units were included of which researchers were participating in one of the working committees of the Medical Science Department of the Dutch Organization for Scientific Research (NWO): cell-

biology and cellpathology, organ systems (exclusive of biomedical technology), and hormone regulation and neurosciences. In order to select the health research institutes, the report 'Advice about the Mission Pattern of Non-university Research Institutes' by the Dutch Research Policy Council (RAWB 1988) was consulted. On page 60 of this report an outline is given of the research institutes in the biomedical field. To provide for homogeneity, only those departments were examined which were involved in molecular biology, medical biology and pharmacology/toxicology (RAWB 1988, table 3 p. 43).

Exhibit 6.3 THE ISN FIELDS IN THE LIFE AND MEDICAL SCIENCES USED AS DEMARCATION LINES FOR BIOMEDICAL RESEARCH

ISN number	life sciences	ISN number	medical sciences
2403	biochemistry	3205	internal medicine (endocrinology)
2407	cell biology		
2409	genetics	3207	pathology
2410	human biology	3208	pharmacodynamics
2411	human physiology	3209	pharmacology
2412	immunology	3214	toxicology
2414	microbiology		
2415	molecular biology		
2418	radiobiology		
2420	virology		

According to Gross (1983), there are only 30 to 35 pharmaceutical companies world-wide which are actively involved in innovation: exploring new areas, synthesizing new molecules or studying how to make use of new discoveries. This is a figure far below the number of companies which claim the status of science-based companies. The actual number may even be less, because of the large number of mergers since then. From the innovative pharmaceutical companies, 20 were chosen with large discovery and/or pharmaceutical development laboratories in Great Britain, Germany, France, Belgium or the Netherlands. Fifteen of them have their head office in one of these countries, five have their head office in the USA. They are all global players in branded ethical drugs. The companies were selected on the basis of their (world-wide and European) sales volume of branded ethical drugs, and on their innovative capacity, measured by the size of the R&D staff and the number of patents submitted with a European priority. In order to prevent bias due to the use of

quantitative data only, four leading Dutch clinicians were asked to name the companies which have introduced the most innovative drugs to their therapeutic areas in the last five years. The information obtained supported the quantitative selection.

Criteria for Inclusion
Because the medical context was one of the inclusion criteria, the research units in universities had to be, at least partly, situated in one of the medical faculties. The minimum number of questionnaires which had to be returned before a research unit could enter the study was two for small and three for larger units, including ReQuest 1. A low research output during the first years after the appointment of a new professor cannot be fully attributed to his/her work, because it takes several years to build up a unit. Therefore, the second criterion for inclusion was that the head of the unit had to have been in charge for at least four years.

6.4.1 Representativeness of the Study Sample

In order to study the representativeness of the study sample the output per researcher was measured for all the biomedical research units in three of the medical faculties and all the participating institutes. Using the annual reports, the number of scientific papers, papers for physicians and reports for governmental and industrial contractors of participating and non-participating units were compared.

In order to establish the representativeness of the individual response, the answers of early, average and late respondents were compared. Oppenheim (1966) suggests that late respondents might resemble non-respondents, rather than early respondents. If similarity is found in the answers of early, average and late respondents, this can provide confidence in the representativeness of the answers. Unfortunately, only in universities was it possible to make such a comparison. The more centralized organization of data sampling in institutes and companies (see § 6.5.3) meant that the questionnaires were often returned in packages, making it impossible to separate early from late respondents.

Both ReQuest 1 and 2 included subjective questions. In ReQuest 1 the heads of the research unit were asked to estimate the time allocated to research, to education, to management and acquisition and to clinical practice, not only for themselves, but also for their scientific staff. Bias may arise in two respects as regards this estimation. First, the actual time-allocation of the professor may differ from the estimated one, as was indicated in a study by the Central Bureau of Statistics (1985). And second, this bias may be even larger if the estimation concerns the time-allocation of others. In order to check the bias in the latter, a selected sample of 19 scientific staff members of different research units in universities was asked to fill in ReQuest 1 for their research group. The answers were compared with those given by their professor. As to the subjective judgements in ReQuest 2, it is not unlikely that the head of the unit, being primarily responsible, has a different perception of the management control situation than the senior scientific staff. Therefore, the answers from the head of the units were compared with those given by their senior scientific staff.

6.4.2 Approach of Study Population

In every empirical management study a high response rate positively influences the generalizibility of the results. Because of the relatively small size of the study population, both in respect to the number of units and the number of respondents per unit, obtaining a high response rate was even more critical for this study. A large practical problem encountered when using a study population embracing professors, scientists, Directors of Research Institutes and industrial R&D Directors, is that most respondents are extremely busy. Therefore, the individual imposition on each of the respondents must be limited. In order to get a satisfactory response rate for this study the following measures were taken:

- all Dutch respondents were approached individually by phone,
- every questionnaire was mailed to the respondents personally.

The method chosen was labour intensive. In order to spread the work load it was decided to approach the study population in succeeding stages. From January until September 1991 the universities were dealt with, followed by the research institutes from September 1991 until January 1992, and the company

Exhibit 6.4 APPROACH SCHEME FOR THE STUDY POPULATION

week	universities	institutes	companies
0	letter of announcement to the faculty board	letter of invitation to the institute board	letter of invitation to the board of directors
2	letter of invitation to the professors; sending of ReQuest 1	telephone enquiry regarding participation	telephone enquiry regarding participation
3	telephone enquiry regarding participation; sending of ReQuest 2	-	-
4	interview with selected sample of professors	site-visit, interview with institute board; leaving of ReQuest 2	-
6	-	collection of ReQuest 2 at the institute	-
8	first telephone reminder; first written reminder	first telephone reminder; first written reminder	site-visit, interview with R&D directors leaving of ReQuest 1 and 2
12	second telephone reminder; second written reminder	second telephone reminder; second written reminder	first telephone reminder first written reminder
16	sending interview text to professors	sending interview text to institute board	sending interview text to R&D directors; 2nd telephone/written reminder
18	end of data collection	end of data collection	end of data collection

laboratories from February until September 1992. In order to minimalize the differences, the approach of the respondents was done according to strict protocols, which were adapted to the specific situation in each of the strata. The different protocols will be discussed below. The approach scheme is summarized in exhibit 6.4.

Universities

Two universities were approached during every month of the study period. The data collection started with a letter in which the study was announced and the background was revealed, which was sent to the Board of the Medical Faculty. After one week an invitational letter, together with ReQuest 1 and 2, was sent to the professors of the research units which met the selection criteria. One week later, the professors were phoned to ask for their consent. If they agreed to participate, ReQuest 2 was mailed to the senior scientific staff. The list of names was checked by the secretary for completeness. The professor filled in both ReQuest 1 and 2. In some cases ReQuest 1 was filled in by one of the senior scientists, and in larger units (or departments) by the unit (department) manager. If the professor did not want the research unit to participate, the reason for non-response was noted. Two weeks later a selected sample of distinguished senior professors was interviewed (about one third of the participating professors). After four weeks the respondents got a telephone reminder. In the case of individual non-response the reason was noted. Some of the potential respondents were non-eligible (for instance because of a long period of foreign leave). A written reminder was sent to the respondents who, even after several attempts, could not be reached by phone. A second reminder followed four weeks later, using the same procedure.

Institutes

Every month an institute was approached. Data collection started with the sending of an invitational letter to the Board of the Institute. After a positive reaction the Research Director(s) was/were interviewed. In a number of institutes, the quantitative questions were answered by a central staff department. Within the institute a contact person was designated, who took care of the distribution of ReQuest 2 among the members of the scientific staff, supported by a letter of recommendation from the Institute Board. ReQuest 1 was also distributed in some of the institutes. In these cases the heads of the units filled in the quantitative questions for their research unit. After two weeks the questionnaires were collected by the contact person. Respondents who had not returned their questionnaires were reminded twice if necessary

with four weeks intervals.

Companies
Because the R&D laboratories of the pharmaceutical companies are situated in different EU countries, another approach was chosen. First an invitational letter was sent to the Board of Directors of the different companies in one country. After approval, all the site-visits were planned in a two week period, about two months after sending the invitational letter. Structured interviews were held with the directors of research, and/or pharmaceutical and clinical development. In these interviews the general data regarding research input and output were checked and general information regarding research management was obtained (see appendix B). In a number of cases ReQuest 2 could be sent to the heads of the different research departments. The questionnaires were collected by a contact person in the company, and returned by mail.

6.5 CONCLUDING REMARKS

In this chapter the methods of data collection have been described. The criteria for selecting the study population and the methods used to guarantee the representativeness of the study sample have been discussed. The next Section presents the results of the empirical study.

SECTION 3

RESULTS

CHAPTER 7

DATA COLLECTION

This Section focuses on the results of the empirical studies. In this chapter the actual data collection, and the assessment of the representativeness of the response and the reliability of the instruments are examined. The results from universities and institutes are presented in chapter 8, separately from those from company laboratories in chapter 9, because of the difference in the level of analysis, i.e. single research units in universities and institutes, compared to chains of research units in industry. To increase the readability of this Section the more extensive tables are presented in the appendices.

7.1 RESPONSE RATE

Universities

All the chaired professors of the 82 biomedical research units in universities were approached. Six could not be reached, as they were abroad for a longer period of time. In total 47 agreed to participate. In 7 research units the inclusion criterion of the minimum number of returned questionnaires was not met. Therefore, the population on which this study is based consists of 40 research units, 53% of the eligible population of 76 (82 - 6) research units. In total 24 preclinical and paraclinical units and 16 clinical units were analyzed. Sixteen interviews were held with professors, and research questionnaires were sent to the 47 who had agreed to participate, and their 218 senior scientific staff members. Sixteen senior scientific staff members were non-eligible. They turned out to be attached to the research unit for only a short period of time (a few months) or could not be reached as they were on leave. The chaired professors returned 44 questionnaires (an individual response rate of 58% of the total eligible population of 76). The senior scientific staff returned 105 questionnaires (an individual response rate of 52% of the eligible population of 202 (218 - 16) senior scientific staff members). Because of the inclusion criterion of minimum participation, 7 questionnaires could not be used. Therefore, 142 questionnaires were analyzed, i.e. 3 to 4 questionnaires per research unit.

Institutes
The health research institutes in which biomedical research is carried out were examined; two para-university institutes, one not-for-profit institute, one dependent on private funding and one dependent on the distribution of and control over vital medical products. One institute, which is part of a government ministry, could not be examined, because of the difficulty of obtaining separate data (see also § 1.7.2). Structured interviews were held with 9 scientific and general directors and 20 questionnaires were sent to the heads of the research units and 52 to their senior scientific staff. Seventeen questionnaires were returned by the heads of the units (individual response rate 85%), and 27 by their senior scientific staff (individual response rate 52%). The reason for this uneven distribution might be that the head of a unit feels more obliged to participate.

Companies
The 20 innovative pharmaceutical companies with large discovery and/or pharmaceutical development laboratories in Great Britain, Germany, France, Belgium and the Netherlands were approached (see § 6.4). Fourteen agreed to take part in this study (a response rate of 70%). Nine companies are among the top 20 companies ranked according to the 1991 world-wide branded ethical drug sales. The other 5 are top 50 pharmaceutical companies. Twenty-two structured interviews were held with the directors of discovery, and with those of pharmaceutical and clinical development (1 to 2 interviews per company). ReQuest 2 was submitted to the heads of the different research departments in 10 companies. In total 59 questionnaires were sent, of which 38 were returned (3 to 4 questionnaires per company laboratory, an individual response rate of 64%).

7.2 ANALYSIS OF NON-RESPONSE

The response rate in the 8 medical faculties differed from 38% to 67%. In 3 faculties the response rate was below 50%. In the faculty with the lowest response rate to telephone enquiry, a negative attitude towards the faculty from which the study was conducted was mentioned in some cases. The other two faculties were involved in a reorganization. A large proportion of the chaired professors did not want to participate, because they had to concentrate on faculty politics. No significant differences were found in the response rates of the different types of Dutch universities, and between the different (sub-)disciplines. One faculty board sent a letter to the departments advising them not to participate, because of pos-

sible misuse of the citation analysis (mentioning the pitfalls described in § 6.1.2). Interestingly, the response rate for this faculty equals the average response rate. Although some professors did not want to participate because of this letter, most of the others indicated that it did not influence their decision. The way the professors disregarded the negative advice of the faculty board stands in clear contrast with the positive reaction of the heads of the research units in institutes to the request of the directorate to participate, which may be an illustration of the difference in vertical integration between the two types of organization (see § 2.5.1).

In telephone enquiries, lack of time or lack of interest because of questionnaire weariness were most often mentioned as reasons for non-response. In institutes about one-third of the non-responding scientific staff indicated that the head of the unit would fill in the questionnaire for all of them, because they agreed upon most of the items. In a few cases, the non-response might have influenced the results. Some professors mentioned that the research unit was already so successful that they did not see the need to enhance it by participating in this study. On the other hand, in some cases, where the faculty was involved in a reorganization, there was concern about possible negative consequences. To decrease the workload for the scientific staff in two of the research institutes, the directorate selected a number of research units to enter the study, which could have led to a possible selection bias in two respects. Firstly, these two institutes might be somewhat under-represented because in the other institutes all relevant research units participated. Secondly, the directorate may have selected the best research units in order to obtain a positive outcome for their institute. However, the study of the representativeness (see § 7.3.1) revealed that the selected research units were only slightly, but not significantly, better than average.

7.3 REPRESENTATIVENESS

7.3.1 Performance and Effectiveness

Universities and institutes

Although the output differed considerably, both between and within the three medical faculties and the five participating institutes in which all the biomedical research units were examined, no significant differences were found between participating and non-participating research units. This provides evidence that the

participating research units, at least as far as their scientific output is concerned, may be regarded as representative of the biomedical research population in Dutch universities and institutes.

The number of publications found in the database of the Institute for Scientific Information (ISI) was on average 20% lower than according to the report of the research management concerned. In the case of a larger difference the reason for this was checked. In most cases the difference could be attributed to the inclusion of national publications, congress proceedings and non-English publications by the research management. In six units the research management reported a lower number of scientific papers than the actual number found in the ISI files. Telephonic enquiry showed that the research management had just underestimated the number of papers. It is interesting that an output measure, which plays such an important role in research policy, is treated so casually by some of the units.

In all cases where an exceptionally high citation score was found (more than twice the world average), independent experts in related research fields outside the study sample were asked to indicate whether outstanding results had been presented by the research unit involved. In all cases one of the researchers of the unit had published new and interesting results. However, the findings also pointed to an inherent problem of citation analysis, namely the time-lag between publishing and the citation measurement. In all cases the researcher had already left the unit to take up a professorship elsewhere.

Companies

The innovative capacity of the companies in this study was measured in order to examine whether they could be regarded as representative for the population of large innovative companies in branded ethical drugs. Patent analysis revealed that from 1985 to 1991 in total 3,874 licensees submitted pharmaceutical patents to the European authorities. The number of licensees is actually less, because most companies and conglomerates in particular, use different licensee names and addresses. The strong innovative capacity of the companies in the study sample was illustrated by the fact that the 14 companies together submitted 25% of all the pharmaceutical patents in this period.

7.3.2 Respondents

Universities and institutes

The answers of early, average and late respondents were compared to investigate whether the returned questionnaires could be considered to reflect, to some extent, also the judgements of non respondents. Early respondents were defined as those respondents who sent their questionnaire back before the first reminder (46 respondents). Average respondents reacted after the first reminder but before the second reminder (54 respondents). Late respondents were those, who returned their questionnaire after the second reminder (49 respondents). There was a somewhat uneven distribution of the study population over the groups of early, average and late respondents. Firstly, in the group of early respondents the number of chaired professors was somewhat, although not significantly, under-represented. This was to be expected because the professor had to fill in both ReQuest 1 and 2, while the senior scientific staff only had to finish ReQuest 2. Secondly, in the group of early respondents, a significantly higher percentage of scientific staff from clinical research units was found. This was not expected, because the work-load in clinical units is generally assumed to be higher than in preclinical and paraclinical units. This finding may be attributed to the demands of patient care. Physicians may be urged to 'clean their desks' more than scientists in preclinical and paraclinical units (see § 10.5). Thirdly, researchers from the larger research units were significantly over-represented in the group of late respondents. This was mainly due to the fact that the scientific staff was more difficult to contact. Often neither the secretary nor their colleagues knew whether a respondent was in or was abroad for a congress etc. No significant differences were found in the reactions of early, average and late respondents, corrected for rank, amount of clinical practice and the size of the unit. For this reason it is assumed that the answers of respondents may resemble those of non-respondents. The answers obtained may therefore be regarded as representing, to some extent, the judgements of the population of researchers in the participating units on the questions concerned.

The individual judgements of the scientists were condensed to an average judgement for the research unit as a whole. In order to check whether the senior scientists in one research unit more or less agreed in their judgements, the intra-unit variation was compared with the inter-unit variation. This analysis showed that the inter-unit variation was higher than the intra-unit variation on all the relevant items. In three university research units, however, clear outliers were found, individual researchers whose judgements differed considerably from those of their

colleagues on nearly all the items. Telephone enquiries taught us that personnel conflicts may have caused the deflecting response.

Companies
The data obtained in one research laboratory are considered to reflect the whole innovative process. However, the different steps in the innovative process of the large pharmaceutical companies are carried out in a number of laboratories located in different countries. In order to reduce the chance of an accidental deflection, the main research laboratory of a company was examined (in 75% of the cases), or in the case of an American company, a major laboratory in Europe. In order to check whether the companies use comparable definitions for the different aspects of R&D and sales, annual reports and public information was combined with the information obtained in the structured interviews. Some of the data, for instance the percentage of scientific versus total R&D staff, could be checked in the laboratory under study, but this was not the case for all the data. Although much care was taken to attain uniform information, it is still possible that differences in interpretation occurred between companies. However, on the global level of the analyses there is no reason to assume that it will have distorted the results.

Exhibit 7.1 TIME-ALLOCATION OF SENIOR SCIENTIFIC STAFF AS ESTIMATED BY THE PROFESSOR AND THE SENIOR SCIENTIFIC STAFF, mean and (s.d.)

time-allocation senior scientific staff (%)	professor n=40	senior scientific staff n=19
research	50 (22)	43 (22)
education	18 (12)	16 (15)
management	11 (10)	21 (19)
clinical practice	21 (26)	20 (27)
total	**100%**	**100%**

7.3.3 Unit head versus Senior Scientific Staff

Universities
In order to investigate the validity of the professors' estimation of the time-allocation of their scientific staff, 19 scientific staff members were asked to fill in Re-

Quest 1 for their research group. A χ^2-test did not show a significant difference in the estimation ($\chi^2 = 0.93$). Exhibit 7.1 shows that the only difference which could be established was in the estimation of the time allocated to the management task. In the perception of the scientific staff, this was nearly twice as high as was estimated by their professor. It was likely that a difference in the estimation of the management task would occur, because it is the most diffuse task and therefore difficult to estimate.

Exhibit 7.2 shows the answers to those items of ReQuest 2, which were judged significantly different by professors and the senior scientific staff. Similar results were obtained when the answers from each research unit were analyzed in a matched pair analysis. The professors and their senior scientific staff agreed on most of the items in ReQuest 2, for instance about the (in)adequacy of the research budget and the technical level of laboratory devices, and about such factual points as the number of research meetings. On more subjective subjects as the importance of research planning, and on aspects of personnel policy, their judgements also turned out to co-vary. However, on a few points significant differences were found. Exhibit 7.2 shows that the professors were more positive about the attention to career planning, and clearly more positive about the possibilities of obtaining favourable working qualifications for external application. Furthermore, the professors counted more reorganizations in the previous five years. The reason given for this difference, which emerged during the structured interviews, was that also smaller reorganizations, affecting only part of a unit, were reported by the professor. The senior scientific staff, in larger units especially, is primarily oriented each towards their own research group. The senior scientific staff was significantly more positive about the possible pace of reallocation of a large part of the resources to a new research line. This can be explained by the relatively small scale of reallocations in research groups compared to whole research units.

Both the professors and their senior scientific staff seem to overestimate their attendancy of the weekly or bi-weekly research meetings, or underestimate the attendancy of the other rank. Considering the central role of research meetings as a tool for maintaining control of the research process, it is interesting to notice that 14% of the professors, according to their own account, and even 23% in the view of their senior scientific staff, do not attend the research meetings on a regular basis. In the light of the above consideration, it is also surprising that nearly 10% of the professors indicated that their scientific staff does not attend the research meetings on a frequent basis, compared to the figure of 2% given by the senior scientific staff themselves. The professors report more lateral linkages with

Exhibit 7.2 ANSWERS ON ITEMS OF REQUEST 2 WHICH ARE JUDGED SIGNIFICANTLY DIFFERENT BY PROFESSORS AND THE SENIOR SCIENTIFIC STAFF, mean and (s.d.)

management control[1]	professor n=40	senior staff n=102	F-value
personnel control			
career planning			
• scientific staff	2.42 (1.10)	2.09 (1.07)	2.80 *
• technical , analytical and administrative staff	2.67 (1.10)	2.26 (1.01)	4.48 **
• external career possibilities	3.41 (0.93)	2.90 (1.09)	5.36 **
number of reorganizations	1.07 (0.42)	0.69 (0.31)	6.40 **
resources control			
pace of reallocation (in months)	8.40 (2.80)	5.40 (2.40)	4.56 **
process control			
attendancy of research meetings			
• professor (%)	86 (26)	73 (25)	2.70 *
• senior scientific staff (%)	91 (24)	98 (14)	3.67 *
• scientists of other units (%)	42 (13)	23 (6)	4.32 **
external control			
meetings with			
• international colleagues (times per year)	4.00 (1.60)	2.40 (0.80)	9.01 ***
• funding agencies (times per year)	2.50 (0.80)	0.50 (0.15)	9.78 ***

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

[1] Likert 5-point scales; higher values indicate a more positive judgement

other research units. More professors than senior scientists indicate that also scientists of other units attend the research meetings. The professors in the study sample present their units to the outside world and monitor the environment for innovative ideas and research funding. They reported significantly more contacts with international colleagues and with funding agencies. The participation in international congresses and on editorial boards of scientific journals was also clearly higher (data not shown).

Institutes

Exhibit 7.3 shows that the differences in the assessment of the items in ReQuest 2 between the heads of the research units and their senior scientific staff were quite similar to those found in universities. The heads of the units in institutes were also more positive on aspects of personnel policy, such as the career situation and the effectiveness of personnel policy. The research unit heads were also more positive about the pace of the administrative procedures regarding appointments and procurement of equipment. Of more interest is the great difference in the perception of the regularity of attendancy of research meetings between the research unit heads and the senior scientific staff. Whereas 92% of the heads of the units report a regular attendancy, this was only 34% according to their senior scientific staff. It was indicated in the structured interviews that in a number of institutes the different research groups within a single unit work so independently, that they organize separate research meetings. It seems that Mayntz's observation (1985) that getting programmatic unity is problematic in German institutes, also applies to Holland. The research unit heads reported significantly more meetings with outside contractors than the senior scientific staff. However, the number of meetings is not very large, on average two a year. Most of the communication with contracting agencies is done by the directorate of the institute and not by the heads of the different research units.

7.4 RELIABILITY OF INSTRUMENTS

7.4.1 The Contingencies and Performance and Effectiveness

The contingencies and the performance and effectiveness variables were analyzed by means of factor analysis. Appendix D presents the factor structures in universities, institutes and companies. Three principal component analyses were conducted to investigate the relationships between the different items. This was fol

Exhibit 7.3 ITEMS OF REQUEST 2 WHICH ARE JUDGED SIGNIFICANTLY DIFFERENT BY THE HEAD OF THE UNIT AND THE SENIOR SCIENTIFIC STAFF IN INSTITUTES, mean and (s.d.)

management control [1]	unit head n=17	senior staff n=27	F-value
personnel control			
effectiveness personnel policy	3.54 (0.32)	2.90 (0.48)	3.79 *
internal career possibilities	3.17 (0.45)	2.58 (0.52)	3.70 *
promotion	3.75 (0.75)	3.12 (1.22)	2.84 *
resources control			
adequacy of resources	3.25 (0.75)	2.61 (1.15)	3.16 *
administrative procedures (in month)	3.00 (1.20)	5.00 (1.80)	3.11 *
process control			
attendancy of research meetings			
• unit head (%)	92 (29)	34 (48)	14.79 ***
• senior scientific staff (%)	91 (29)	94 (25)	0.06
external control			
meetings with contractors (times per year)	2.00 (0.95)	0.75 (0.47)	6.77 **

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

[1] Likert 5-point scales; higher values indicate a more positive judgement

lowed by varimax rotation to reach maximal independency (clusters of items with a high correlation). Only the factors with an 'eigenvalue' above 1.0 and the items with a factor loading above 0.4 are presented. The factors are listed in the order

of presentation in the variable lists. Whenever possible, the factors are named in accordance with the names of the corresponding predefined empirical concepts. If items out of different empirical concepts occur in the same factor, the factor is called after that empirical concept whose items contribute most to the factor loading.

Comparison of the exhibits D.1 to D.5 with the exhibits 4.5 and 4.6 show that the factor structures to a great extent confirm the predefined structures of the empirical concepts of the contingencies and performance and effectiveness. Nevertheless, the individual items and not the factor structures as such will be used in the comparative analyses in the next two chapters, because, as will be shown below, the factor structures in universities, institutes and companies differ in places. In the case of multi-collinearity (such as the strong negative correlation of time-allocation to research and clinical practice in universities), the item with the highest factor loading is chosen for the analysis.

Universities
In universities technological support capacity and signatory authorization capacity load on two different factors, not only on the empirical concept defined, but also on size. In § 8.1.2 more attention will be paid to the relationship between the proportion of the technical, analytical and administrative support staff on the one hand and the size of the unit on the other. The negative association between signatory authorization capacity on the one hand, and external funding and junior to senior scientist rate on the other was expected in light of the hypothesized contrast between internal and external orientation (*hypothesis 2.4*)[1]. The negative relationship between signatory authorization capacity and size is more surprising. It indicates that professors in smaller research units can invest more without the previous consent of higher management than professors in larger units. Another interesting point is the inverse relationship between time allocated to research and time allocated to clinical practice, which seems to be a clear confirmation of *hypothesis 2.2*. It is interesting to notice that the measures of scientific credibility, such as the number of papers received for peer review and the participation in editorial boards, form one factor with international scientific publishing. Apparently there are research units which clearly have a cosmopolitan orientation. It will be interesting to see in the next chapter whether or not these units overlap

[1] Because the factor loadings are a reflection of the correlation matrix it is not surprising that signatory authorization capacity is negatively associated with external funding ($r = -0.34^{*}$), supervision rate ($r = -0.28^{*}$) and size ($r = -0.29^{*}$).

with the externally oriented units mentioned above.

Institutes

In institutes, only those empirical concepts were used in the factor analysis which could be attributed to the research unit level, to avoid loss of statistical power. Therefore, the items external funding, material resources and annual growth rate, which concern the institute level, were not used. Junior to senior scientist rate was not included, because real supervisory relationships, comparable to the ones between senior scientists and PhD students in universities, are not found in institutes. Project size was not distinguished as a separate factor, it loads negatively on size (so in larger units the relative size of the projects was smaller) and positively on power. A reason for the negative relationship between project size and the size of the research unit may be that a project (in fact a research group) is bound to a certain maximum level. As a consequence, in the larger units the relative weight of the largest research project will be less than in the smallest research units. The predefined empirical concepts organizational age, technology and power are reduced to two factors. This is probably due to the fact that the items material resources and external funding are not included in the factor structure. The items research and management experience were combined with technological support capacity into the factor age and technology. The items research experience and project size also occur in the factor power, together with signatory authorization capacity. The negative sign of this last item may indicate that, whereas the size of the unit increases with increasing age, the average signatory authorization capacity decreases. This would be surprising. It is therefore expected that a third factor, such as the difference between the institutes, may have caused this relationship. The participation in editorial boards seems to concern both scientific journals and journals for physicians, because it relates to research and user effectiveness.

Companies

The fact that the technological support capacity and the percentage of the total R&D budget spent on discovery, load on one factor, indicates that within the study sample, companies conducting a more radical strategy could be distinguished from those conducting a more incremental R&D strategy (see § 5.3.1). In § 9.3 this contrast will be examined in more detail.

7.4.2 Management Control

Exhibit 7.4 shows that in all cases Cronbach's α is sufficiently high (> 0.62) to warrant confidence in the internal consistency of the scales constituting the empirical concepts of management control (Van de Ven and Ferry 1980). A factor analysis revealed that three of the items loaded on different empirical concepts in universities on the one hand, and institutes and companies on the other. In the comparison of universities, institutes and companies, these questions were omitted from the analysis.

Exhibit 7.4 INTERNAL CONSISTENCY OF THE EMPIRICAL CONCEPTS OF MANAGEMENT CONTROL IN UNIVERSITIES, INSTITUTES AND COMPANIES

management control	number of items	Cronbach's α		
		universities	institutes	companies
personnel control				
effectiveness	12	0.77	0.87	0.85
resources control				
adequacy	4	0.72	0.79	0.90
administrative control	4	0.66	0.64	0.78
process control				
planning	3	0.81	0.79	0.79
research process communication	3	0.69	0.63	0.79
external control				
external communication	5	0.63	0.68	0.79

- The length of the appointment procedures loaded on personnel control in universities and on resources control in institutes and companies.
- The pace of resource allocation loaded on contractor communication in universities and on resources control in institutes and companies.
- The adequacy of personnel and material resources loaded on adequacy, and administrative control in universities, whilst in institutes and companies it only loaded on adequacy.

These differences in the factor structure seem to reflect a difference in the position of the professional in the organization. In the more vertically organized institutes and companies, appointment procedures and allocation of resources may be merely dependent on the internal rules, and thereby are primarily related to organizational flexibility. In universities the individual professor has to struggle for resources within the faculty, and therefore these items may be more related to control capacity.

7.5 CONCLUDING REMARKS

The response rate and the analysis of the non-response suggest that the study population can be regarded as representative for biomedical research in Dutch universities and institutes, and for R&D in global innovative pharmaceutical companies. Furthermore, the high factor loadings of the individual items and the level of the 'eigenvalues' provide confidence in the reliability of the operationalizations of the contingencies and performance and effectiveness. The height of Cronbach's α provides confidence in the reliability of the operationalizations of management control. In the next chapter the results found in universities and institutes, and in chapter 9 those found in companies, will be presented.

CHAPTER 8

UNIVERSITIES AND INSTITUTES[1]

This chapter concentrates on the results from universities and institutes. In the first three paragraphs comparisons are made between the contingencies, management control and performance and effectiveness. In order to show the differences connected with patient care, preclinical and paraclinical units are presented separately from clinical units. The Spearman rank correlations and the neural network associations between the contingencies and management control and performance and effectiveness are presented in the next two paragraphs. This chapter ends with a qualitative analysis at the university and institute level.

8.1 CONTINGENCIES

Exhibit E.1 compares the contingencies in universities and institutes. It shows that on average 20 staff members work in a research unit, and that more than half of them are scientists. The average project size in universities is larger than in institutes. In universities more than half of the scientific staff works on the main

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[1] Different aspects of the contingencies and management control in universities and institutes and the comparison of unversities, institutes and companies are reported in:

Omta, S.W.F., L.M. Bouter and J.M.L. van Engelen 1993, A Comparative Study of Management and Organization of Biomedical and Pharmaceutical Research in Universities, Institutes and Companies, in *Bedrijfskunde en Technologie*, ISBN 90-365-0635-2, UT Service, Enschede, pp. 97-105.

Omta, S.W.F., L.M. Bouter and J.M.L. van Engelen 1993, *Contingencies related to Research Performance in Academia: a Comparative Study of 40 Biomedical Departments in the Netherlands*, Research Report 1993-11, ISSN 0926-4485, Groningen, 20 pp.

Omta, S.W.F., and J.M.L. van Engelen 1995, *Research Performance and Effectiveness: a Comparative Study of 57 Biomedical Laboratories in Universities and Institutes*, 3e NVAM-congres Technologie, Innovatie en Diensten, Erasmus Universiteit Rotterdam.

research line, whereas in institutes this is about one-third. The difference in time-allocation between preclinical and paraclinical units and institutes on the one hand and clinical units on the other, is significant ($\chi^2 = 16.68^{**}$). Whereas researchers in preclinical and paraclinical units and institutes spend about three-quarters of their time on conducting and supervising research, the average time spent in clinical units is only half of that. The self-estimation of 38% is somewhat higher than the findings of the Central Bureau of Statistics (CBS 1985), which recorded an actual time spent on research in clinical medicine of approximately 30%. The time spent on clinical practice shows an inverse relationship. While in the preclinical and paraclinical units the time spent on clinical practice is almost zero (some diagnostic testing), this increases to more than 40% in clinical units.

As could be expected, the time-allocation to education is significantly larger in universities. Nevertheless, the institute staff indicated spending on average 6% of their time on educational tasks. In institutes more time is allocated to management and acquisition than in universities. It was indicated in the structured interviews that the latter task in particular gets more attention now than it did about 5 years ago. This extra time spent does not seem to have led to a higher percentage of external funding. Both in universities and institutes this percentage is high, 36% to 43% of the personnel and material resources stems from external funding. It is often argued that if more than one-third of the resources of a research unit stems from external funding the (programmatic) continuity would become at risk. For most of the research units this is already the everyday situation. Both in universities and institutes, the head of the unit has had about 18 years of research experience. In institutes, less than four years after attaining a PhD he/she is appointed head of department, whereas in universities it takes the professor on average eight years to attain a chair. The running costs in biomedical research, being part of 'Big Science' (Spiegel-Rösing and De Solla Price, eds. 1977) is rather high. The material costs per researcher amount from US$ 9,000 in clinical units to US$ 20,000 in institutes. The signatory authorization capacity is comparably high, from on average US$ 4,500 in clinical units to US$13,000 in preclinical and paraclinical units. However, the differences between the academic research units are considerable, in a number of research units the signatory authorization capacity is only US$ 750. The number of junior scientists equals the number of senior scientists in clinical units and goes up to about 1.5 times the number of senior scientists in preclinical and paraclinical units.

8.1.1 Staffing Structure and Age Distribution

Exhibit 8.1 shows that the staffing structure in universities and institutes is more or less the same. The head of the unit and the senior scientific staff together account for between 23% (preclinical and paraclinical units) and 30% (clinical units and institutes) of the total staff, whilst the junior scientific staff accounts for between 27% (clinical units) and 36% (preclinical, and paraclinical units and institutes), and the technical, analytical and administrative support staff counts for between 40% and 44%. Nearly half of the scientific staff and two-thirds of the support staff hold a tenure appointment (data not shown).

Exhibit 8.1 COMPARISON OF STAFFING STRUCTURE, mean and (s.d.)

staffing structure	universities		institutes n=17
	pre/para-clinical units n=24	clinical units n=16	
unit head	1.0	1.0	1.0
senior scientific staff	3.4 (2.5)	5.4 (4.2)	4.3 (6.3)
junior scientific staff	6.8 (4.1)	5.9 (3.8)	6.2 (5.0)
support staff	7.6 (6.6)	9.8 (10.6)	7.6 (5.1)
total	18.8 (11.7)	22.1 (15.0)	18.8 (11.5)

Exhibit 8.2 shows that the staff of the research units is rather young, with one half (in institutes) to three-quarters (in preclinical and paraclinical units) of the total staff under the age of 40. The senior scientific staff members in preclinical and paraclinical units are, on average, younger than their colleagues in clinical units, and significantly younger than those in institutes. As could be expected, in universities almost the entire junior scientific staff, for the largest part PhD students, is under 40. In institutes 40% of the junior staff is over 40 years of age. This shows that, in contrast to universities, the term junior scientific staff in institutes relates to a hierarchical category more than to a supervisory relationship. The age distribution of the unit heads shows an inverse relationship. Whereas only 1% to 4% of the professors are under 40, this percentage increases to 19% of the research unit heads in institutes. As has already been mentioned in the last paragraph, the unit heads in institutes are appointed to their management

Exhibit 8.2 PERCENTAGE OF STAFF IN THE DIFFERENT RANKS UNDER THE AGE OF 40, mean and (s.d.)

staffing structure	universities		institutes %	F-value
	pre/para-clinical units %	clinical units %		
unit head	1 (7)	4 (13)	19 (39)	3.02 *
senior scientific staff	52 (33)	32 (31)	26 (18)	3.78 **
junior scientific staff	100 (2)	100 (1)	60 (29)	3.66 **
support staff	69 (27)	78 (25)	72 (36)	0.45
total	73 (19)	64 (18)	50 (18)	3.05 *

* $p < 0.1$; ** $p < 0.05$

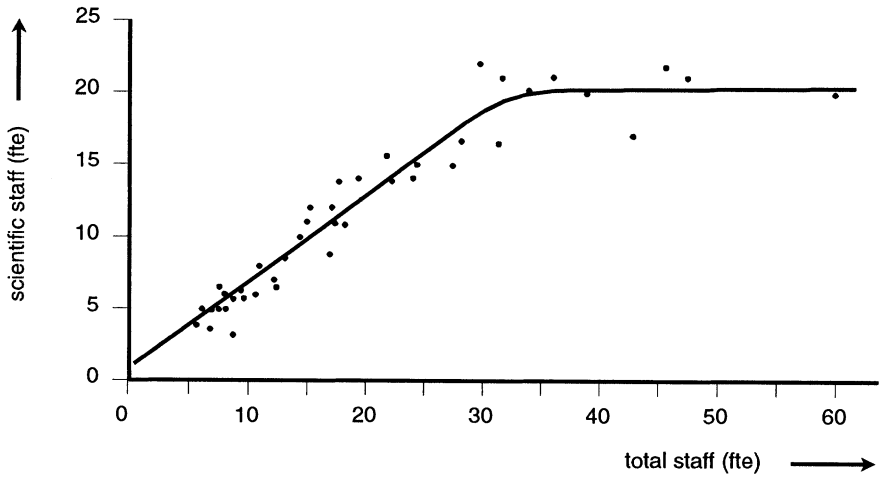
positions on average earlier in their careers than the professors. The high percentage (69% to 78%) of young technical, analytical and administrative support staff is remarkable. Because the majority of the support staff members hold a tenure appointment, the personnel flow must be considerable.

8.1.2 Staffing Structure and Size

The results indicate that in institutes both the scientific staff and technical, analytical and administrative support staff increase linearly with unit size (Y). The regression equations are ($Y = 0.6X + 0.3, r^2 = 0.94^{****}$) for the scientific staff and, consequently ($Y = 0.4X - 0.3, r^2 = 0.95^{****}$) for the support staff. As exhibit 8.3 shows, this is not the case in universities. Until about 30 fte the number of scientific staff rises almost linearly ($Y = 0.6X + 0.8, r^2 = 0.91^{****}$). Above this size the number of scientific staff seems to reach a plateau level of around 20 fte. The curve presented in exhibit 8.3 has been assessed with the aid of neural network modelling ($r^2_{neural\ network} = 0.94^{****}$). To avoid misinterpretation, the reader must bear in mind that the number of research units upon which this observation of a possible plateau level is based is rather low, at only 10 research units. In contrast to the scientific staff the number of support staff continuously increases linearly with size ($Y = 0.6X - 2.8, r^2 = 0.90^{****}$). Until a unit size of around 35 fte

is reached the absolute number of researchers is higher than the number of support staff; thereafter the number of support staff is higher. An explanation for this finding could be that the tasks are not evenly distributed with size. For instance, the larger research units may employ more technical and analytical staff for clinical laboratory work. However, no significant differences were found between the size and the preclinical, paraclinical or clinical background of the research units. The dis-proportionate increase of the scientific and the support staff has a large impact on the research effectiveness of the units. This point will be returned to in the discussion of exhibit 8.4.

Exhibit 8.3 SCIENTIFIC STAFF VERSUS TOTAL STAFF OF THE RESEARCH UNITS IN UNIVERSITIES IN 1991 (n=42)



8.2 MANAGEMENT CONTROL

Exhibit E.2 shows that the average assessment of the variables of system control in institutes is significantly higher than in universities. Whereas the effectiveness of personnel policy and the adequacy of resources is judged slightly positively in institutes, it is judged negatively in universities (the average assessment is below 3 on the Likert 5-point scale). As regards process and external control, the differences are small. The scientific staff members in institutes attend more international congresses as a participant, whereas the university researchers present significantly more papers at congresses. The differences between preclinical and

paraclinical compared to clinical units are small, only the variables of external control are somewhat higher in preclinical and paraclinical units.

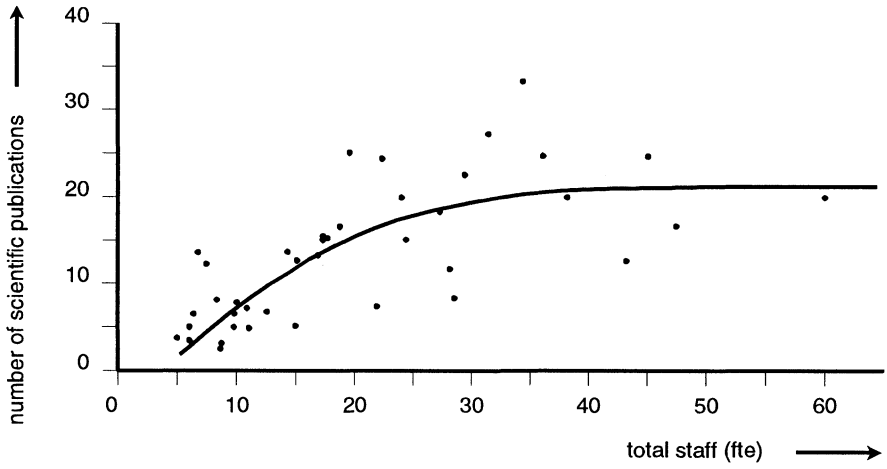
8.3 PERFORMANCE AND EFFECTIVENESS

Exhibit E.3 shows that most of the units were growing, at 8% to 10% per year, despite of the budget retrenchments. This could merely be attributed to the increase in external funding, which grew from around 20% in 1985 to 40% in 1990. The potentially destabilizing effect on the programmatic continuity of such a high percentage of external funding is already mentioned in § 8.1. The research effectiveness in terms of scientific papers per researcher is higher in universities than in institutes. In universities the researchers published (and supervised) more than one scientific paper per researcher annually. Calculated per PhD student, this is approximately 2 to 2.5 papers per year. A PhD student defends a thesis on average 5 years after starting a research project. The difference in user effectiveness between preclinical and paraclinical units on the one hand and clinical units on the other is significant. Whereas researchers in clinical units published a paper in a journal for physicians once a year, researchers in preclinical and paraclinical units did this only once in 3 to 4 years. The research units in institutes took an intermediate position with about 2 articles in three years. Both in universities and institutes the number of citations per paper numbers somewhat above the journal average and the world average for the (sub-)discipline(s) involved. The citation score weighed for (sub-)discipline is significantly higher for institutes. Interestingly, the citation score of the research units in which the scientific staff publishes less than 1 scientific paper per researcher per year (11 units in universities and 9 in institutes) is significantly higher than in units in which more than 1 paper per year is published (29 and 8 units, respectively). This difference is the largest for the citation score, weighed for (sub-)discipline (***1.65 versus 1.10, $F_{\text{one-way ANOVA}} = 4.9^{**}$***).

8.3.1 Size and Research Performance

Exhibits 8.4 shows the consequence of the disproportionate increase of the scientific and the support staff on the research performance in universities. Up to

Exhibit 8.4 NUMBER OF SCIENTIFIC PAPERS VERSUS TOTAL STAFF OF THE RESEARCH UNITS IN UNIVERSITIES IN 1991 (n=40)



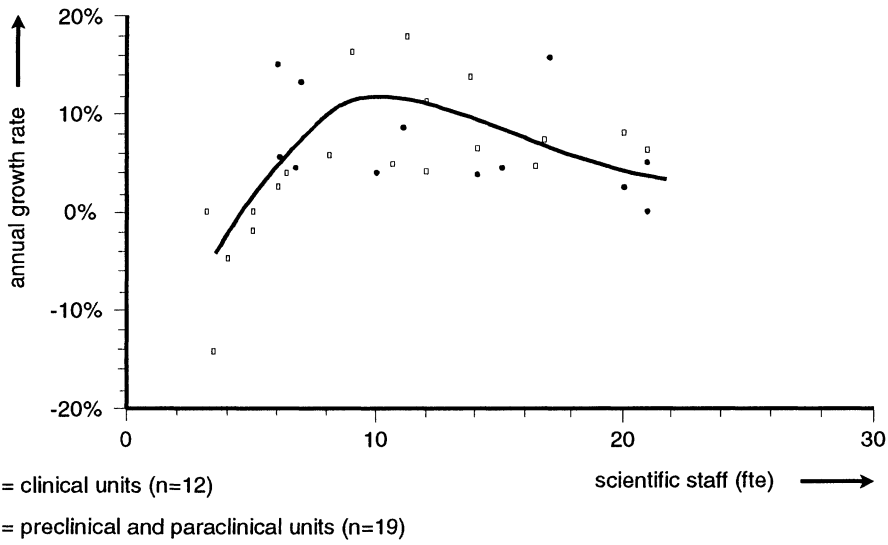
about 30 staff members the number of scientific papers increases gradually with size, thereafter the curve deflects ($r^2_{neural\ network} = 0.51^{**}$). Further increase in staff does not result in additional scientific papers. However, if the average number of scientific papers is plotted against the number of scientific staff, the picture changes. Then the number of papers increases almost proportionately with size ($Y = X + 1.8, r^2 = 0.61^{***}$). The same relationship is found in institutes. Here the regression equation is ($Y = 1.1X - 0.9, r^2 = 0.58^{***}$). The correlation with user publications is weaker in both universities and institutes.

8.3.2 Annual Growth Rate

Exhibit 8.5 ($r^2_{neural\ network} = 0.45^{**}$) shows that the annual growth rate differed considerably, from a decline of more than 10% at one end of the scale, to an increase of more than 15% per year at the other end. It should be remembered that the differences are less spectacular in absolute numbers, because of the limited size of most of the units. However, the smallest research units seem to be at risk. The 5 research units with 5 or less researchers, corresponding to a total unit size of less than 9 staff members, are the only ones which remain constant or declined. These are all preclinical and paraclinical research units. Above the

level of 5 researchers a steady increase in annual growth rate occurred to a level of about 10 researchers, whereafter the annual growth rate had a tendency to decline again. The annual growth rate also showed a tendency to decline significantly with increasing organizational age (see exhibit 8.6).

Exhibit 8.5 ANNUAL GROWTH RATE VERSUS THE NUMBER OF SCIENTIFIC STAFF OF THE RESEARCH UNITS IN UNIVERSITIES IN 1991



8.4 BIVARIATE ASSOCIATIONS

Exhibit F.1 shows some interesting similarities and differences between preclinical and paraclinical units on the one hand and clinical units on the other:

- The time allocated to research and clinical practice shows an inverse relationship with research and user effectiveness. If more time is allocated to research, a higher research effectiveness is measured, and if more emphasis is laid on clinical practice (or clinical advising and laboratory testing in preclinical and paraclinical units), a higher user effectiveness is measured. These contrasts can only partly be attributed to a difference in size. Both in preclinical and paraclinical, as well as in clinical units,

the correlation of size with time allocated to research is slightly negative ($r = -0.15$ and $r = -0.23$, respectively) and the correlation of size with time allocated to clinical practice is slightly positive ($r = 0.27$ and $r = 0.08$). These correlations are too weak to serve as an explanation for the differences found.

- The different relationship between annual growth rate and the size of the units has already been shown in exhibit 8.5. It can be chiefly attributed to the combined impact of the difference in the size and the organizational age (see the next point).
- The contingencies organizational age and size are inversely associated with the preclinical and paraclinical or clinical background of the research units. In clinical units, research experience and management experience are positively ($Y_{man.\,exp.} = 0.6X + 4.5$, $r^2 = 0.52^{***}$), and in preclinical and paraclinical units negatively ($Y_{man.\,exp.} = -0.5X + 15.7$, $r^2 = 0.18^{*}$) associated with the size of the research staff.
- In clinical units signatory authorization capacity is positively, and junior to senior scientist rate negatively, associated with user effectiveness, which seems to point to a more internal orientation. In preclinical and paraclinical units in contrast, signatory authorization capacity is negatively, ($r = -0.33^{*}$) and external funding is positively, ($r = 0.43^{*}$) associated with research performance[1], which seems to point to a more external orientation.

Furthermore, exhibit F.1 shows the following contrasts between clinical research units which concentrate more on research and those which concentrate more on clinical practice. The clinical units which allocate more time to research are somewhat smaller, have a higher annual growth rate, and spend less time on clinical practice. The professor is on average younger and shows a more external orientation. There is relatively more junior staff, and there is significantly more international communication. Interestingly, the citation score is lower than in the units which concentrate more on clinical practice. The relatively older professor of these units has a higher signatory authorization capacity, and a higher percentage of senior scientific staff compared to junior scientific staff. Finally, the amount of international communication is relatively low in these units.

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[1] Because these units are also larger (size vs. sign authorization capacity: $r = -0.46^{**}$; size vs. external funding: $r = 0.48^{**}$), this difference is not found in the correlation with research effectiveness.

Exhibit F.2 shows that in preclinical and paraclinical units, the effectiveness of personnel policy is positively associated with all the different effectiveness measures, except user effectiveness. Effectiveness of personnel policy is also positively associated with all the effectiveness measures in clinical units, although not at a significant level. The other management control variables in clinical units present unclear relationships, probably due to the confounding influence of patient care. Because the contrast between institutes and universities is much larger than between preclinical and paraclinical units compared to clinical units, these units are taken together in the multi-variate comparison of universities and institutes.

8.5 MULTIVARIATE ASSOCIATIONS

Exhibit 8.6 shows the multivariate models of the contingencies and management control with performance and effectiveness, as calculated by the neural network. The most important results are supported by the Spearman rank correlations (see the exhibits F.3 and F.4). The size of the research staff contributed most to the explained variance of research and user performance. To compensate for its obvious influence, size was entered as the first variable in the learning process. The best models are found for research performance in universities and user performance in institutes, with a total explained variance of 68% and 77%, respectively. This is combined with a good test set fit of above 50%. In both cases the contingency size and the management control variables, effectiveness of personnel policy, administrative control and international and contractor communication, and in the case of research performance in universities, the closely to contractor communication related contingency external funding, count for a fair amount of the explained variance. Relatively weaker models are found for user performance in universities and research performance in institutes, with a total percentage of explained variance of 52% and 43%, respectively. The relatively high test set fit in the case of user performance in universities stems from the strong correlation with the time spent on clinical practice and the related contingencies, smaller project size and older organizational age (see the last paragraph). The annual growth rate is not correlated with management control. It correlates positively with time allocated to research, and negatively with organizational age and signatory authorization capacity . This relationship can also be related to the preclinical and paraclinical versus clinical background of the units (see the last paragraph). The strength of the model, however, is weaker, with a percentage ex

plained variance of 37%.The model of the citation score in universities and to a lesser extent in institutes, shows a similar pattern to that for research performance in universities, but both models are very weak, with a total of explained variance of around 25%, and a very low test set fit.

8.6 ORGANIZATIONAL LEVEL

In order to investigate whether an uneven distribution of the quality of the research units among the different universities and institutes could be established, thus indicating a possible difference in the management control situation, the results were also analyzed using the average scores of the units in the 8 universities (numbered 1 to 8) and the five institutes (numbered 1 to 5). Because of the high level of aggregation it was decided to do a qualitative analysis only. A median split has been made. The 5 universities and/or institutes which got the highest scores for a certain empirical concept are depicted as a plus sign (further referred to as positive scores), the 3 organizations around the median are depicted as neutral (neutral scores), and the 5 with the lowest scores with a minus sign (negative scores). This means that those 5 organizations which have, on average, the largest research staff per unit, for instance, or the most positive assessment of personnel control, or the highest number of PhD graduations are indicated with a plus sign (see appendix G).

The exhibits G.1, G.2 and G.3 show that, if universities and institutes are compared, the figures in exhibit E.1 become more contrasted. In all institutes the average project size is smaller than in universities, the average assessment of system control is clearly more positive, and the frequency of international communication is higher. Contrary to this, the contacts with outside contractors are more frequent in universities, and higher scores are obtained for the measures of research effectiveness. Interestingly, the figures for user effectiveness are also clearly higher in universities, not only the number of articles in journals for physicians, but also the number of articles in user journals. The contrast in the citation score is quite remarkable. Only one university could match the number of citations per article received for institutes.

There is clearly an uneven distribution of the average quality of the research units in the different universities and institutes. Two medical faculties (universities 3 and 6) seem to house some of the best research units. Both these universities are

Exhibit 8.6a PERCENTAGE EXPLAINED VARIANCE OF PERFORMANCE AND EFFECTIVENESS BY THE CONTINGENCIES AND MANAGEMENT CONTROL

contingencies	universities (n=40)				institutes (n = 17)		
	performance		citation score	growth rate n=31	performance		citation score
	research %	user %	%	%	research %	user %	%
size							
research staff	46	13	-	-	33	37	-
project size	-	(-)5	(-)6	-	5	-	-
time-allocation							
research	-	-	-	8	-	-	-
education	-	-	-	-	-	-	-
management and acquisition	-	-	-	-	-	-	-
clinical practice	-	19	-	-	-	-	-
age							
research experience	-	-	-	(-)16	-	-	-
management experience	-	15	-	-	-	-	-
technology							
technological support capacity	-	-	-	-	-	-	-
material resources	-	-	-	-	na	na	na
power							
signatory authorization capacity	-	-	-	(-)13	-	-	9
external funding	3	-	-	-	na	na	na
junior to senior scientist rate	-	-	2	-	-	-	-

Exhibit 8.6b PERCENTAGE EXPLAINED VARIANCE OF PERFORMANCE AND EFFECTIVENESS BY THE CONTINGENCIES AND MANAGEMENT CONTROL

management control	universities (n=40)				institutes (n=17)		
	performance		citation score	growth rate n=31	performance		citation score
	research %	user %	%	%	research %	user %	%
system control							
effectiveness	5	-	4	-	5	14	3
adequacy	-	-	(-)4	-	-	-	-
administrative control	4	-	6	-	-	10	-
process control							
planning	-	-	-	-	-	-	-
frequency	-	-	-	-	-	-	-
attendancy mix	-	-	-	-	-	-	-
external control							
international communication	2	-	-	-	-	7	-
contractor communication	8	-	5	-	-	9	12
R^2 total	68	52	27	37	43	77	24
R^2 training set	69	51	30	37	75	80	32
R^2 test set	53	65	10	37	19	64	7

(-) = negative association with performance and effectiveness - = no additional explained variance na = not applicated (n=5)

in the top five as regards to both aspects of research effectiveness, the number of international scientific publications and the number of PhD graduations per scientist. This is also the case as regards to the closely related recognition variables (number of editorial boards and peer review). The relationship with management control is the same as that which was found at the research unit level. In both cases positive scores for research effectiveness go hand in hand with positive or neutral scores for effectiveness of personnel policy, and administrative and external control (together with adequacy of resources).

The research units in the other universities clearly attain lower scores for the empirical concepts of system control. Two universities (2 and 8) receive negative scores on most of the effectiveness measures. In addition most of the management control variables were assessed negatively by the scientific staff. Interestingly, one of these universities scores high on the number of scientific publications, and the other on the annual growth rate of their units. In two universities (4 and 7) positive scores are found for user effectiveness, combined with positive scores for annual growth rate and citation score. The positive scores for user effectiveness were not due to a higher percentage of time allocated to clinical practice. As has already been concluded for the research unit level, the output parameters, citation score, user effectiveness and annual growth rate are not very closely related to management control. This is especially surprising for the last variable. One would expect beforehand that the researchers in a situation of growth would be more positive about variables of management control. A positive growth rate provides, for instance, more job security, and it seems to produce a more rewarding working environment. The relatively small size of the research units may have caused these results because, whilst in relative terms such a research unit may grow vigorously, in absolute terms the growth may be limited to only a few researchers.

Three universities (1, 4, and 5) achieve positive scores for process control. Although the research units in these universities attain positive effectiveness scores on a few points, no uniform pattern could be established. The negative relationships of annual growth rate with organizational age and internal orientation and the positive one with time allocated to research are also (roughly) found at the university level. In universities 4 and 8 a relatively high annual growth rate is combined with negative scores for organizational age and internal orientation and a positive score for time allocated to research (university 4), whereas in university 2 a relatively low annual growth rate is combined with the opposite relationships. For universities 1 (relatively high annual growth rate) and

7 (relatively low annual growth rate), however, no clear relationships are found.

One institute in particular (number 3) seems to be very successful, not only compared to the other institutes, but also compared to universities. It is not only successful in terms of user effectiveness, but also in terms of research effectiveness, scientific recognition and citation score. Institutes 4 and 5 are also particularly effective in terms of citation score, annual growth rate and recognition (institute 4). If the user effectiveness in institutes is compared, these institutes are ranked second and third (data not shown). Both institutes also attain higher scores for the management control variables, effectiveness of personnel policy, administrative control, and external control. The relationships are less clear than in universities, due to the relatively higher scores which are obtained in institutes. Institute 2 scores relatively low. It scores below the average for almost all the empirical concepts. According to the scientific staff, the only managerial task which is relatively well organized is administrative control. The managerial outlook of research institute 1 is comparatively much better. Almost all the management control variables are judged positively by the scientific staff. Nevertheless, institute 1 scores negatively on aspects of user effectiveness. It scores better on research effectiveness and scientific recognition, but compared to universities the results are still lower.

8.7 CONCLUDING REMARKS

Clear differences have been found separating the more-than-average from the less-than-average performers in universities and institutes. In the next chapter the attention will be directed towards industry. It will be interesting to learn whether similar or contrasting results will be found for high and low performers.

CHAPTER 9

COMPANIES[1]

This chapter starts with the descriptive statistics and the relations between the variables measured at ratio-level; i.e. size, technology and performance and effectiveness. In § 9.2 the management control variables measured at ordinal level are described. In the next paragraph the contingencies and management control variables are associated with performance and effectiveness using different bi-variate and multi-variate statistical techniques. This chapter ends with different cross-sections of the study sample on specific characteristics. Companies with a more radical orientation are compared with those with a more incremental orientation, autonomous companies (the pure play pharmaceuticals) are compared with dependent divisions of conglomerates, and companies with an Anglo-American head office are compared with those with a continental European head office.

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[1] Recently, four articles have been published reporting on different aspects of the industrial part of the study:

Omta, S.W.F., L.M. Bouter and J.M.L. van Engelen 1994, Innovative and Industrial Performance in Pharmaceutical R&D, a Management Control Perspective, *Omega, The International Journal of Management Science*, 22 (3) pp. 209-19.

Omta, S.W.F., L.M. Bouter and J.M.L. van Engelen 1994, Managing Industrial Pharmaceutical R&D. A Comparative Study of Management Control and Innovative Effectiveness in European and Anglo-American Companies, *R&D Management*, 24 (4) pp. 301-13.

Omta, S.W.F., 1994, The Effectiveness of Management and Organization of Pharmaceutical R&D. A Comparative Study, in *Managing the R&D Process*, P.C. de Weerd-Nederhof, I.C. Kerssens-van Drongelen, R. Verganti (eds.), ISBN 90-365-0709-X, Twente Quality Centre, pp. 143-52.

Omta, S.W.F., L.M. Bouter and J.M.L. van Engelen 1995, A Management Control Perspective on Industrial Pharmaceutical R&D, in *Proceedings of the Twenty-Eights Annual Hawaii International Conference on System Sciences, Vol. III Information Systems - Decision Support and Knowledge-Based Systems*, J.F. Nunamaker and R.H. Sprague (ed.), ISBN 0-8186-6940-3, IEEE Computer Society Press, Los Alamitos, pp. 552-62.

9.1 SIZE, PERFORMANCE AND EFFECTIVENESS

Exhibit 9.1 shows that the companies in the study grew vigorously between 1986 and 1991, at about 10% a year. The average sales volume of branded ethical drugs amounts to US$ 3,4 billion, with a operating profit margin of 24%. As could be expected of a science-based industry, the average R&D expenditures are high, about 15% of the total sales volume of ethical drugs. About 25% of the total R&D expenditures is spend on discovery, which results in about six patents on NCEs per US$ 10 million per year. The development phase has a long duration. It takes the companies on average more than 9 years to finish the pharmacological and clinical testing necessary to bring an NCE to the prescription drug market.

Exhibit 9.1 DESCRIPTIVE STATISTICS OF SIZE, PERFORMANCE AND EFFECTIVENESS (n=14)

size, performance and effectiveness	mean	standard deviation
size		
sales (US$ million)	3,372	1,913
R&D expenditure (US$ million)	540	248
• discovery (US$ million)	126	70
• development (US$ million)	390	209
performance and effectiveness		
number of patents	73	62
patents / US$ 10 million in discovery	5.3	2.6
length of development (years)	9.3	2.1
annual growth rate (%)	10.5	4.5
operating profit margin (%)	23.6	11.2

Exhibit 9.2 describes the R&D process in more detail. An estimation is given of the length of the different phases of the R&D process, the percentage of the R&D budget spent on these phases, and the number of compounds examined. The data are based on literature and were checked in the structured interviews. The total length of the R&D process from the start of the discovery phase until the final launch of the drug amounts to 7 to 13 years in total. Although the discovery phase can take much longer than the 1 to 2 years mentioned in exhibit

Exhibit 9.2 AN ESTIMATION OF THE AVERAGE DURATION, THE PERCENTAGE OF THE R&D EXPENDITURE AND THE NUMBER OF CHEMICAL COMPOUNDS UNDER RESEARCH IN THE DIFFERENT PHASES OF THE R&D PROCESS

phase in R&D process	duration (years)	R&D exp. (%)	number of compounds
1. discovery phase	1-2	20-30	>10,000/ 500-1,000
2. pharmaceutical development	2-4	25-30	20-50
3. clinical development I, II and III	3-6	15-30	5-7 (I) 3-4 (II) 1-2 (III)
4. registration and launch	1-3	3-5	1
5. clinical development IV	-	15-25	1

sources: Centre for Medicines Research 1993, Taggart 1993 and this study

9.2, most of the time is spent on development (typically 6 to 12 years, depending on the disease), half of it on clinical trials. As a consequence, the largest part of the R&D budget is spent on clinical development, with 30% to 55% of all R&D costs being allocated to phase I to IV clinical trials. About one-third of the costs of the phase IV clinical trials are paid for from the development budget, and two-thirds comes from the marketing budget of the company. The number of chemical compounds which have to be synthesized and screened roughly amounts to 10,000 or more in the case of high capacity screening and 1,000 in rational drug design for a single 'hit' (see § 3.3.2). All companies have claimed a considerable number of launches of innovative products in the last ten years. However, most of them turn out to be therapeutic or pharmaceutic extensions of earlier innovations. Although these extensions can be of major therapeutic importance, they are not considered to be a valid measure for innovative potential. In fact, only 6 of the larger companies launched innovative drugs in the 1980s. However, these innovative drugs accounted for a large part of the company's profitability. Between 10% to 50% (on average 32%) of the total pharmaceutical sales revenues of 1991 stem from these innovative drugs.

Exhibit 9.3 shows the Pearson product-moment correlations of size, technology and performance and effectiveness. The volume of the world-wide sales of branded ethical drugs is significantly correlated with the R&D expenditures and the performance and effectiveness variables, except the annual growth rate. However, the R&D expenditures spent on development do correlate significantly with annual growth rate. Exhibits 9.4 to 9.6 will show these relationships more precisely.

Exhibit 9.3 PEARSON PRODUCT-MOMENT CORRELATIONS OF SIZE, TECHNOLOGY, PERFORMANCE AND EFFECTIVENESS (n=14)

	sales	R&D exp.	patents/ US$10m	dev. length	profit margin	growth rate
sales	x					
R&D expenditure	0.94***	x				
patents / US$10 million	0.63**	0.58**	x			
development length	0.87***	0.87***	0.53*	x		
operating profit margin	0.57**	0.47*	0.05	0.47*	x	
annual growth rate	0.28[1]	0.36	-0.22	0.42	0.36	x

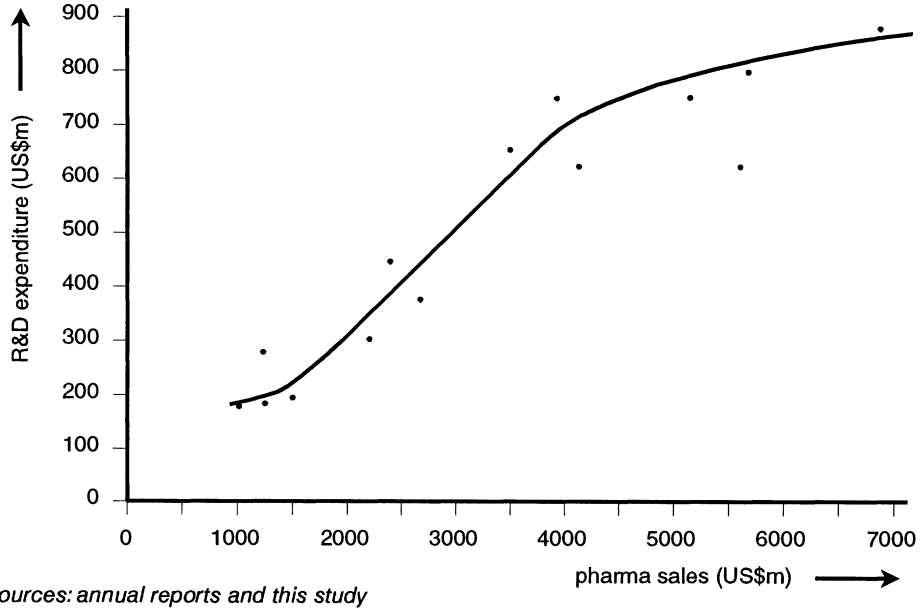
* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$; 2-tailed significance

[1]R&D expenditure spent on development is significantly correlated with annual growth rate (r=0.58**)

Exhibit 9.4 compares the R&D expenditures with the sales of branded ethical drugs in 1991. The curve rises almost linearly until the sales of ethical drugs approaches approximately US$ 4 billion. Thereafter, the R&D expenditures rise only moderately, from about US$ 700 million to a maximum of about US$ 875 million, while the sales of branded ethical drugs rise to approximately US$ 7 billion.

In order to examine the effectiveness of the discovery phase, the average annual expenditures for discovery between 1988 and 1991 are plotted against the average annual number of pharmaceutical patents submitted in the same period. The curve in exhibit 9.5 starts at around US$ 50 million and increases to approximately US$ 200 million, while the average number of patents rises from 10 to 175 patents submitted annually.

Exhibit 9.4 SALES OF BRANDED ETHICAL DRUGS VERSUS THE R&D EXPENDITURE PER COMPANY IN 1991 (n=14)



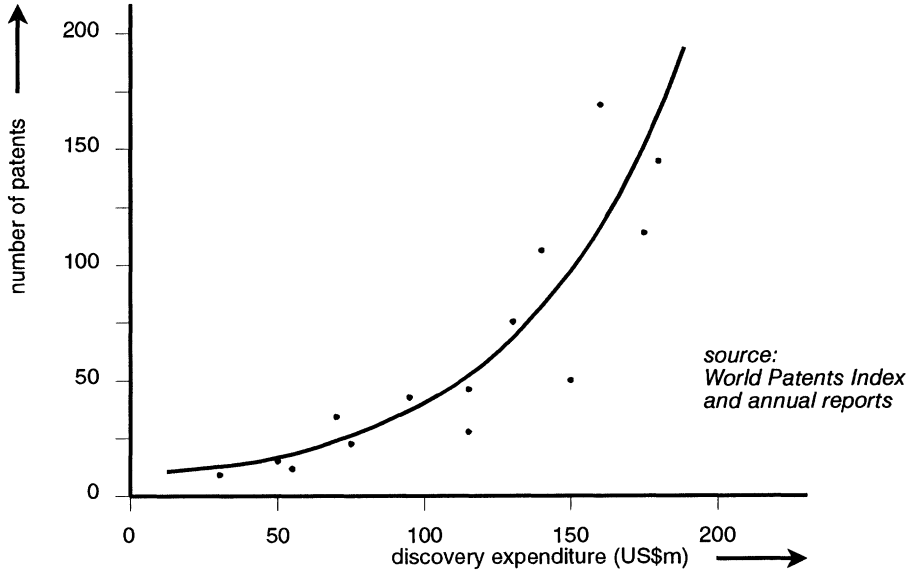
sources: annual reports and this study

A t-test was performed to examine whether a difference in effectiveness could be established between large and small companies. Calculated per US$ 10 million investment in discovery, the large companies submit 9.6 patents per year, while the smaller ones submit only 2.7*[1] patents per year. In addition, the number of therapeutic areas in which the pharmaceutical companies carry out research increases with the size of the R&D expenditures from 5 to 6 therapeutic areas in the smaller companies to 8 to 9 in the larger ones.

In exhibit 9.6, the length of the development phase is plotted against the expenditures spent on development. There turns out to be a significant correlation; the higher the expenditures, the shorter the duration of the development phase. Initially, the length drops steeply, from 12 years at about US$ 120 million, to 9 to 10 years at US$ 250 million. Then it remains constant until around US$ 450 million, and drops again to a length of around 6 to 7 years at above US$ 600 million.

1 * $p < 0.1$

Exhibit 9.5 AVERAGE ANNUAL NUMBER OF PATENTS FOR NEW CHEMICAL ENTITIES SUBMITTED WORLD-WIDE VERSUS THE AVERAGE ANNUAL EXPENDITURE FOR DISCOVERY PER COMPANY FROM 1988 TILL 1991 (n=14)



9.2 MANAGEMENT CONTROL

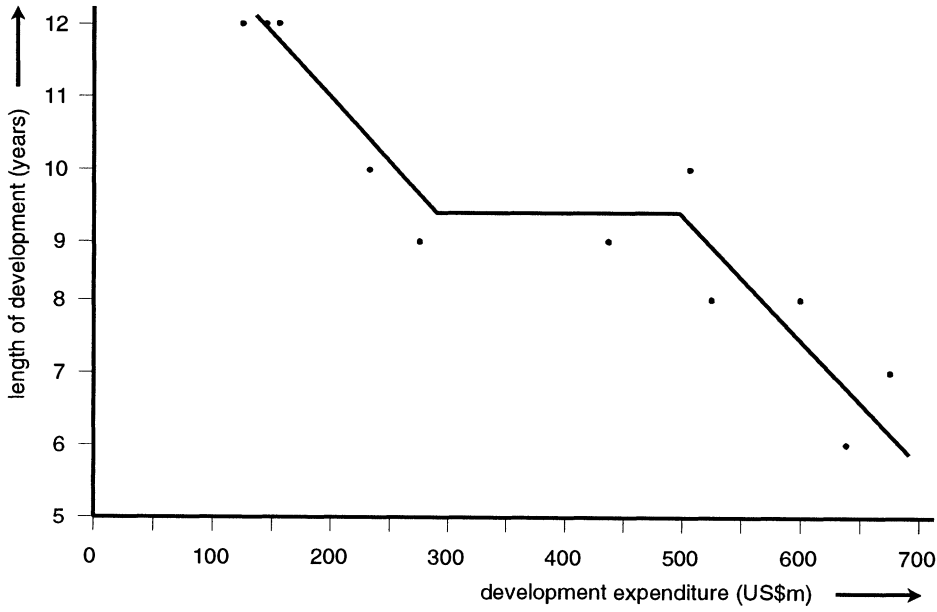
Exhibit 9.7 shows that the average assessment of the management control situation is rather positive. The assessment of the effectiveness of personnel policy, the adequacy of the research budget, laboratory equipment and devices, as well as the pace of administrative procedures, is assessed at above 3 on the Likert 5-point scale.

9.2.1 Bivariate Associations

In exhibit 9.8 the Spearman rank correlations of management control with the variables of innovative and industrial performance and effectiveness are presented. Because of the possible influence of the size of the company, the correlations with the sales volume are also shown. The sales volume shows a high,

although not significant, correlation with effectiveness of personnel policy. The closely related size of the R&D expenditures correlates significantly with the adequacy of resources. The effectiveness of personnel policy and the intensity of international communication are significantly correlated with the operating profit margin. The empirical concepts of resources control are not significantly correlated with any of the performance variables. The frequency of project team meetings is significantly correlated with the number of patents, as is the attendancy mix with shorter development length and annual growth rate. The management control variables are hardly correlated at all (data not shown).

Exhibit 9.6 LENGTH OF THE DEVELOPMENTAL PROCESS VERSUS THE R&D EXPENDITURE SPENT ON DEVELOPMENT PER COMPANY IN 1991 (n=11)



Exhibits H.1 and H.2 show the differences in the mean values of the answers, comparing high and low performers for the different performance and effectiveness measures. A median split was made, based on the answers on ReQuest 2. In most cases a clear division could be made at the median level. Only in the case of the operating profit margin was a clear separation found at another level. In six companies the operating profit margin was below 17%, whereas in the other eight companies it was above 28%. Because operating profit margins between

Exhibit 9.7 DESCRIPTIVE STATISTICS OF MANAGEMENT CONTROL

management control[1]	mean (n=38)	standard deviation
personnel control		
effectiveness	3.33	1.02
resources control		
adequacy	3.56	0.63
administrative control	3.48	1.26
process control		
planning	3.78	1.57
frequency	3.07	0.88
attendancy mix	2.37	0.51
external control		
international communication	3.46	1.31

[1] Likert 5-point scales; higher values indicate a more positive judgement

17% and 28% were not found in any of the companies, the separation is made at this level. The significant relationships of size and management control with the different performance and effectiveness variables, already shown in exhibits 9.3 and 9.8, are evident again here, with additional information about the group means. Of more interest is the observation that the effectiveness of personnel policy turns out to be significantly correlated with 3 of the 4 performance and effectiveness measures. It is true for all four performance and effectiveness measures that the assessment is clearly negative (below 3 on the Likert 5-point scale) in the low performing companies, and clearly positive in the high performing companies. However, because of the inter-correlation of size and the effectiveness of personnel policy, shown in exhibit 9.8, only a multi-variate analysis can give conclusive evidence of whether the effectiveness of personnel policy provides additional explaining power. A short development phase is also significantly associated with the adequacy of resources, the importance of short-term, middle-term and long-term planning and the attendancy mix, indicating a higher level of lateral and cross-functional communication. The frequency of the project team meetings turns out to be significantly higher in the case of high performance in

the discovery phase and is also significant for annual growth rate. Finally, the operating profit margin is also significantly correlated with international communication.

Exhibit 9.8 SPEARMAN RANK CORRELATIONS OF MANAGEMENT CONTROL WITH PERFORMANCE AND EFFECTIVENESS (n=10)

management control	sales	patent number	dev. length	profit marge	growth rate
personnel control					
effectiveness	0.50	0.36	0.43	0.71**	0.44
resources control					
adequacy	0.43[1]	0.24	0.54	0.51	0.30
administrative control	0.14	0.17	0.42	0.39	0.05
process control					
planning	0.31	0.06	0.62*	0.42	0.19
frequency	0.44	0.75**	0.30	0.08	0.48
attendancy	0.18	0.13	0.66**	0.18	0.80***
external control					
international communication	0.25	-0.02	-0.26	0.73**	0.06

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$; 2-tailed significance
[1]adequacy is significantly correlated with R&D expenditure (r=0.67**)

9.2.2 Multivariate Associations

The multivariate associations of size and management control with the different performance variables are presented in exhibit 9.9. Neural network models could be established for all performance measures, 60% to 80% of the total variance being explained by the size of the R&D expenditures and the different management control variables. In all cases the test set fitness is above 50% and the F-value is significant. Size contributes more than 50% of the explained variance. Only for annual growth rate is this percentage lower, namely 30% of the explained variance. The effectiveness of personnel control is the most important factor of the management control variables. All performance and effectiveness

Exhibit 9.9 PERCENTAGE EXPLAINED VARIANCE OF PERFORMANCE AND EFFECTIVENESS BY SIZE AND MANAGEMENT CONTROL (n=10)

	patent number %	develop-ment length %	operating profit margin %	annual growth rate %
size				
R&D expenditure	44	52	43	24
personnel control				
effectiveness	18	4	17	3
resources control				
adequacy	-	-	-	-
administrative control	-	-	11	-
process control				
planning	-	2	-	-
frequency	14	-	-	-
attendancy mix	-	5	-	52
external control				
international comm.	-	-	10	-
R^2 total	76	63	81	79
R^2 training set	79	59	80	79
R^2 test set	53	85	82	75

- = no additional explained variance

measures are associated with effectiveness of personnel policy in the multi-variate models. The link between the other management control variables and the different performance measures is less clear. Administrative control and internation-

al communication are associated with operating profit margin, planning and attendancy mix with the length of development, and the frequency of project team meetings with the number of patents. The attendancy mix is significantly associated with annual growth rate 70% of the explained variance of annual growth rate can be attributed to this variable.

9.3 DIFFERENT CROSS-SECTIONS OF THE STUDY SAMPLE

Exhibit H.3 shows that a more radical orientation and a more incremental orientation can be distinguished. Radical companies spend on average more than 30% of the total R&D budget on discovery, and employ more than 30% scientists in R&D. Incremental companies spend less than 20% on discovery, and employ 20% or fewer scientists in R&D ($r = 0.69^{**}$). The idea that the difference found in the height of the discovery budget relative to the total R&D budget is merely depended on the size of the companies, smaller companies having to spend more on discovery to get sufficient 'leads' for further development, is only partly true. The companies conducting an incremental strategy are somewhat, but not significantly, larger than those conducting a radical strategy. As expected, a radical strategy is significantly correlated with international communication, whereas an incremental strategy correlates significantly with research process communication. However, no significant correlation is found between a more radical strategy, and the (absolute or relative) number of patents. In addition, no significant correlation is found between a more incremental strategy and the length of the developmental process (data not shown). Contrary to this, a significant correlation is found with annual growth rate. The companies conducting an incremental strategy grow nearly twice as fast than those conducting a more radical strategy.

Exhibit H.4 compares autonomous pharmaceutical companies (the pure play pharmaceuticals with dependent pharmaceutical divisions of conglomerates, and compares Anglo-American with continental European companies. The pure play pharmaceuticals perform better than the divisions of conglomerates. They are somewhat, but not significantly, larger than the divisions of the conglomerates. Comparatively, the differences between Anglo-American and continental European companies are much larger. The average sales volume, the R&D expenditures and the operating profit margin in Anglo-American companies are more than twice as high as in the continental European companies. In both comparisons the difference in the assessment of the effectiveness of personnel policy is

significant. The emphasis on career planning, and, although to a lesser extent, the way reorganizations are performed, count for a large proportion of this difference. Both items are assessed very negatively in the pharmaceutical divisions of conglomerates; the average values on a Likert 5-point scale are considerably below 3. In pure play pharmaceuticals, in contrast, the assessments are much more positive; the average values are considerably above 3. In the comparison of Anglo-American and continental European companies, the difference in the assessment of career planning is even more pronounced. The employees in the Anglo-American companies appear to be considerably more positive about the possibilities of career planning than their colleagues in the continental ones. In addition, a more positive opinion about the possibilities of career planning is found in the larger companies than in the smaller ones. However, this difference is smaller than that between pure play pharmaceuticals and conglomerates and even much smaller than between Anglo-American and continental European companies. Therefore, it is assumed that the differences in the assessment of career planning, although partly scale dependent, can to a great extent be attributed to the Anglo-American or continental European background of the company. However, in the comparison of Anglo-American or continental European companies, the difference in the assessment of the conduction of reorganizations disappear almost totally. Consequently, it is likely that this difference must mainly be attributed to the (level of) autonomy of the company involved. International communication is significantly correlated with the background of the company; scientists in Anglo-American companies attend significantly more international congresses and workshops than their colleagues on the continent.

9.4 CONCLUDING REMARKS

In the last two chapters the results from universities, institutes and company laboratories have been discussed separately. In this concluding paragraph the data will be integrated into two tables, showing the differences and similarities between the three strata. Exhibit 9.10 integrates the exhibits E.2 and 9.7, and exhibit 9.11 integrates the exhibits 8.6 and 9.9.

Exhibit 9.10 shows that clear differences are found in the level of management control in universities, institutes and companies. The scientific staff members in companies are, on average, more positive about the effectiveness of personnel policy than their colleagues in universities and institutes. Although a large differ

Exhibit 9.10 A COMPARISON OF THE LEVEL OF MANAGEMENT CONTROL IN UNIVERSITIES, INSTITUTES AND PHARMACEUTICAL COMPANIES, mean and (s.d.)

management control	universities n=142	institutes n=44	companies n=38	F-value
personnel control				
effectiveness	2.52 (0.77)	3.09 (0.73)	3.33 (1.02)	6.96***
resources control				
adequacy	2.54 (0.93)	2.89 (0.85)	3.56 (0.63)	3.65**
administrative control	2.00 (0.99)	2.41 (1.03)	3.48 (1.26)	8.96***
process control				
planning	3.62 (1.17)	3.64 (1.17)	3.78 (1.57)	0.06
frequency	4.25 (0.78)	4.49 (0.96)	3.07 (0.88)	10.50***
attendancy mix	2.81 (0.44)	2.80 (0.65)	2.37 (0.51)	3.37**
external control				
international communication	2.54 (0.97)	3.06 (1.02)	3.46 (1.31)	3.64**

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

ence could be established between scientists in the different companies (see appendix H), on average their judgement in terms of renumeration, career possibilities and recognition was clearly more positive. The other empirical concepts of system control, adequacy and administrative control are also judged more positively in companies. The estimated pace of the administrative procedures is nearly twice as high as in universities, which could indicate that the hypothesis of higher organizational flexibility in companies, at least concerning operational flexibility, is correct. The generally negative judgements of the researchers in universities concerning the empirical concepts of system control, has already been mentioned as a possible illustration of the diminishing organizational flexibility due to the budget retrenchment. The monitoring of the scientific network is more intensive and the participation in international congresses is significantly higher in industry. The researchers in institutes take an intermediate position between universities and companies on all the empirical concepts of system and external control. Research process control is significantly more intensive in universities and institutes than in companies, and the frequency of research meetings and the attendancy mix is significantly higher.

Exhibit 9.11 shows the neural network associations of the contingencies and management control with performance and effectiveness. It is interesting to notice that the effectiveness of personnel policy, administrative control and external control, together with size explains (in strictly statistical sense) most of the variance of research performance in universities, user performance in institutes and operating profit margin in companies. The fact that the empirical concepts of process control do not add additional explained variance to all the performance and effectiveness measures in universities and institutes and to the industrial performance and effectiveness measures in pharmaceutical companies, is also worth mentioning.

The results presented in this section will be discussed in more detail in the final Section. In the trajectory of theory construction, conclusions will be drawn regarding the theoretical framework of this study. A critical reflection on the validity of the different theories and methods will be combined with strong references to management impact, following the trajectory of theory application.

Exhibit 9.11 PERCENTAGE EXPLAINED VARIANCE BY CONTINGENCIES AND MANAGEMENT CONTROL OF PERFORMANCE AND EFFECTIVENESS

	universities n=40			institutes n=17			companies n=10		
	rp %	up %	cs %	rp %	up %	cs %	pn %	dl %	pm %
size									
research staff	46	13	-	33	37	-	44	52	43
contingencies	3	39[1]	8	5	-	9	na	na	na
personnel control									
effectiveness	5	-	4	5	14	3	18	4	17
resources control									
adequacy	-	-	(-)4	-	-	-	-	-	-
administrative control	4	-	6	-	10	-	-	-	11
process control									
planning	-	-	-	-	-	-	-	2	-
frequency	-	-	-	-	-	-	14	-	-
attendancy mix	-	-	-	-	-	-	-	5	-
external control									
international communication	2	-	-	-	7	-	-	-	10
contractor communication	8	-	5	-	9	12	na	na	na
R^2 total	68	52	27	43	77	24	76	63	81
R^2 training set	69	51	30	75	80	32	79	59	80
R^2 test set	53	65	10	19	64	7	59	85	82

- = no additional explained variance
(-) = negative association with performance and effectiveness
[1] = clinical practice

rp = research performance
up = user performance
cs = citation score

pn = patent number
dl = development length
pm = profit margin
na = not applicable

SECTION 4

DISCUSSION AND CONCLUSIONS

CHAPTER 10

UNIVERSITIES AND INSTITUTES

In this Section the main conclusions are drawn following the hypotheses formulated in chapter 5. In this chapter the conclusions for universities and institutes are discussed, and in chapter 11 those for companies. In the final chapter the management control situation in the three strata is compared.
Following the trajectory of theory construction, theory modifications are suggested based on the empirical findings, in order to improve the understanding of the observable reality. The weak and strong sides of the study design are evaluated and the character of the follow-up studies is discussed. Following the trajectory of theory application, and based on the contextual documentation supplied in this study, design parameters are deduced for practical use for research management, system designers, administration and research policy.

10.1 HIGH AND LOW PERFORMERS

Supportive evidence has been found for the main hypothesis, *hypothesis 1*, that high performers will obtain more positive scores on a number of empirical concepts of management control than low performers. The empirical concepts effectiveness of personnel policy, administrative control, external control (together with the closely related contingency external funding) and the contingency size turn out to associate strongly with research performance and effectiveness in universities and user performance and effectiveness in institutes. Management control is not, or only weakly, associated with user performance and effectiveness in universities and research performance and effectiveness in institutes. Together these results provide confirming evidence for the *hypothesis 1.1*, which predicted that robust and similar associations would be found between management control and those performance and effectiveness measures which are considered to reflect the primary goals and objectives of the research organization, which are conducting basic and strategic research in universities and applied research in institutes, and weak and different associations with those measures which are considered to reflect the secondary management goals and objectives. The above findings

are, to some extent, supported by the multivariate models of the citation score. This measure is considered to reflect the use of the results by scientific colleagues and physicians. Both in universities and institutes, the effectiveness of personnel policy and contractor communication are positively associated with the citation score, while in universities administrative control is also positively associated with this effectiveness measure. However, the relatively low explained variance and low test set fit indicate that it is difficult to draw conclusions. This could be expected because of the inverse association of the citation score with research effectiveness in the lowest segment of scientific production.

Another interesting observation is that process control turns out to be a relatively unimportant factor in discriminating between high and low performers. Although large differences were established in the way and manner in which research is supervised (see, for instance, the differences between the units in the attendancy of the research meetings by the unit head and/or the senior scientific staff, presented in exhibits 7.2 and 7.3), these differences are not found in the multivariate analyses examining the performance and effectiveness measures (exhibit 8.6). Apparently, performance and effectiveness in universities and institutes are primarily related to system and external control, and only secondarily to process control. It is perhaps more accurate to say that both ways of supervision (hands-on supervision by the head of the unit or hands-off supervision, which leaves the direct guidance of the research process to the scientific staff) can lead to high performance and effectiveness, provided that the fundamental requirements of system and external control are met. System designers and research policy makers can profit from this knowledge, by concentrating their efforts on one or both these aspects.

10.2 ORGANIZATIONAL LEVEL

As has already been stressed in chapters 1 and 5, the above relationships may be focused in the opposite direction to that originally suggested. For instance, the researchers in the better research units may have responded more positively in regards to the effectiveness of personnel policy than their colleagues in the lower performing ones, although the 'objective' situation is the same. Furthermore, researchers in the better units may have more opportunities of presenting papers at international congresses as a keynote speaker, with the expenses paid by the organizing committee. Also, contractors will try to select the best research

units for contract research. However, as was pointed out in § 5.1.1 it can be imagined that the management control situation in some research organizations is 'objectively' better than in others. There might be universities or institutes which really get the best out of their scientific staff, by limiting the bureaucratic constraints and improving the human resources situation. Such a university or institute will clearly be more attractive to the better researchers.

In confirmation with *hypothesis 1.2*, differences could be established between the different universities and institutes. Two universities and especially one institute seem to house some of the best research units. In all three cases high scores for performance and effectiveness go hand in hand with the above-mentioned management control features of a successful research unit. Two universities score relatively low on most of the performance and effectiveness measures. These universities also attain lower scores on the different factors of management control. One institute scores extremely low. The only managerial task which seems to be relatively well organized, according to its scientific staff, is administrative control. Although precautions must be taken, not to over- emphasize results obtained at such a high level of aggregation, it can be concluded that at the organizational level too, supportive evidence has been found for the hypothesis that the quality of research units is not randomly distributed over the different universities and institutes, but that there may be some 'objective' differences in the management and organization. These may favour good research in one organization and hinder it in others. Researchers in medical faculties have to divide their time between research, education and clinical practice. Some faculties define themselves more in terms of research, others in terms of education or patient care. Interestingly, one of the best performing faculties is known for its research orientation, while the faculty which profiles itself in problem (disease) oriented education scores high in terms of user effectiveness. The objectives and goals of the best performing institute, however, are not primarily related to research but to services.

10.3 DIFFERENCES BETWEEN UNIVERSITIES AND INSTITUTES

In accordance with *hypothesis 1.4*, the elements of system control, i.e. effectiveness of personnel policy, adequacy of resources and administrative control, are judged more positively in institutes than in universities. Part of this difference can probably be attributed to the difference in the level of integration between universities and institutes. As has already been stressed in § 2.5.1, in a professional bureau-

cracy there is always a certain tension between the professionals and the administration (Mintzberg, 1979, 1983). This tension may have resulted in a negative attitude towards elements of system control. As has already been observed in § 7.2, in the more vertically integrated institutes, the tension between the administration and professionals is clearly less than in the largely decentralized universities. However, the system control situation in institutes may, in some respects, indeed be better compared to universities (see also § 2.5.3). A research director of one of the institutes, a former university professor, compared the management control situation in universities and institutes as follows: '*The management control situation in institutes is better than in universities. There is more room for leadership. In my institute the important decisions are made together with the heads of the different research departments, in close consultation with the scientific staff. After the decisions are taken, they can be carried out with minor objections. Because of the limited power distance, the process of decision-taking itself takes too much time, let alone the carrying out of these decisions.*'

The largest difference in the judgement of system control between universities and institutes is that concerning the effectiveness of personnel policy. In an earlier study into job satisfaction, mobility and commitment of scientists in Dutch universities, Slootman (1991) also found a negative judgement of the human resources situation. However, the judgements in the present study are relatively more negative. In Slootman's study, the junior scientists in particular judged the personnel situation negatively. The higher the scientific rank, the better the human resources situation was judged to be (compare the differences in the judgements of the heads of the units and their senior scientific staff, in exhibits 7.2 and 7.3). In this study, however, only the higher scientific ranks were questioned. The negative judgements may indicate that the budget retrenchments of the Dutch government have destabilized the biomedical research units in universities. It has forced the units to acquire additional external funding to such an extend that the (programmatic) continuity might become at risk. This, in combination with the unclear decision structure mentioned above, should be a point of concern for research policy makers.

10.3.1 Citation Score

According to citation measures, Dutch biomedical research scores somewhat above the world average. The time-lag between publishing and measurement may

provide an explanation for the relatively weak models found for the citation score. As was shown in § 7.3.1, in all cases where an exceptionally high citation score was found, the contributing researcher had already left the unit to take up a professorial chair. It is interesting to observe that the average citation score in institutes is higher than in universities. An explanation for this finding might be that the pressure to publish has increased tremendously in recent years, rightly condensed in the expression: 'publish or perish'. In order to reach the highest number of publications, it becomes necessary to divide the gathered information over as many scientific papers as possible. Furthermore, the PhD theses in Dutch biomedical research have gradually become readers, composed of several articles in scientific journals. The relatively short period of time in which a PhD has to be finished (4 years) increases the tendency to distort the information. However, because publishing is not their primary task in institutes, the publishing pressure might be lower. This, in combination with the fact that the researchers in institutes are generally more experienced than the young PhD students, may lead to their publications attaining more attention from the scientific community and the community of users. Another explanation might be that the citation pattern in applied research is different from that in basic research, because of the direct interest of the community of users. An indication for such a difference could be that the average citation score in clinical units is somewhat higher than in preclinical and paraclinical units. Additional evidence for the first explanation is provided by the fact that the citation score, in institutes especially, is negatively associated with the number of papers published. The researchers in the units with a relatively low scientific production probably wait longer before publishing, gather more empirical data, and attain a higher density of new information in their papers.

10.4 ECONOMIES OF SCALE, THRESHOLD LEVEL AND PROGRAMME HOMOGENEITY

As was expected, the contingency size has a large impact on performance; 46% of the variance of research performance in universities, and 37% of user performance in institutes can be explained (in strict statistical terms) by this contingency. But the real question is whether larger size is also positively related to effectiveness. According to *hypothesis 2.1*, an optimum size of the research unit is expected, above which the effectiveness declines. Exhibit 8.4 shows that for total staff a plateau is reached of about 20 publications per 30 staff members. Increase

in staff does not seem to be converted into extra papers. Because Bresser and Dunbar (1986) operationalized size as total staff, this finding corresponds with their observation of a negative association of size and research effectiveness. However, if compared to the number of researchers, the number of scientific papers rises in an almost one-to-one relationship. The conclusion must be that in our sample, if calculated per researcher, no 'economies' nor 'diseconomies of scale' could be observed. Indeed, many high performing units were not large. In some cases this was the strategic choice of the head of the unit. As one of the professors of a research unit with extraordinary results indicated: '*I don't want to have a large research unit, because I strongly believe that only in a unit of limited size can the core of our unit, the junior researchers, get the optimal guidance.*'

Exhibit 8.3 shows that, in universities, above a level of around 20 researchers the number of researchers does not increase any further, whereas the number of technical, analytical and administrative support staff increases further almost linearly. The reason for this finding might be that at a level of 20 researchers the span of control of the head of the unit and/or of the senior scientific staff is reached. The fact that the junior to senior scientist rate differs considerably across those units with about 20 researchers may indicate that the span of control of the head of the unit can be considered the limiting factor. Because of the comparably low task uncertainty of technical, analytical and administrative work, it can be supervised by senior and junior scientists (or in larger laboratories by the support staff of higher rank). Therefore, the span of control of the head of the unit may not limit the size of the support staff. Mayntz (1985) indicates that keeping a coherent pattern of research goals and interests is one of the major challenges of the research management. A too large differentiation in research goals and interests was one of the major disintegrating factors, according to the directors of the institutes in her study. The possibility of the integration of research goals and interests being a major reason for the observed maximum in the size of the research staff was also indicated by one of the professors in the structured interviews: '*If the researchers do not consider the weekly research meetings of direct interest for their work, the unit will split up sooner or later. To my experience this is the case at a level of around 25 researchers.*' This might also supply an explanation for the major differences in research unit size in the different disciplines in universities. The higher the level of integration in a discipline in terms of research goals, values and techniques, in other words the higher the level of paradigm development (Kuhn, 1970), the larger the possible span of control of the professor and thereby the research unit size.

Exhibit 8.5 seems to indicate, in confirmation with *hypothesis 2.1*, that there is a threshold level of about 5 researchers, corresponding with about 9 staff members, below which the units do not grow, or even may decline. Above this level abundant growth can be observed until a level of about 10 researchers is reached, above which the growth stabilizes at a somewhat lower level. The decline of the smaller units could be an indication for a low level of performance, leading via a diminishing loop to reduction of the size of the units (see exhibit 3.5). However, the research effectiveness of these units turned out to be only slightly below average. None of these units was 'small but beautiful', but nor were they extremely low performing. Another explanation might be found in the budget retrenchments of the Dutch government. The staff of the larger units might be in a more favourable position to acquire additional external funding. In smaller units the primary tasks (research, education and, in clinical units, also clinical practice) may take relatively so much time of the research management, that time for acquisition is lacking. Young professors, 'inheriting' a small unit, may have (great) difficulties in attaining independency. How difficult this can be is demonstrated by the following statement of a young professor, taken from outside the study sample: '*I put much emphasis on acquisition. But if I do attain a large research grant, preparing and supervising are so laborious that time for further acquisition is lacking. I have the feeling that in the last five years I have constantly been running, just to maintain my unit.*' However, at the very moment that the 'subsistence level' is overreached, abundant, even exponential growth may start, following the amplifying loop A in exhibit 3.5. Additional supportive evidence for a sort of 'subsistence' level in university research, might be found in the fact that an inverse relationship was found between annual growth rate and age. Some of the older professors of smaller units may lack the physical strength or the fighting spirit to survive in the competitive world of scientific research. Of course, the number of units on which these considerations are based is too small to draw definite conclusions. Further research is needed to settle this point and to look for possible threshold levels in other disciplines. However, if these considerations contain a certain amount of truism, then research policy should consider setting a minimum staff level per chair. In the long run it might be more fruitful to have fewer but better staffed chairs, rather than more and understaffed ones.

Sub-hypothesis 2.1.1 is not confirmed by the data; no optimum project size can be established. Therefore, no firm conclusions can be drawn about possible differences in programmatic homogeneity between units. However, the average project size in institutes is significantly smaller than in universities, which might be interpreted as confirming evidence for the Mayntz's observation (1985), that attaining

programmatic homogeneity is more difficult in institutes than in universities, because of the bargaining power of outside contractors.

10.5 RESEARCH AND CLINICAL PRACTICE

In accordance with *hypothesis 2.2*, the time allocated to research and that allocated to clinical practice shows an inverse relationship. The scientific staff in preclinical and paraclinical units can spend twice as much time on research as the staff in clinical units. Interestingly, this extra time spent is not translated into higher research and user effectiveness. The researchers in the clinical units publish on average about the same number of scientific papers and three times as much papers in journals for physicians than their colleagues in the preclinical and paraclinical units. An explanation for this unexpected finding could be that researchers working in clinical units have easier access to a larger and more differentiated number of scientific journals, due to the number of clinical specialisms. A second explanation emerged from the structured interviews. Several clinical professors indicated that the average time spent of their scientific staff amounted more than 40 hours a week. Researchers, who had worked both in clinical and preclinical or paraclinical units also indicated that the total work-load in clinical units is significantly higher. Apparently, the necessity of '24 hours a day availability' for patient care, considerably increases the total work-load. This extra time spent may compensate for the lack of time during the official working hours. This could also be the explanation for the initially surprising fact that more early respondents were found in clinical units than in preclinical and paraclinical units. Franklin (1988) concludes that longer hours lead to more output per researcher, at discipline, individual and project level. Spangenberg (1989) also points at the 'after-working' research as one of the major performance indicators in clinical medicine.

Interesting differences are found between preclinical and paraclinical units on the one hand and clinical units on the other regarding the association of age, time-allocation and power with effectiveness and growth rate (see exhibit F.1). When integrated, these findings present the following picture. Thomas (1979) typifies clinical medicine as 'half-way technology'. Although in the last twenty years tremendous progress has been made in acquiring knowledge about the origin, cause and effective treatment of diseases, clinical medicine has still not come further than 'half-way'. The physiological background of the treatment of a num-

ber of diseases is still largely unknown (for instance the use of gold in the treatment of rheumatoid arthritis). The often observed healing effect of the confidence of the physician in his treatment indicates that a physician needs more than just scientific and technical knowledge. Clinical medicine is therefore often referred to as knowledge *and* art. An art which a young clinician has to learn by extensive practical training under the supervision of an experienced clinical expert. Spangenberg (1989) cites Picasso's statement that '*the arts, like crafts, are more associated with transpiration than inspiration.*' In fact, transpiration can be considered as the bridge between the two analogies of science, namely top sport and art. This may well be the reason for the older average age of the senior scientific staff in clinical units (see exhibit 8.2), and the positive relationship of age with the size of these units. The great number of therapeutic specialisms, each requiring their own clinical expert(s), may account for the higher percentage of professors and senior scientists in clinical units compared to preclinical and paraclinical units (see exhibit 8.1). Furthermore, researchers in clinical units seem to be more internally oriented and in preclinical and paraclinical units more externally oriented. The positive association of signatory authorization capacity with user effectiveness in clinical units may indicate that the more a clinical unit is oriented towards patient care, the larger the financial power, probably due to the extra flow of insurance money. It seems that Spangenberg's (1989) observation is confirmed that the more a clinical unit is directed towards the scientific community, the worse their financial position. Policy directed towards stimulating clinical research to be effective should take account of this mechanism.

10.6 THE LIFE CYCLE CONCEPT AND AGE DISTRIBUTION

As predicted, increasing organizational age is negatively associated with annual growth rate (see exhibits F.1 and F.3). This, combined with the positive association with internal orientation, supplies confirmative evidence for *hypothesis 2.3* which is that the life cycle concept can be applied to academic research. If the research units which are supervised are small, an absolute decline of the size of the unit before super-annuation (and not after super-annuation, see box 5.1, decay) can even be observed. By plotting management experience and size, it becomes apparent that young professors often do not start with the smallest research units (as expected, see box 5.1, incubation). Professors who attained their chair before 1980 and after 1985 supervised larger research units than those starting in the beginning of the 1980. This finding can probably be explained by the

fact that a great number of non-chaired professors (lectors) in the Netherlands attained a professorial chair at the end of the 1970s. In addition, no confirming evidence has been found for a direct relationship between the age distribution of the scientific staff and research effectiveness. The age distribution seems to be more related to the other tasks of the units, for instance the supervision of graduate and postgraduate (PhD) students and the demands of patient care.

10.7 INTERNAL AND EXTERNAL ORIENTATION

The positive association of junior to senior scientist rate with research performance in preclinical and paraclinical units may show the important role of young PhD students in scientific production. The positive link of external orientation to research performance and annual growth rate may further indicate that a positive reinforcing loop of presenting new and innovative ideas and the size of the unit is at work here. On the other hand, the negative association with internal orientation may indicate that research units with more in-faculty power are less interested in international scientific exposure than those with less in-faculty power, which would be in accordance with *hypothesis 2.4*. It seems that Gouldner's division of researchers into 'locals' and 'cosmopolitans' can be extended to whole research units. The question which remains is whether some of the 'cosmopolitans' may in fact be 'locals' who are forced to go out, because of their weak in-faculty position, or whether some of the 'locals' in fact are 'cosmopolitans' who could not make it in the outside scientific world.

10.8 CUSTOMER ORIENTATION

A point worth mentioning, although it was not an item of the investigation, is the difficulty encountered when trying to reach the research units in universities and institutes by phone. Nearly half of the research units had to be phoned more than once before a secretary could be reached. Even large departments which rely considerably on contract research, and even one institute, were nearly inaccessible. The few secretaries who used an answering machine were, in most cases, reluctant to call back. In the case of one of the largest university departments it took more than a month to reach the central secretariat. Besides this, the where-abouts of the researchers was largely unknown, especially in the larger departments. Even

the fact that researchers were on leave for several months was often not known at the secretariat. This is not the grumble of a frustrated researcher (the actual phone calls were made by assistant researchers and not by the author), but an attempt to stress the importance of accessibility. As has been shown in this study, contract research has become increasingly important for universities and institutes. Seen in the light of the policy of the Dutch government to continuously decrease the budget levels of universities and institutes, it is likely that the importance of contract research will further increase in the future (whether this policy is good for the technological advancement of the Netherlands is another question). Therefore, if universities and institutes want to compete in the increasingly competitive world of contract research, they must start by improving their accessibility in order to avoid frustration and unnecessary loss of time and money[1].

During the structured interviews examples were given of lack of customer orientation in universities and institutes. R&D directors which had experienced cooperation in the field of biomedical research with some of the Dutch universities and institutes, expressed their opinions that a cooperative project is often more technology push, in terms the selling of projects by the university or institute, rather than market pull, which involves listening to the needs and wishes of the customer. An additional problem in the field of cooperation with research units in universities, which emerged in the structured interviews, is the lack of contractor communication during the conduction of the project. As one of the R&D directors put it: '*In latter years a number of cooperative projects failed, because the objectives were changed by the university department without previous consultation. Apparently, they are used to getting money from sponsoring foundations with only limited evaluation whether the original objectives are met.*' The main criticisms in the case of institutes not only concerned the lack of listening to the customer, but also weak project acquisition and management. Prompt sending of clear offers and contracts, conducting the contract research according to time schedules, and, in international projects, reporting in the home language of the customer (if required), were notable areas of criticism. Of course, these opinions are not representative, because most of the R&D directors have no experience in cooperation

[1] That the problem of accessibility has a larger scope was shown by a Dutch survey in which more than 750,000 phone calls were made. In trading, utility, services, banking and insurance 19% to 24%, and in government and health care, 35% of the departments and staff members could not be reached by the first phone call. The Netherlands Economic Institute calculates the annual loss for the Dutch economy due to inaccessibility to about US$ 275 million (quoted in the *NRC* February 9 1995 p. 17).

with Dutch universities and institutes. However, in a recent survey into the cooperation between Dutch universities and the pharmaceutical industry, similar points were raised (Ministry of Economic Affairs 1993). Seen in the light of the mutual interest in R&D network cooperation, it is important that the customer orientation improves.

10.9 CONCLUDING REMARKS

A brief outline is given below of the main conclusions which are to be drawn from this chapter.

- The empirical concepts effectiveness of personnel policy, administrative control, and external control associate strongly/weakly with those performance and effectiveness measures which reflect the primary/secondary goals and objectives of the research management.
- Hands-on supervision by the head of the unit or hands-off supervision leaving the direct guidance of the research process to the scientific staff can both lead to high performance and effectiveness, provided that the fundamental requirements of system and external control are met. System designers and research policy makers can profit from this knowledge, by concentrating their efforts on one or both these aspects.
- The elements of system control (effectiveness of personnel policy, adequacy of resources and administrative control) are judged more positively in institutes than in universities. However, the assessment of personnel policy in universities, and, to a lesser extent, in institutes, is so negative that it should be a point of concern for research policy makers.
- The average citation score in institutes is higher than in universities. This is probably due to the greater disruption of new scientific knowledge in a number of articles which together constitute a biomedical PhD thesis in universities. The finding of a negative relationship between the number of papers per researcher and the citation score, in institutes especially, could point in the same direction. Probably, the researchers in (part of) the units with a lower scientific production wait longer before publishing, gather more empirical data, and attain an higher density of new scientific information. This could indicate the special importance of citation analysis, in addition to publication counts, as a quantitative evaluation tool in research policy.

- No 'economies or diseconomies of scale' can be observed in biomedical research.
- The empirical evidence may indicate that the span of control of the head of the unit may limit the size of a research unit to about 20 to 30 researchers. No size limitations were found for technical, analytical and administrative work. Further research into the span of control in relation to paradigm development could be an interesting extension of this study.
- A threshold level seems to exist, below which it is difficult to survive in the competitive world of scientific research. In biomedical research this level lies at about five researchers, corresponding with about nine staff members. The number of units on which these considerations are based is too small to draw definite conclusions. Further research is needed settling this point and to look for possible threshold levels in other research fields. Research policy may consider to have fewer but better staffed chairs, by establishing a minimum staff level per chair, taking into account the specific characteristics of the different research fields.
- The positive association of signatory authorization capacity and user effectiveness in clinical units may indicate that the more a clinical unit is directed towards the scientific community, the worse the financial position. Policy directed towards stimulating clinical research to be effective should take account of this mechanism.
- The fact that the average project size is significantly smaller in institutes may be interpreted as a confirmation of Mayntz's observation (1985), that programmatic homogeneity is weaker in institutes.
- Despite that researchers in preclinical and paraclinical units spend twice as much time on research than researchers in clinical units, no difference in research effectiveness can be established. Probably, researchers in clinical units have more easy assess to a larger and more differentiated number of scientific journals, due to the number of clinical specialisms. In addition, the '*24 hours a day availability*' in clinical practice may have compensated for the lack of time during the official working hours.
- Confirming evidence has been found that the life cycle concept can be applied to academic research.
- No direct relationship between age distribution of the scientific staff and research effectiveness can be established.
- Researchers in clinical units seem to be more internally oriented and those in preclinical and paraclinical units more externally. The positive association of junior to senior scientist rate with research performance

association of junior to senior scientist rate with research performance in preclinical and paraclinical units, proves the important role of young PhD students in scientific production in basic biomedical research. The positive link of external orientation to research performance and growth rate may further indicate that a positive reinforcing loop of presenting new and innovative ideas and the size of the unit is at work here. On the other hand, the negative association with internal orientation may indicate that research units with more in-faculty power are less interested in international scientific exposure than those with less in-faculty power. It therefore seems that Gouldner's division of researchers into 'locals' and 'cosmopolitans' can be extended to whole research units.

- Clear differences are found in management control and performance and effectiveness between the different universities and institutes, supporting the idea that the quality of the research units is not randomly distributed over the universities and institutes, but that there are 'objective' differences in the management and organization, favouring good research in some and hindering it in others.
- Seen in the light of the interest in R&D network cooperation with industry, it is important that the accessibility and the customer orientation of the research units in universities and institutes improves.

This chapter has taught the important lesson that management and organization as such can make a difference between success and failure. It has also taught the lesson that both hands-on or hands-off supervision of the individual research manager can lead to success or failure. It is the organisational flexibility which sets the boundaries. The comparison with the company laboratories in the next chapter will show just how far these findings can be extended to management control of industrial R&D.

CHAPTER 11

INDUSTRIAL PHARMACEUTICAL INNOVATION

In this chapter the main conclusions from the results obtained from the pharmaceutical companies are discussed in relation to the hypotheses formulated in chapter 5.

11.1 HIGH AND LOW PERFORMERS

One of the most striking results is that, in confirmation with the main hypothesis, *hypothesis 1* the best performing companies in terms of innovative and industrial performance, as well as in terms of effectiveness clearly differed from their lower performing competitors on a number of managerial and organizational features. The most important of these is the effectiveness of personnel policy. No matter which measure of performance and effectiveness is taken, the perceived effectiveness of personnel policy proves to be the most important management control factor dividing the more-than-average from the less-than-average performers. In the companies with the larger operating profit margins, the perceived quality of personnel policy is much better than in the average companies. In addition, the average duration of administrative procedures is clearly shorter, and international communication with scientists and physicians at congresses and workshops is more intense. It can be argued, however, that the causality may be the opposite to that which has been suggested. The more effective companies are also the most profitable and can therefore afford to spend more on elaborate laboratory equipment, to have more frequent international contacts and can have quicker procurement and appointment procedures. Also, the R&D staff in the better companies is likely to respond more positively to such studies than their colleagues in the less performing ones. However, because of the size of the companies it can be expected that spending budgets will not be so much of a bottleneck for procurement, appointment and international travelling. The consistency of these results with those of previous studies (e.g. Allen 1977, Biemans 1992, Pelz and Andrews 1976, Twiss 1992 and Volberda 1992) leads us to prefer our interpretation.

11.2 ECONOMIES OF SCALE

In order to evaluate *hypothesis 2.1*, which concerns whether or not 'economies of scale', in terms of increasing returns on investment, can be observed in pharmaceutical innovation, the outcome of the different parameters of innovative and industrial performance and effectiveness are discussed below.

- ***R&D expenditures as percentage of sales.***
  At lower sales levels the R&D expenditures increase almost linearly with size, indicating that the companies in this category increase their innovative potential in proportion to the sales-volume. At the highest sales-volumes, however, a saturation level seems to be reached. Apparently, there is no further need to invest the extra sales-volume in innovative potential.

- ***Number of patents in relation to the investment in discovery.***
  The larger firms clearly submit more patents per invested dollar than the smaller ones. This could be a clear indication of their higher innovative effectiveness. Another explanation could be that larger companies submit their patents relatively earlier than smaller ones. Basberg (1987) and Pavitt (1988) suggested that some companies play for safety and apply for a patent at an early stage of the innovative process, while others wait longer. This strategy decreases the risk that a competitor will submit a patent for a similar compound, but increases the patents fees and translation costs and can put a competitor on the track. The second strategy has complementary (dis-)advantages. The patent fees and the translation costs constitute a smaller part of the R&D budget of the larger companies, and therefore they are more likely to play for safety. In the structured interviews, however, most research directors indicated that the chosen patent strategy mostly depended on the therapeutic area. In a highly competitive area, such as Aids, patenting is completed at an early stage of the innovative process. The normal procedure is to wait longer, until about one year before the start of clinical testing. Only two research directors stated that their companies executed a restrictive patent policy. In point of fact, the data of these companies lay somewhat beneath the curve presented in exhibit 9.5. The research director of a third company with a relatively low number of patents, however, complained of backward innovative potential. A further explanation may be that the development phase, not the discovery phase, is the limiting factor in pharma-

ceutical innovation. Indeed, in the structured interviews many research directors indicated that the increasing cost of innovation was mainly due to the continuously rising cost of the developmental process, especially of the large scale clinical trials.

- ***The number of new products launched.***
  The larger companies in the sample were the only ones who introduced innovative drugs, giving strong support to the thesis of higher innovative strength in larger companies. This result should be interpreted with some caution. Ethical drugs differ from almost all other consumer goods, in that the buying decision is not made by the final consumer, but by the prescribing physician. Frequent face-to-face contact of a highly knowledgeable sales force, combined with direct mail and advertisements in medical journals, and the organization of medical congresses and other meetings, are considered to be necessary to exert influence on the physicians. Only the largest companies can finance the huge marketing and sales effort necessary for influencing the prescribing pattern in a desired direction. Consequently, it is possible that smaller companies introduced innovative drugs which did not receive the recognition they deserve. Indeed, a research director of a smaller company stated that one of their most innovative drugs performed only moderately until it was licensed-out to one of the major companies. Only then did it prove to be a success on the market.

- ***The length of the developmental process.***
  According to the model developed by Grabowski and Vernon (1987), each year that an innovative drug can be launched earlier than would normally be expected, counts for an additional patent protection time of three years. The length of the developmental process transpires to be shorter in the larger companies. This finding can mainly be attributed to the greater size of the developmental budget. In the structured interviews, some research directors gave, as a further explanation, the view that larger companies have more opportunities for parallel development, because it is easier to shift R&D staff between projects.

Although all these parameters can be separately criticized on solid grounds, when combined they point in the same direction, namely, that economies of scale can be observed in pharmaceutical innovation. Therefore, it appears that the recent strategy, developed to cope with the political and economic risks, of increasing

concentration by mergers and joint ventures and strategic alliances, is also justifiable from the viewpoint of scale economics in pharmaceutical innovation. How can this finding be explained in the light of the Soete's conclusion (1979) of diminishing returns on R&D investment? Perhaps the main difference between now and the 1970s is that the governmental regulations have become much stricter. For that reason, the investments needed, especially for the large scale clinical trials, have increased considerably, while the possibilities to recoup these investments have decreased, especially for the smaller companies which cannot afford a huge marketing and sales force.

11.3 THRESHOLD LEVEL

In order to evaluate *hypothesis 2.1*, which concerns whether the costs in pharmaceutical R&D are still increasing, or whether the data might indicate any sign of a steady state, the following very rough calculation, based upon the information from the research directors, was made. For the conduction of the R&D process for one new drug, an investment of about US$ 200 million is needed (US$ 150 million according to Ballance et al. 1992, and US$ 230 million according to DiMasi et al. 1991). Roughly speaking, one in every four drugs is successful on the prescription drug market and once in every four years a pharmaceutical company develops a successful drug. Considering that the successful drugs account for the profitability of a pharmaceutical company, it can be calculated that a minimum annual R&D expenditure of US$ 200 million is needed to maintain the innovative potential. The curve in exhibit 9.4 starts at around US$ 180 million, which could indicate the entrance of a steady state. However, further research is needed to confirm these data systematically.

In confirmation with *hypothesis 1.3*, the operating profit margin, being an industrial performance and effectiveness measure, is not closely related to process control. As was shown in § 11.1, the operating profit margin is related to effectiveness of personnel policy, administrative control and external control and not to planning and research process communication. The annual growth rate, however, is significantly correlated with the attendancy mix, originating from the significant association of this performance and effectiveness measure with the R&D expenditures spent on development (see exhibit 9.2). In the discussion of the merits of a radical orientation compared to an incremental orientation will be returned to this point.

11.4 DISCOVERY VERSUS DEVELOPMENT

In the structured interviews it became apparent that the best performing pharmaceutical companies are increasingly shifting their attention from the screening of thousands of chemical compounds in pharmacological and animal models, to the understanding of the biochemical and physiological background of diseases. According to Griffin et al. (1994), 10% to 20% of the total R&D budget is spent on collaborative fundamental research and sponsorships in academia and medical research institutes. The screening process itself is becoming increasingly automatized. According to *hypothesis 1.5*, the growing task and environmental uncertainty which derives from this shift from systematic screening to fundamental research, will lead to a higher need for information. Therefore, it is expected that the more-than-average discovery departments will pay more intention to international communication than their less-than-average competitors. This was not found, exhibit 9.11 shows no additional explained variance of performance and effectiveness by international communication. All companies seem to pay equal attention to maintaining the R&D network. It is interesting, however, that the frequency of research meetings is significantly higher in the more-than-average discovery departments. Apparently, the increased informational need is met by intensive in-house communication with colleagues in discovery.

Considering the limited patent protection time, shortening the length of the developmental process is essential for attaining profitability in a pharmaceutical company. As one of the Research directors expressed it: '*Each day a successful drug reaches the market earlier earns US$ 200,000 for the company.*' With this figure in mind, it is obvious how large the benefits can be for companies which are able to shorten the development phase by more than a year by use of parallel development and close monitoring of the developmental process. All pharmaceutical companies make use of parallel development. The structured interviews showed that the fine-tuning is more precise in the more-than-average performers, and the lateral and cross-functional communication more intense, leading to an interactive concurrent process. Concurrent development so fundamentally changes the pharmaceutical R&D process that it can best be described as a chain of integrated learning loops. In accordance with these observations, and with *hypothesis 1.6*, is the finding that a positive correlation exist between shorter development length on the one hand and planning and the attendancy mix on the other. Researchers of different phases of the R&D process stand in close contact with each other and with marketing and production in multidisciplinary project teams. Interestingly, the close monitoring of the developmental process does not go hand

in hand with a high frequency of project team meetings. Most of the pharmaceutical companies in this study are multinationals with laboratories in different countries. Therefore, a high frequency of meetings in the development phase would mean a lot of travelling. Mutual adjustment is therefore achieved mainly by telecommunication. In the cases of frequent project team meetings, a tendency towards ineffectiveness can even be observed.

A number of problems were mentioned during the structured interviews concerning how the multi-centred (international) clinical trials are conducted. In principle one large, well designed, multi-centred clinical trial can be a substitute for a large number of smaller ones, and can therefore be helpful in shortening the R&D process. However, large problems are encountered. First of all, cultural differences and differences in the practice of medical care make it difficult to get the cooperation of physicians in a large number of countries for the same clinical trial design. Moreover, coordination problems tend to arise and travelling expenses are considerable. Therefore, some of the companies have turned to the 'core country' concept. If the number of available patients permits, a country is chosen in which the whole trial is executed. In the longer run the main advantage of this new approach may turn out to lie in the resulting 'empowerment' of the clinical research associates. The large multi-centred clinical trials are designed and analyzed at the parent company. The clinical research associates are merely responsible for monitoring of the process and sending the resulting data to a central biostatistical department, where they are analyzed for registration. In the 'core country' concept, however, they are responsible for the whole trial, ideally, from the starting design until the final analysis of the data. That the 'core country' concept can help in enhancing motivation was affirmed by one of the clinical trial directors: '*The motivation of the clinical research associates has increased tremendously. Now they feel responsible, calling during their holidays to check if everything is going according to schedule.*'

11.5 RADICAL VERSUS INCREMENTAL ORIENTATION

Apparent differences in innovative strategy can be traced between the companies in this study, when they are considered in the light of *hypothesis 3.1*. In companies conducting a more radical strategy a higher percentage of the R&D staff has been educated to university level, a greater part of the R&D budget is allocated to research and the researchers attend more international congresses and work-

shops than in companies adopting a more incremental strategy. An incremental strategy turns out to be related to lateral and cross-functional communication. As the R&D process continues, more and more structured consultations are needed with staff members of marketing, sales and production to speed up development. In terms of annual growth rate, the companies conducting a more incremental strategy turn out to be more successful. The strong correlation of annual growth rate with the attendancy mix, originating from the strong association of this performance measure with the R&D expenditures spent on development (see exhibit 9.2), points in the same direction. That is to say, that speeding up product development, in order to introduce drugs with small improvements on a regular basis (Taggart 1993), is currently a more rewarding strategy than concentrating on discovery. It seems to be less attractive for a pharmaceutical company to invest in innovative potential of which the uncertain revenues can only be expected after a decade or more, than in incremental improvements which can be marketed after a short period of time.

A related development is the recent tendency to contract-out parts of the R&D process. Contract research with universities and institutes has already been mentioned, but in pharmaceutical and clinical development, too, increasingly activities are being carried out by outside contractors. The demand from regulatory agencies for 'objective' clinical trials, conducted by institutions outside the pharmaceutical industry, and the opportunities for conducting pharmaceutical and clinical development relatively cheaply in Eastern Europe, may speed up this process. In the unfavourable times to come, the pharmaceutical companies may find themselves under increasing pressure 'to do more with less'. However, if too much emphasis is placed on incrementation and contracting-out, a company may fall into the trap of staffing below the critical mass of experienced and talented people, necessary for keeping up the innovative potential. Also companies adopting an incremental strategy still need to maintain considerable 'in-house' skills in order to be able to evaluate the potential of the lead compounds on offer. Therefore, such a strategy, which may seem sensible in the short-run, may prove to be the opposite in the long-run.

As a consequence of the long duration of the developmental process, new medicines will often be more expensive than those already on the market. The recent political emphasis on price for the admission of a new medicine into the reimbursement system may therefore further discourage innovation. However, society has a need for a constant stream of new and innovative medicines. Government has therefore the public duty to encourage innovation by working closely together

with branded ethical drug firms in reducing time-to-market. For instance, much time could be gained if registration authorities and clinical trial designers would regularly discuss the desired end-points for registration in an early stage of clinical development.

11.6 PURE PLAY PHARMACEUTICALS AND CONGLOMERATES

Although it is possible that, in accordance with Taggart's prediction (1993), the conglomerates will become more successful in the long run, at present, in confirmation with *hypothesis 3.2*, the pure play pharmaceuticals are performing better. At the level of management control, the main difference between the pure play pharmaceuticals and the conglomerates turns out to be the pace, the way and the manner in which reorganizations are performed. The positive judgement of the pace is considered a reflection of the eagerness of the management of pure play pharmaceuticals to survive on the market. It is not possible for them to fall back on a parent company in less favourable times. The positive judgement of the way and manner in which reorganizations are performed is considered a reflection of the knowledge about and the interest in the specific needs of the research staff and the greater opportunities available to meet such needs. In a conglomerate, the directorate of a division has to comply with the general rules, which may not match the pharmaceutical market. As one of the Research Directors of a conglomerate put it: '*We need the [financial] comfort, not the [bulk chemistry] culture.*' Conglomerates, facing the unfavourable times to come, could therefore consider transforming their pharmaceutical divisions into independent subsidiaries. In this way they may profit from the best of two worlds, i.e. the financial power and the world-wide sales-network of the parent company, combined with the flexibility of the pure play pharmaceutical.

11.7 ANGLO-AMERICAN AND CONTINENTAL EUROPEAN COMPANIES

The respondents from the Anglo-American companies report a much larger variety of incentives and career opportunities than their colleagues in the continental European companies. A number of incentives are reported for extraordinary contributions in the structured interviews, such as pay for performance, bonuses, use of a company car and the provision of company shares and options. All research

directors indicate, however, that there is a driving force, which is even more important than material incentives. This driving force is the receiving of recognition for scientific merits, externally by the scientific audience, and internally by the company management. The opportunity to publish and, although to a lesser extent, to attend congresses, are strong incentives for the scientific staff. The R&D staff in Anglo-American companies report a significantly higher attendance of congresses, possibly because of their universal mother language. Aside from those containing research results concerning the non-patented leads in the discovery phase, only minor restrictions are placed on publishing results. Bibliometric research by Koenig (1983) revealed that the research staff of the large pharmaceutical companies in the USA published so many articles in top journals that they could compete with university departments. Although in Europe the companies are less publication-oriented, the scientific production can still be considerable. For instance, in 1990 the pharmacologists and clinical research associates of Hoechst-Roussel were authors or co-authors of 699 articles, congress contributions and abstracts (Hoechst-Roussel 1990).

Several research directors of 'continental' European companies indicated, that the lack of career possibilities for the scientific staff was one of their major managerial problems, tersely rendered in the expression '*If you want to get on, get out of research*'. A dual (or hybrid) ladder system, which can compensate for such a problem, is used on a wider scale in Anglo-American companies. One of the Anglo-American research directors characterized the advantages as follows: '*The possibility of getting recognition for scientific efforts appears to be an especially important feature for scientists, because a relatively flat organization, like a laboratory, offers only limited opportunities for promotion in terms of responsibility. The dual ladder goes all the way up to 'vice-president' on the managerial and to 'distinguished research scholar' on the scientific ladder.*' One of the R&D directors of a pharmaceutical division of a continental conglomerate, who registered loss of commitment of the R&D personnel (they developed '*a nine to five mentality*'), noted that the introduction of a dual ladder system could contribute to improving the motivation of the scientific staff, but that the parent company opposed it. Many authors have stressed the limitations of the dual ladder system (e.g. Gunz 1980 and Tuininga 1990). Essentially, it can only function if there is recognition and appreciation of scientific achievements within the company. Although the differences between Anglo-American and continental European companies are many, both in management and culture, this apparent difference in recognition and appreciation of scientific achievements could be one of the major reasons for the observed difference in innovative and industrial performance and effectiveness.

11.8 CONCLUDING REMARKS

The conclusions of this chapter are summarized below.

- The data suggest that a threshold annual investment of around US$ 150-200 million is needed to maintain the innovative potential of a branded ethical drug company. Above approximately US$ 750 million, 'economies of scale' seem to appear in pharmaceutical innovation.
- The perceived effectiveness of personnel policy proves to be the most important management control factor, dividing the more-than-average from the less-than-average performers in terms of explained variance.
- In the companies with the largest operating profit margin the perceived quality of personnel policy is better than in the average companies. The average duration of the administrative procedures is also clearly shorter, and there is a more frequent international communication with scientists and physicians at congresses and workshops.
- The best performing pharmaceutical companies in the discovery phase, are increasingly shifting their attention from the screening of thousands of chemical compounds in pharmacological and animal models to the understanding of the biochemical and physiological background of diseases. The screening process itself is becoming increasingly automatized.
- The best performing companies in development are able to shorten the development phase by more than a year, by use of parallel development and close monitoring of the developmental process. In the more-than-average performers the fine-tuning is more precise, and the lateral and cross-functional communication more intense leading to a concurrent process. However, pharmaceutical companies could consider reducing the number of face-to-face contacts and substitute it by e.g. electronic forms of contact, because of the time-losses involved.
- The 'core country' concept could help to motivate the clinical research associates, by 'empowering' them to take responsibility over the whole clinical process, from the design of the study until the final data analysis.
- An incremental strategy, directed towards speeding up product development in order to introduce drugs with small improvements on a regular basis, by concurrent development for instance, seems to be more successful in terms of growth rate than a radical strategy, which emphasizes discovery.
- Pharmaceutical companies are under increasing pressure 'to do more

with less'. However, if too much emphasis is placed on incrementation and contracting-out parts of the R&D process, a company can fall into the trap of staffing below the critical mass of experienced and talented people needed to maintain an acceptable level of in-house scientific skills to invent leads or to evaluate the merits of lead compounds on offer.

- Pure play pharmaceuticals seem to be more successful than pharmaceutical divisions of conglomerates on the pharmaceutical market. In particular, the pace, the way and the manner in which reorganizations are performed, is assessed more positively in pure play pharmaceuticals. Conglomerates could consider transforming their pharmaceutical divisions into independent subsidiaries. In this way they may profit from the best of two worlds. The financial power of the parent company, and the flexibility of the pure play pharmaceutical company.
- Society has a need for a constant stream of new and innovative medicines. Government has therefore the public duty to encourage drug innovation by working closely together with branded ethical drug firms in reducing time-to-market. For instance, by discussing the desired endpoints for registration in an early stage of clinical development.
- The greater emphasis on recognition and the larger career opportunities for the R&D staff in Anglo-American companies in comparison to continental European companies could be important explanatory factors for their greater success in the pharmaceutical market. In a flat organization like an R&D laboratory, the opportunities for promotion in terms of responsibility are limited. Therefore, promotion on the basis of scientific merits, such as in a dual (or hybrid) ladder system, and other incentives for scientific staff, should be considered.

CHAPTER 12

GENERAL CONCLUSIONS

In this final chapter the general research questions will be answered, which were formulated in chapter 1. The scope of this study, and the possible contribution that the empirical results could make to the theory of management and organizational studies and to management practice, will also be evaluated.

12.1 THE RESEARCH QUESTIONS

In chapter 1 of this book the fundamental question was raised, whether success or failure in biomedical research is merely dependent on the quality of the researchers or other aspects of management and organization also determine the success of a research laboratory. The following general research questions were formulated in order to help to answer this main question.

1 *Do certain aspects of management control affect R&D performance and effectiveness in a positive way?*
2 *If so, to what extent do these aspects affect R&D performance and effectiveness, and which instruments should be used to increase R&D performance and effectiveness?*
3 *What is the impact of the organizational setting on this relationship?*

The first two questions concern the comparison of management control in high and low performers within the three strata, while the third concerns the comparison between the strata.

12.1.1 High and Low Performers

The results of the empirical studies provide strong evidence for a positive answer to *research question 1*. One of the most striking results of this study is that the

high performers clearly differed from their low performing competitors on a number of socio-dynamic and system-technical features, regarding both organizational flexibility and control capacity. As is shown in exhibit 9.11, positive associations could be established in all three strata between the derived concepts of system control and external control on the one hand and performance and effectiveness on the other. This means that confirming evidence has been found for the main hypothesis, *hypothesis 1*, namely that more-than-average performers show different scores than less-than-average performers on a number of empirical concepts of management control. Furthermore, the fact that replication of the study design in the three strata has yielded consistent results, enhances confidence in the generalizibility of the findings to 'Big Science' in general.

In regards to *research question 2*, which refers to the establishment of a control mix separating high from low performers. As has been previously stated, large differences could be established in organizational flexibility and control capacity between the more-than-average and less-than-average performers. In universities and institutes, as is shown in exhibit 9.11, personnel control, administrative control and external control correlate positively with the performance and effectiveness measures which reflect their primary goals, which are basic and strategic research in universities and applied research in institutes. Interestingly, the same three concepts separate the more-than-average from the less-than-average performers, if the operating profit margin, one of the industrial performance and effectiveness measures, is considered. Possibly, the operating profit margin reflects not only the ultimate goal of the company of maintaining profitability, but also, at least to a certain extent, the contribution of the R&D function in attaining this goal. This would be in accordance with the conclusion drawn by Van Engelen (1989) for the marketing function. If this assumption is correct, it can be concluded that the same derived concepts of management control separate the more-than-average from the less-than-average performers in all three strata. These findings mean that the following factors separate the more-than-average from the less-than-average performers.

- The perceived effectiveness of personnel policy a socio-dynamic factor of organizational flexibility and control capacity, combined.
- The average duration of the administrative procedures, a system-technical factor of organizational flexibility. For example, it took the best performing research laboratories on average 3 to 12 months less to reallocate a major part of their resources to a new research area.
- The communication with contractors and the international communica-

tion with colleagues at congresses and workshops; a socio-dynamic factor combining elements of organizational flexibility (e.g. available travelling budget) and the control capacity of the research management.

The most important empirical concept of management control turned out to be the effectiveness of personnel policy. This is a clear confirmation for a central thesis in socio-dynamic literature, which is that stimulating and rewarding environments, which enhance the motivation of the scientific personnel, are needed for high performance and effectiveness. Probably just as interesting is the observation that process control is relatively unimportant as a discriminating factor between high and low performers. Although large differences could be established in the way and manner research was supervised, those differences were not found in the multivariate analyses. Apparently, research and user performance in universities and institutes, respectively, and industrial performance in industry are mainly related to system and external control, but only weakly to process control. More accurately, perhaps, one can say that both ways of supervision (tight control, with strict planning of every step of the research process, or loose control, leaving the individual researcher room for manoeuvre) can lead to high performance and effectiveness, provided that the fundamental requirements of system and external control are met.

12.1.2 Comparison of the Strata

In regards to *research question 3*, exhibit 9.10 shows great differences in the average assessment of the empirical concepts of management control in the three strata. In most cases the research units in universities are found at one end of the scale and the industrial laboratories at the other end, with the research units in institutes taking up an intermediate position. Most of the relevant hypotheses, based on the theoretical suppositions of the relative strength of the system variables in the three strata (see exhibit 2.5), are confirmed by the empirical findings. In confirmation with *hypothesis 1.4*, the respondents in companies are clearly more positive in their judgement of the different empirical concepts of system control than those in universities and institutes. The average assessments in industry of the effectiveness of personnel policy and the adequacy of the personnel and material resources are about 0.8 point higher on a Likert 5 point scale than in universities, and 0.2 to 0.6 points higher than in institutes. The difference in the average assessments of administrative control is even larger, a difference of

about 1.5 points between industry and universities and more than 1 point between industry and institutes. For instance, according to the scientific staff in more than 50% of the university research units, it would take more than a year to reallocate a major part of the resources to a new research line, while in industrial laboratories the average estimation is (less than) six months. This substantial difference in the assessment of system and external control may indicate that, despite the recent policy to improve market orientation, the fundamental differences between profit and not-for-profit organizations still exist.

Seen in the light of the great difference in task uncertainty between university and industrial R&D which emerges from the relevant literature (i.e. Weick 1984 and Spangenberg 1989), it was remarkable that the differences found were not so large. In accordance with the idea that the informational need is higher in universities and institutes than in industrial laboratories, both the frequency of research meetings and the attendancy mix are significantly higher in universities and institutes. In contrast to this, international communication, meeting scientists, physicians and colleagues at congresses and workshops, turns out to be most frequent in industry and least frequent in universities. The company researchers have more than twice as much international contacts compared to the researchers in universities. The first finding can be partly explained by the much larger size of the R&D process, whereas the second finding is probably due to the larger available travelling budget in industry. In accordance with the idea of lower task uncertainty, the assessed importance of planning is the highest in industry, but the differences are far from significant. An explanation might be, that the task uncertainty in pharmaceutical discovery has grown considerably in recent years, because of the shift from random screening to basic research. Another explanation might be, that the task uncertainty in basic research is not as high as generally assumed. The fact that the results in basic research are highly unpredictable may not be that disadvantageous, because, in contrast to institutes and industrial R&D, negative results may also have a positive impact on research performance and effectiveness. Even, if no supporting evidence has been found for a hypothesis, it can still lead to a new research line, theory or even (on rare occasions) to a new paradigm. The possibility of presenting negative results partly depends on the receptiveness of the scientific community. That this can be a serious problem was indicated by Easterbrook et al. (1991). They established that medical studies in which statistically significant differences between study groups were found were more likely to be published than those finding no difference. This tendency towards publication bias was not only due to the referees and editors of the scientific journals, but had already begun at the level of the research group

itself. Many researchers with non-significant results decided not to go through all the trouble of publishing. The referee system itself may also act as a publication barrier. Especially in research areas with a low level of paradigm development, in which different schools are in contest with each other, authors may be reluctant to send scientific papers to journals, the editor and referees of which they suspect of being unfavourable to their research concepts.

A final remark must be made regarding the most important contingency, size. Size has, of course, a major impact, not only on performance, but also on the effectiveness of personnel policy. This is not surprising, as size enlarges the range of possible incentives in terms of career planning, remuneration, and possibilities for replacement in situations of conflict. Interestingly, only in industry was a positive association found between size and the adequacy of resources. This finding is in agreement with Spangenberg's observation (1989) in universities, that 'objective' and 'subjective' size are hardly associated. This difference in the assessment of the adequacy of the resources could be considered as a reflection of a difference in competitive orientation between universities and industry (Fisscher 1986). In confirmation with this is the observation which emerged from the examination of a subgroup of the sample, that researchers in universities are more competitively oriented than those in industry.

12.2 STUDY EVALUATION

Following the trajectory of theory construction, theory modifications will be suggested to improve the understanding of the observable reality. Then, following the trajectory of theory application, design parameters will be deducted for practical use for research management, system designers, administration and the makers of research policy. It will be started below with the evaluation of the weak points and the strong points of the study design in terms of contributions made to the trajectory of theory construction, and indicating fruitful directions for further research and complementary follow-up studies.

12.2.1 Strengths and Weaknesses of the Study Design

The strengths and weaknesses of this study are all connected with the *MS*

(TC_{medium}/TA_{small}, see exhibit 1.2) taxonomy of this study.

- The first weakness stems from the cross-sectional nature of the design. All the independent, and nearly all the dependent (except annual growth rate), variables were taken at one point in time. Although this approach enables to evaluate the hypotheses about the sign of the relationships and the relative strength of the different independent variables, it does not inform about causal relationships. A longitudinal design would be more informative in this respect.
- A survey approach has been used in the empirical studies. The strength of this approach is, at the same time, its weakness. On the one hand, it has provided a list of features dividing the more-than-average from the less-than-average performers. In addition, different cross-sections could be made (for instance, more radical compared to more incremental oriented companies and preclinical and paraclinical research units compared to clinical research units), which gave insight into specific aspects of the study population. On the other hand, this type of study observes from a distance through standardized questionnaires. In this particular study this problem was overcome by also obtaining in-depth information through structured interviews. Therefore, the study design was referred to as a set of case studies.
- Other criticisms may centre on the obvious defects of any empirical management study, such as the relatively small study population leading to an unfavourable variable/observation ratio. Moreover, there are probably more factors related to performance and effectiveness which have not been taken into consideration. This, combined with the inevitable measurement imperfections, implies that the conclusions presented should be interpreted with some caution.

This study also has a number of particular strengths:

- the most important is, that the study design concerns a transversal cross-section of three different (sub-)contexts of one technology field, providing the possibility to evaluate the importance of management control in relation to performance and effectiveness and to generalize the findings to related contexts in other technology fields.
- The relatively high response rate for an empirical management study may provide further confidence in the representativeness, and therefore, the generalizibility of the findings.

- It has been attempted in this study to apply the best available ('state of the art') methods for evaluating performance and effectiveness. Although all these measures can be separately criticized on solid grounds, when combined they may provide a more or less 'objective' picture. This has made it possible to relate 'subjective' judgements about management and organization to more or less 'objective' performance and effectiveness measures, which has improved the impact of the findings.
- This approach provided the opportunity to evaluate the validity of the different performance and effectiveness measures. Some performance and effectiveness measures turned out to be more valid than has been generally assumed in the relevant literature (such as the number of articles in universities and institutes and the number of patents in industry), and the criticism of others proved to be true (for instance, the time-lag between publishing and citation). This measure turned out to be useful in the comparison of the strata universities and institutes, and for identifying important differences in publication strategies.
- A last important strength of this study is the use of a neural network to analyse the multi-variate relationships. Up to now a neural network has seldom been used in empirical management studies, because of the problem of 'overfitting'. The neural network 4Thought deals with this problem by use of an independent test set.

12.2.2 Theory Modification

Concerning the methodology of management and organization this study has demonstrated:

- that a transversal cross-section of different types of organization can be a fruitful way to shed light on the complex world of management control in research organizations. Different angles of analysis have been chosen, which each provide their essential contribution to the elucidation of the underlying control mix. The methodology of 'context-comparison', through cross-sectional transverses of different strata in one technology field, combined with cross-sections through different technology fields in one stratum, can therefore be advocated as an important tool for the further investigation of technology management.

- The distinction of having the trajectories of theory construction and theory application condensed into the TC/TA matrix, has proved to be a helpful classification tool and can be used as a paradigm on completeness for application-oriented management and organizational studies.
- Neural network modelling has proved to be a fruitful tool for evaluating the multi-variate relations in this study. It can therefore be advocated for use in empirical management studies including variables operationalized at different measurement levels.

Concerning the theoretical foundation of management and organization studies the following merits can be mentioned:

- The demonstration of the importance of integrating socio-dynamic with system-technical factors in one integrated control mix and the empirical confirmation of the central, but only scarcely proved, thesis of the special importance of human motivation in the socio-dynamic literature.
- The theoretical construct of task uncertainty must be redefined in the light of the findings in this study. The relatively small difference in task uncertainty between basic research in universities, applied research in institutes and discovery in pharmaceutical companies, indicates that, not only do the uncertainty of task input (number of input resources, Galbraith 1973), conduct and outcome (diversity of output, level of goal difficulty, Galbraith 1973) determine the level of task uncertainty, but that the receptivity of the customer function is equally important. This also shows that the shifting of the system boundaries in the model of the double unity cell (Van Engelen 1989), to incorporate the supplier and the customer function, is justified.
- The analogy of the life cycle might prove to be a fruitful theoretical construct for predicting the longitudinal development of research units in universities.

12.2.3 Suggestions for Further Research

The results of this study give rise to further research. Following the trajectory of theory construction, comparative studies into the results of theory application as influenced by contextual differences and further studies into the theoretical and technical aspects of the application of neural network modelling in empirical

management studies, can be mentioned. This can be combined with further studies into the minimum threshold level and span of control in relation to paradigm development in universities and institutes, which could be interesting extensions of the study by Bresser and Dunbar (1986) into educational and research performance and effectiveness across low and high level paradigm fields. Following the trajectory of theory application, in-depth studies into the managerial aspects concerning the building-up and maintaining of the R&D network of universities, institutes and biotechnological and pharmaceutical companies would be important. This study will also be used as a baseline for two follow-up studies. Firstly, the data set will be used as a base line for a longitudinal study in which a number of the laboratories will be examined at regular intervals. An advantage of a longitudinal study is that it can be used for a 'quasi-experimental' design. For instance, the 'objective' situation of some of laboratories has already changed. One of the divisions of a conglomerate, for example, has recently become independent. This change in the 'objective' situation makes it possible to test hypotheses regarding the (dis-)advantages of autonomy compared to dependency at a (near) causality level. Secondly, in order to get an insight into the rich pattern of underlying structures and processes leading to the 'clear-cut' relationships presented in this monograph, this study will be complemented by further case studies.

12.2.4 Theory Application

Following the trajectory of theory application, the control mix which has been established in the trajectory of theory construction can be translated into the following six design parameters for a successful biomedical research laboratory.

- Much attention is paid to human resources management.
- The administrative procedures are carried out quickly.
- There is a flexible adjustment to changing situations.
- Much attention is paid to the building and maintaining of an (international) R&D network.
- The research process in the discovery phase is characterized by intensive 'in-house' communication.
- Much attention is paid to planning and lateral and cross-functional communication during the development phase.

Although these design parameters do not constitute a blueprint, they enable the research management, system designer, management consultant or research policy maker, to concentrate their efforts. It is interesting in this respect, that process control turns out to be a less important factor in association with performance and effectiveness. Apparently, the socio-dynamic and system-technical factors constituting organizational flexibility are more important in the control mix than the control capacity of the research management. There are many ways for good research managers to reach their goals. But what they cannot change is the flexibility of the organization as a whole. This stresses the importance of organizational change being directed towards staff empowerment and motivation. In the 'Harvard Business Review', Kanter (1989) mentioned the following immaterial incentives directed at enhancing motivation:

- Mission; helping people believe in the importance of their work.
- Agenda control; giving people greater control over their own activities and direction.
- Share of value creation; giving individuals or teams entrepreneurial incentives.
- Learning; access to training, mentors and challenging projects, providing the opportunity of continuous learning.
- Reputation; enhancing recognition and bringing people into organizational and professional networks.

According to our scientific findings these immaterial incentives are indeed important. Give scientists the chance to enhance their reputation, and provide opportunities for attaining recognition. This can be done by encouraging them to publish and attend congresses as a speaker, bringing them into contact with outside peers, or by giving them visible rewards (e.g. fellowships, and awards for project team achievements) and by a dual (or hybrid) ladder system in industry.

An alarming result is the negative judgement of system control, and the effectiveness of personnel policy especially, in universities (see exhibit 9.14). This finding should be interpreted with some caution, because in a professional bureaucracy, such as a medical faculty, there is always a certain tension between professionals and the administrative staff (Mintzberg 1979, 1983), which can result in a more negative judgement of the measures of organizational flexibility. Nevertheless, the very negative judgement, also in comparison to earlier research, could indicate that the budget retrenchments have reached a border which should not be surpassed. The recent fierce reactions of the Dutch universities to further budget

retrenchments seem to support this supposition. However, a number of policy measures could be taken to improve the situation.

- Governmental policy could be directed towards assisting universities in improving the unclear decision structure. Up to now, important decisions can be hindered for years by ever-changing coalitions of interest groups.
- Provide opportunities for gaining recognition, for instance, by supplying a sufficient travelling budget for attending international congresses, or by specialized training facilities.
- Provide the opportunity for talented PhD students to continue in research after attaining their PhD by an extensive fellowship programme for postgraduate appointments.
- Reduce the overhead by reducing the corporate staff and by critically evaluating the number of administrative procedures.
- Improve the communication within the faculty, for instance by organizing faculty-wide seminars and workshops.

The triangular model indicates that management control and performance and effectiveness stand in a dynamic equilibrium. The researchers of a leading research laboratory are more often asked as editor, referent or key note speaker, reinforcing their position in the scientific or users' community. However, a motivated young leader of a research unit can certainly enlarge the chance of success by using the tools presented in this study. Most important of those is the choice of a 'research niche', a new and interesting theme (e.g. a new theory or a new approach to tackle a fundamental or applied research problem), which inspires and motivates the scientific staff and can be used as a key to open the door to the scientific or users' world. If working at an under-exposed research terrain it is more easy to get access to journals, to organize a congress or to start a journal. Prof. Kistemaker (1982 and 1985), the former Director of the Institute for Atomic and Molecular Physics and as such leader of the Dutch ultracentrifuge enrichment project, states that a well-balanced research programme should consist of four research themes, in order to combine the required concentration of research efforts with a certain amount of risk-spreading. The choice of a theme should meet the following criteria.

- It should be new, with only a few research groups working on the same subject, world-wide. A subject about which large international congresses are organized is less suitable.
- It should be of scientific or public relevance and affiliate with the expert-

ise of the group.
- if after some years no interesting results are found it should be possible to switch to another research theme without considerable loss of expertise and equipment.

He states that any innovation has to be realized against the following forces.

- Fear for failure.
- Absence of vision.
- Disgust of excellency.

According to Kistemaker, these are powerful forces against which research leaders have to fight and usually loose. They can be recognized by the continual asking for more extensive explanation and more external comments by central authorities, and sharp criticisms by highly intellectual and democratic feeling people. Also research leaders in pharmaceutical innovation, in discovery especially, have to cope with these forces. However, more aspects must be taken into consideration, because of the more extensive character of the pharmaceutical R&D process. A well-balanced pharmaceutical R&D programme should therefore comply with the following 'Ten Basic Rules for Success in Pharmaceutical Innovation'.

- Orientate R&D staff towards the company's mission, objectives, and goals and identify these at all organizational levels.
- Adhere to the highest scientific, medical and ethical standards.
- Strive to concurrent development by stimulating lateral and cross-functional communication. Encourage openness, honesty, cooperation, teamwork and shared goals within and between functions (R&D, production, marketing and sales).
- Focus activities in a relatively limited number of therapeutic areas. Develop a portfolio of investigational drugs that balances risk.
- Create an international R&D network. Put much emphasis on cooperation with universities, institutes and biotechnological and innovative pharmaceutical companies.
- Formulate a strategy for each therapeutic area, and within each area a strategy for each drug, indication and formulation. Establish minimum criteria that must be achieved to continue development and specify key decision points.

- Set priorities and assign personnel and resources accordingly. Evaluate each project and the overall portfolio at frequent intervals, minimize duplication and stress efficiency. Identify rate-limiting steps and tackle them collectively in an early stage, through lateral and cross-functional communication.
- Create operating systems which avoid bureaucracy and work with short (tele-)communication lines. Empower scientific staff to provisionally stop a project if one of the parameters is negative, without previous hierarchical consent.
- Develop a clear licensing strategy that allows all technology, product, process and other opportunities (e.g. acquisitions) to be rapidly reviewed.
- Develop an integrated registration and reimbursement strategy, directed towards cooperation with the relevant authorities. Keep up-to-date files of everything important to deal with questions and criticisms.

It is often said that workers are resistant to change. However, the respondents in about 60% of the research units considered the results of previous reorganizations to be positive. In universities the reduction in the number of less productive groups, in institutes the aim of improved market orientation, and in industry the creation of multidisciplinary project teams were mentioned as improvements. The positive overall judgement is, of course, for a great deal due to the fact that only those staff members answered the questions who still worked in the organization. However, the results show that if a reorganization is based on obvious necessities the remaining staff will assess the results to be positive for the organization as a whole. In this context, it is of interest that the largest difference between autonomous pure play pharmaceuticals and dependent conglomerate divisions turned out to be the way that reorganizations were carried out, which was done with greater pace and with more knowledge of the specific needs of the scientific staff in the pure play pharmaceuticals.

Numerous researchers have stressed that stimulating and rewarding environments are needed to enhance R&D performance and effectiveness(e.g. Allen 1976, Pelz and Andrews 1976 and Badawy 1988). The importance of a flexible organization to proactively react on changing situations at strategic, tactic and operational level (e.g. Volberda 1992) and the importance of the maintaining of an extensive R&D network, are also stressed in many studies (e.g. Biemans 1992, Della Valle and Gambardella 1993, and Albertini and Butler 1994). However, until now only limited evidence has been presented to prove these statements in the real world of management practice, partly because of the large methodological and practical

problems. It is the merit of this study that it has provided confirming evidence for these theses by using the methodology of 'context-comparison'. Taking into account the large contextual variation, the comparison has shown rather consistent results. Consequently, the results may be generalized to management control of biomedical research, and probably to 'Big Science' and R&D at large.

12.3 CONCLUDING REMARKS

Now the everyday management situation in research organizations has been analyzed in some detail, will be returned to were was started from, in the ideal world of Nova Atlantis. If is looked at the evidence presented above, it can be concluded that the keywords for success prove to be organizational flexibility, autonomy and empowerment of staff. Below these theoretical constructs are used to show the reader three mental pictures, of an ideal university, institute and company laboratory.

Picture high quality universities, which compete for prestige in the scientific world and which try to provide the best medical care and education possible. These universities try to get the most highly qualified academic staff, which is broadly educated and able to see problems in their broad context. The staff is flexible, cooperative and ready to accept and to proactively react to changes and new challenges. The laboratory equipment is advanced and the number of regulations is small. There are numerous opportunities for continuous learning in excellent universities or institutes abroad (fellowships, sabbaticals etc.). There is a large travelling budget for attending scientific congresses and for visiting the leading scientists abroad and for the appointment of visiting professors and scientific guest-workers. Optimum use is made of telematica facilities for remote working. Most of the research is done at home, but in direct contact with the other members of the multidisciplinary research team and the scientific community around the globe. Long-distance learning methods are used avoiding the one-way education of mass lectures. The educational programme itself is problem-oriented and based on individual learning. The staff is appointed on a temporary basis, reappointment depends on the evaluation by students, the person's prestige in medical care, or their quality in basic or strategic research. Most of the research money is acquired through grants, supplied by a large number of grant agencies. Part of which have the objective to assist basic and strategic research in different scientific fields, while others are oriented to the important challenges which face

society (pollution, Aids etc.) In order to avoid in-crowd selection, educated laymen also take part in the granting committees. The administration of the unit is small and assists the scientific staff as much as possible. There is a clear decision structure with short lines from the research floor level up to the level of the university board, with groups of research units working together in temporary cooperative structures directly under the supervision of the university board.

The picture of an ideal institute is nearly the same, with research units working together in temporary, often multidisciplinary projects directly under the supervision of the institute board. A large part of the applied research, which traditionally had to be carried out in a laboratory, is done at home by use of virtual reality techniques such as computer aided drug design. The staff is appointed on a temporary basis, depending on the projects they are working on. There is a high market orientation. The staff has a clear vision of what the customer wants, and much care is taken that the customer gets value for money. The requisite knowledge for this is build up by frequent customer communication.

If this picture is realized, universities and institutes will be fully integrated into organizations in which basic and applied research are combined in an optimum way. The innovative pharmaceutical company will then become adjusted to this new situation. Imagine the resulting picture. Most of the basic and applied research in discovery is done in the biomedical departments in universities and institutes. The companies concentrate on their main strength, bringing a lead to the market in a short period of time. As the market orientation in universities and institutes improves, there is an ever-growing flow of scientific staff between universities, institutes and companies. Regularly, R&D staff members from companies are appointed in universities or institutes and vice versa for temporary research projects, providing to strong links between basic research, applied research and experimental development. Part of experimental development is contracted-out, but the pharmaceutical companies keep the lead in organizing the R&D process. Urged by patient interests, the registration authorities understand that reducing time-to-market is in the mutual interest of the company and society. They stay in close consultation with the pharmaceutical companies to avoid unnecessary loss of information through non-accepted clinical trials. The pharmaceutical R&D process is conducted by independent pure play pharmaceuticals, which work at arm's length but under the umbrella of large chemical conglomerates, which provide a world-wide marketing and sales network. The marketing and sales force is smaller, but better educated than before. The main point of attention has shifted from effecting the prescription behaviour of the physician

to convincing drug specialists from government and insurance companies of the superiority of their new products, by confronting them with the relevant scientific evidence. Ethical drug costs are greatly reduced by vertical integration. The physician's receipt is sent directly to the pharmaceutical company via authorized electronic mail, which in-turn sends the ethical drug directly to the patient.

This picture is a *fata morgana*. Due to the uncertain context, Nova Atlantis can never be reached. If one expects to be there, it drifts away. For instance, the 'fallacy of composition' will work against us. Although a particular measure may be attractive for a few organizations, when adopted by everybody its popularity - becomes self-defeating. It is impossible that all universities and institutes can achieve excellency or that all companies will stand at the forefront of the invention of new drugs. Nevertheless, it will be a great challenge to start the journey by untying universities and institutes from too strict government regulations and giving autonomy to pharmaceutical divisions in industry. After these first steps are taken, the organizations will be confronted with new and unexpected challenges. But by then they will certainly be in a better position to conquer them.

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APPENDIX A

Definitions of the different terms used in ReQuest 1 and 2

Research unit
Consists of a number of researchers, supported by technical, analytical and administrative staff under supervision of a research manager, working on one or more specific research projects.

Full-time equivalents (ftes)
The extent of the appointment, i.e. a staff member with a full-time job accounts for 1.0 fte, a staff member working half-time for 0.5 fte.

Research manager
Directs a research unit, for instance a professor heading an academic research group, or a department leader in an institute or industrial laboratory.

Senior scientific staff
Accountable to the research manager, in charge of one or more research or development projects and leading attached junior scientific staff members and the technical, analytical and administrative support staff.

Junior scientific staff
Supervised by the senior scientific staff, carry out research projects (for instance PhD students).

Technical, analytical and administrative support staff
Provide technical, analytical and administrative support (e.g. a secretary, a chemical analyst, in as far as they are attached directly to the research unit).

Education
Providing and receiving education (specifically PhD students).

Administration and management
Administrative functions outside the research unit (for instance preparing and attending Faculty Council meetings and meetings of the Faculty directorate and cooperative meetings) and administrative and managerial activities within the unit.

Acquisition
Research supplies acquired through, for instance, funding agencies and industry. Also

comprises writing and checking project proposals, consulting with contracting parties and reporting on contract research.

Research project
A group of interrelated research activities aimed at obtaining original results, for instance through developing new theories and methods, or new products and processes, or by way of opening unexplored fields of research. Project progress is, in most cases, reported to the higher hierarchical levels within the organization (for instance Faculty Council, directorate) or to funding agencies supporting the project.

Personnel means
Includes the scientific and the analytical, technical and administrative support staff of the research unit.

Material means
Running costs and replacement and purchasing costs of apparatus.

Funding
Basic funding plus external funding (= 100%).

Basic funding
The structural funding of the research unit (direct funding at universities; structural and target funding in institutes.

External funding
Means received by the research units, not on a structural basis but owing to projects submitted to funding agencies or through contracts with government and industry.

ReQuest 1

1 How many staff members work in your research unit? How many of these are under 40 years of age (in full-time equivalents, ftes)?

	Total number of staff members	Under 40
Research manager(s)	.....	.....
Senior scientific staff	.....	.....
Junior scientific staff	.....	.....
Technical, Analytical & Administrative support staff	.....	.....

2 Please indicate below how the working hours of the research unit scientific staff are roughly spent.

	Research Manager	Senior Sci. Staff	Junior Sci. Staff
Research	.....	.....	.....
Education	.....	.....	.....
Management & Administration	.....	.....	.....
Acquisition	.....	.....	.....
Clinical practice	.....	.....	.....
Other activities,	.....	.....	.....
Total	100%	100%	100%

3 Please indicate below the number of scientific staff members of your research unit involved in the three largest research projects currently in progress?

First (largest) project	..... ftes
Second project	..... ftes
Third project	..... ftes

4 How many scientific staff members are employed on a permanent basis?
..... ftes

5 How many technical, analytical and administrative support staff members are employed on a permanent basis? ..... ftes

6 How many scientific staff members have obtained a PhD within the past three years?
..... ftes

7 Please indicate below the development of the personnel and material means during the last 10 years.

	1980	1985	1990
Personnel means	..... ftes	..... ftes	..... ftes
Material means	..... US$	..... US$	..... US$
Basic funding	..... %	..... %	..... %
External funding	..... %	..... %	..... %

8 How many international congresses, symposia or seminars did your research unit organize over the last three years?

..... congresses etc.

9 How many papers have you presented at international congresses in the last year?

..... papers

10 How many colleagues from abroad visited your research unit in the last year?

..... colleagues

11 How many working hours have the scientific staff of your research unit spent, in the last year, on joint projects with

- other research units within your organization? .....
- research units outside your organization but within the Netherlands? .....
- research units outside the Netherlands? .....

12 How many editorial boards do you sit on?

- International journals ..... ftes
- National journals ..... ftes

13 How many articles have scientific staff members received for peer review in the last year, from

- international journals? ..... articles
- national journals? ..... articles

14 How many articles of which a member of your research unit is the first author have been published over the last three years in

- international journals? ..... articles
- national journals? ..... articles
- professional journals for physicians, medical specialists or pharmacists? ..... articles
- journals for patients' associations? ..... articles

ReQuest 2

1 How long have you been attached to this research unit? ..... years

2 How long have you been directing this research unit? ..... years

3 How many years' experience have you had since obtaining your PhD?
..... years

4 Please indicate using the figures 1 to 5 inclusive how frequently a research plan is usually drawn up by the senior executive staff of your organization (strategy department, laboratory directorate, scientific committee).

Short-term plan (annual plan) .....
Medium-term plan (2 to 5 years) .....
Long-term plan (more than 5 years) .....

1 = once a year; 2 = once in 3 years; 3 = once in 5 years; 4 = less than once in 5 years; 5 = never

5 'The research plan serves as a significant guideline for our research programme'. Please indicate your response to this statement by circling a figure or 'n/a' = not applicable.

Short-term plan: agree entirely - 1 2 3 4 5 - disagree entirely (n/a)
Medium-term plan: agree entirely - 1 2 3 4 5 - disagree entirely (n/a)
Long-term plan: agree entirely - 1 2 3 4 5 - disagree entirely (n/a)

6 Please indicate the frequency of meetings held to discuss progress of research or development projects? Please circle the answer which best describes the situation.

1 = once a week; 2 = once in 2 weeks; 3 = once a month; 4 = once in 3 months; 4 = less than once in 3 months

7 Which staff members are usually present at these meetings (see question 6)? You may indicate more than one group.

Research manager .....
Senior scientific staff .....
Junior scientific staff .....
Technical, analytical and
administrative support staff .....

Scientific staff of other research units .....
Staff of other non-scientific sections
(e.g. product development) .....
Staff ranking higher in the organization .....
People from outside the organization
(e.g. colleagues) .....

8 Please indicate the frequency of research unit evaluation by
(Please fill in the figure corresponding most to the actual situation)

authorities ranking higher in the organization (e.g. research committee, laboratory directorate etc. (internal evaluation) .....
authorities outside the organization
(e.g. an expert panel, external evaluation) .....

1 = once in 6 months; 2 = once a year; 3 = once in 3 years; 4 = once in 5 years; 5 = less than once in 5 years

9 How many working hours are on average spent on an evaluation round (including preparation, evaluation and reporting)?

Internal evaluation		External evaluation	
0 - 8 hours	.....	0 - 8 hours	.....
9 - 20 hours	.....	9 - 20 hours	.....
21 - 40 hours	.....	21 - 40 hours	.....
41 - 80 hours	.....	41 - 80 hours	.....
> 80 hours	.....	> 80 hours	.....

10 If the internal or external evaluation showed that a large part (e.g. 20%) of personnel and material means should be allocated to a new field of research, how long would it take for this reallocation to be realized? Please circle the appropriate figure.

1 = (less than) 1 month; 2 = 1 to 3 months; 3 = 3 to 6 months; 4 = 6 to 12 months; 5 = (more than) a year.

11 Have there been any reorganizations within the last 5 years (for instance in task assignment and task concentration) in which your research unit was involved? Please circle the appropriate figure.

1 = no reorganizations; 2 = one reorganization; 3 = more than one reorganizations

12 What is your opinion with the respect to positive or negative consequences for your research unit of such reorganizations?

very positive - 1 2 3 4 5 - very negative

13 How often do you have meetings (concerning work content) with

colleagues within your research unit?	1	2	3	4	5	
colleagues from other research units within your own organization?	1	2	3	4	5	
staff members working at product development (industry)?	1	2	3	4	5	n/a
staff members working in marketing (industry)?	1	2	3	4	5	n/a

1 = daily; 2 = weekly; 3 = monthly; 4 = once in 3 months; 5 = less than once in 3 months; n/a = not applicable

14 How often do you have meetings (concerning work content) with

colleagues outside the research organization but within the Netherlands?	1	2	3	4	5	n/a
colleagues from abroad?	1	2	3	4	5	n/a
colleagues from other disciplines?	1	2	3	4	5	n/a
medical specialists?	1	2	3	4	5	n/a
funding agencies (e.g. the Dutch Foundation for Cancer Research)?	1	2	3	4	5	n/a
industrial or governmental contractors?	1	2	3	4	5	n/a
interest groups (e.g. patient organizations)?	1	2	3	4	5	n/a

1 = weekly; 2 = monthly; 3 = once in 3 months; 4 = once every half year; 5 = (less than) once a year; n/a= not applicable

15 Please indicate whether the number of personnel is adequate to conduct the current research projects and/or scientific assignments.

certainly adequate - 1 2 3 4 5 - very inadequate

Please indicate whether the material resources are adequate to conduct the current research projects and/or scientific assignments.

certainly adequate - 1 2 3 4 5 - very inadequate

The laboratory accommodation is

certainly adequate - 1 2 3 4 5 - very inadequate

16 Please indicate the degree of the limitations imposed on the research unit by administrative regulations (e.g. regarding travelling, budget, etc.).

very large - 1 2 3 4 5 - very slight

17 What is the limit on the sum that can be appropriated for an apparatus without previous approval by a budget committee or any other regulating authority?

..... US$

18 Please indicate using the figures 1 to 5 inclusive the estimated time-span between a request for an appointment or for purchasing an expensive apparatus and its approval, in the following instances.

A temporary appointment of a staff member .....
A permanent appointment of a staff member .....
The purchase of expensive apparatus (US$ 10,000 or more in universities and institutes and US$ 50,000 or more in industry) .....

1 = less than 1 week; 2 = 1 week to 1 month; 3 = 1 to 3 months; 4 = 3 to 6 months; 5 = more than 6 months

19 How can the personnel resources management within your organization be characterized?

very flexible - 1 2 3 4 5 - very rigid
very decisive - 1 2 3 4 5 - very indecisive
very effective - 1 2 3 4 5 - very ineffective

20 Are attempts made within your organization to guarantee research quality through a policy on career planning for the following groups?

Scientific staff:
very great emphasis - 1 2 3 4 5 - no emphasis at all

Technical, analytical and administrative support staff:
very great emphasis - 1 2 3 4 5 - no emphasis at all

21 Compared to 'competitors' (industrial laboratories, institutes and university departments), you can offer scientific staff the following incentives.

Primary terms of employment and fringe benefits (salary, thirteenth month)

Industrial laboratories	1	2	3	4	5
Institutes	1	2	3	4	5
University departments	1	2	3	4	5

Good reputation of organization and research unit

Industrial laboratories	1	2	3	4	5
Institutes	1	2	3	4	5
University departments	1	2	3	4	5

Career opportunities within the organization

Industrial laboratories	1	2	3	4	5
Institutes	1	2	3	4	5
University departments	1	2	3	4	5

Career opportunities outside the organization (for instance, after obtaining a PhD)

Industrial laboratories	1	2	3	4	5
Institutes	1	2	3	4	5
University departments	1	2	3	4	5

1 = very unattractive; 5 = very attractive

In order to gain insight into the practise of the personnel resources management, a number of examples are given of personnel situations that could occur. In order to be clear, to some extent extreme examples have been chosen.

22 A staff member with a temporary appointment functions so well that you wish to keep him/her in the organization. The applicable regulations leave no room for offering a permanent appointment. However, the legal maximum term for a temporary contract has expired. What will happen, in your view?

The person involved will be dismissed after the contract's expiry date .....
The person involved will be reappointed temporarily within the organization .....
The person involved will be offered a permanent contract, e.g. by means of external funding .....

23 A staff member functions so far above the required level that you wish to move him/her up to a salary scale higher than the maximum which the person involved is entitled to, according to job evaluation. What will happen, in your view?

The person involved will remain in the same salary scale .....
The person involved will remain in the same scale,
but will get an extra allowance (e.g. a once-only bonus,
an extra periodical payment, prolonged maximum salary scale) .....
The person involved will be put on a higher salary scale .....

24 A staff member appointed on a permanent basis functions so badly that dismissal has to be considered. The procedure is started. What will happen, in your view?

The person involved will get a different position
within the research unit .....
The person involved will be transferred .....
The person involved will be dismissed .....

25 How long do you think this procedure will take?

Less than a month .....
1 - 3 months .....
3 - 6 months .....
6 - 12 months .....
Longer than 1 year .....

26 How many scientific staff members of your research unit have, within the last year,

followed a training programme (of at least 2 weeks)? .....
received external practical training in research?
(for at least 3 months) .....

27 Please indicate whether, and how often, arrangements are made within your research unit, such as daytrips, joint Christmas celebrations, etc.

never - 1 2 3 4 5 - very frequently

APPENDIX B

General questions about R&D management

1. Organization of the R&D process

- What is the input of personal and material means in the different phases of the R&D process (discovery (synthesis and test phase), pharmaceutical development and clinical development phases I to IV)?
- In which countries are the different phases of the R&D process located?
- How much time do the separate steps in the R&D process roughly take? Would it be possible to shorten the time span of the different steps in the R&D process? If so, which measures have to be taken to shorten the different steps of the R&D process?
- How are the research and development laboratories organized (e.g. linear, matrix or project organization). What is the average department and project size and the lateral and multi-functional staff composition of the projects in the different steps of the R&D process? What is the percentage of the scientific staff in the total R&D staff in the different steps of the R&D process?
- Can clear differences be pointed out between research laboratories and laboratories for development (e.g. concerning size and hierarchy)?
- How are the clinical development phases I to IV organized (e.g. quality control of clinical research)?

2. Portfolio planning and evaluation (product-line development)

- Which medical indication areas do your company cover?
- Which criteria determine the strategy concerning the initiating or phasing out of research lines?
- Where in the R&D process are the most important Go/No-Go moments?

3. Innovation

- By which methods are innovation areas localized?
- What percentage of the R&D budget is spent on basic research, what percentage of this budget is spent on cooperative projects with universities and research institutes?
- What is the policy concerning basic research, also with regard to contracting out to universities and/or to institutes, or execution by your own company's laboratories?

- What policy is maintained on cooperation with universities and institutes?
- Approximately how many compounds have to be analyzed and patented in order to develop one new product?

4. Human resources

- Is there a dual (or hybrid) ladder system (managerial or scientific)?
- How can the primary and secondary working conditions in your company be assessed in comparison to those in other innovative pharmaceutical companies?
- What incentives are being given to scientific staff (both material and immaterial)?
- What is the company policy on scientific publishing?

5. Management

- Comparison of the management of your company with that of universities and of institutes (weak and strong points).
- Budget responsibility - at which level in the organization?
- How are investments decided upon?
- In which phase, in terms of 'corporate' to 'entrepreneurial', would you place your company?

6. Output

- How many patents obtained through research and development efforts by your industrial laboratory (no licences-in, no me-too licences) have resulted in marketable products over the past 5 years?
- What percentage of the research and development efforts by your company's laboratory was recovered last year on the basis licensing-out to other companies?
- What was last year's operating profit margin (pre-tax on profit to turnover ratio) of your company?

APPENDICES C TO I

Appendix C
The exhibits C.1 to C.4 inclusive, show the operationalizations of the contingencies, management control and performance and effectiveness.

Appendix D
The exhibits D.1 to D.5 inclusive, show the factor structures of the contingencies, management control and performance and effectiveness.

Appendix E
The exhibits E.1 to E.3 inclusive, show the comparisons of preclinical and paraclinical units with clinical units in universities and with the research units in institutes, by use of one-way ANOVA.

Appendix F
The exhibits F.1 to F.4 inclusive, show the Spearman rank correlations of the contingencies and management control with performance and effectiveness in preclinical and paraclinical units, and clinical units in universities and the research units in institutes.

Appendix G
The exhibits G.1 to G.3 inclusive, show a qualitative comparison of the different universities and institutes.

Appendix H
The exhibits H.1 to H.4 inclusive, show different cross-sections of the industrial study sample, by use of one-way ANOVA.

Exhibit C.1a OPERATIONALIZATION OF THE EMPIRICAL CONCEPTS OF THE CONTIGENCIES

size	**sales (companies)** world-wide sales of branded ethical drugs in 1991 in US$ billion
	R&D expenditure (companies) world-wide R&D expenditure in 1991 in US$ million (the total expenditures and the separate expenditures for drug discovery, pharmacological and clinical development, and postmarketing surveillance (phase IV clinical trials, no patent and registration costs)
	total staff (universities, institutes and companies) number of scientific and technical, analytical and administrative support staff working in the research unit or in the R&D process in 1991 in full time equivalents (ftes)
	research staff (universities, institutes and companies) number of scientific staff working in the research unit or in the R&D process in 1991 in ftes
	project size (universities and institutes) percentage of the total research time of the unit directed to the largest research line (group of inter-related research activities)
time-allocation (universities and institutes)	percentage of total working time of the scientific staff allocated to research, education (teaching and receiving education by PhD students), management and acquisition, and clinical practice

Exhibit C.1b OPERATIONALIZATION OF THE EMPIRICAL CONCEPTS OF THE CONTIGENCIES

organizational age (universities and institutes)	**research experience** number of years of research experience of the head of the research unit
	management experience number of years that the current head has supervised the research unit
technology	**technological support capacity (universities, institutes and companies)** technical, analytical and administrative support staff as a percentage of total staff (in ftes)
	material resources (universities and institutes) research budget per fte scientist in 1991 (in US$/ftes)
	percentage discovery (companies) percentage of the total R&D expenditure, allocated to the discovery phase
power	**signatory authorization capacity (universities and institutes)** amount of procurement (in US$) the research unit leader can make without previous consent of higher management
	external funding (universities and institutes) percentage of the total research unit budget originating from external funding (grants, contract research etc.)
	junior to senior scientist rate (universities) number of junior scientists (PhD students and post-docs without a tenure, in ftes) divided by the number of supervising senior scientists (non-chaired professors, associate and assistant professors with tenure) in ftes = (supervision rate)$^{-1}$

Exhibit C.2a OPERATIONALIZATION OF THE EMPIRICAL CONCEPTS OF MANAGEMENT CONTROL

<table>
<tr><td rowspan="3">system control</td><td rowspan="2">personnel control</td><td>effectiveness of personnel policy

subjective assessment by the head of the research unit and the senior scientific staff in universities and institutes, or the heads of the different research departments in company laboratories, of the effectiveness of personnel policy e.g.:
• pace and manner in which reorganizations are executed
• cases concerning appointment, promotion and dismissal

material incentives:
• primary and secondary working conditions (for instance salary level, stocks and use of company car etc.).
• extra payment for extraordinary research efforts

immaterial incentives:
• career planning and training facilities
• good reputation of the organization or the research unit leader
• career possibilities within the organization or as a step-up towards other organizations
• recognition, eg. possibilities for scientific publishing and presentation, or a dual ladder system in industry</td></tr>
<tr><td rowspan="2">resources control</td><td>adequacy of resources

subjective assessment of the adequacy of:
• personnel and material resources
• advanced laboratory equipment, devices and space</td></tr>
<tr><td>administrative control

subjective assessment of the speed of the administrative procedures:
• appointment and procurement of equipment (US$ 5.000 in universities and institutes and US$ 50,000 in industry)
• reallocation of a large part (20%) of the personnel and material resources to a new research field.</td></tr>
</table>

Exhibit C.2b OPERATIONALIZATION OF THE EMPIRICAL CONCEPTS OF MANAGEMENT CONTROL

process control	**planning** subjective assessment of the importance of short and middle range planning by higher management for the everyday research work (for instance research committees in universities and institutes or the head office in industry) **research process communication** frequency • frequency of research meetings attendancy mix • general attendancy of research meetings: is the head of the research unit present, along with the scientific staff or also with the technical and analytical support staff and researchers from other laboratories in universities and institutes, or staff members from other R&D phases and/or marketing and production in industry (lateral and cross-functional communication)
external control	**international communication** • frequency of international contacts with scientists and physicians and colleagues from other companies, for instance at congresses and workshops • number of joint research projects with other research units outside the own institution in the Netherlands or abroad (universities and institutes) **contractor communication (universities and institutes)** frequency of contacts with (industrial and governmental) contractors

Exhibit C.3a OPERATIONAL DEFINITIONS OF PERFORMANCE AND EFFECTIVENESS MEASURES IN UNIVERSITIES AND INSTITUTES

research performance and effectiveness	**scientific publications (universities and institutes)** the average number of papers (articles, letters to the editor, notes, reviews and proceedings) published in international scientific journals between 1985 and 1990, entered in the Science Citation Index, the Social Science Citation Index and the Arts and the Humanities Index per total scientific staff (research performance) and per fte scientific staff (research effectiveness)
	number of PhDs (universities) the average number of PhD theses defended between 1987 and 1991 (research performance) and per fte junior researcher (research effectiveness)
	scientific credibility (universities and institutes) the number of papers received from scientific journals for peer review, and the participation in Editorial Boards by the senior scientific staff
	citation score the average number of citations per scientific paper, published between 1985 and 1987, in the three years following publication; self-citations and citations by research unit members were omitted; the number of citations was divided by the average number of citations of all papers published in that period in the same journals (journal weighed) and in the same (sub-)disciplines (weighed for discipline)

Exhibit C.3b OPERATIONAL DEFINITIONS OF PERFORMANCE AND EFFECTIVENESS MEASURES IN UNIVERSITIES AND INSTITUTES

user performance and effectiveness	**physician papers** the average number of papers published annually by scientists of the research unit in national journals, and journals for physicians and patients between 1987 and 1991 (user performance) and per fte scientific staff member (user effectiveness); to avoid overlap the papers published in international medical journals, such as the British Medical Journal and The Lancet, were considered to be part of the research performance
	contractor papers the average number of papers published annually by scientists of the research unit between 1987 and 1991 for industrial or governmental contractors
general performance and effectiveness	**annual growth rate** the average annual growth rate of the total staff (in ftes) between 1986 and 1991 (number of staff in 1991/ number of staff in 1986)$^{-2}$

Exhibit C.4 OPERATIONALIZATION PERFORMANCE AND EFFECTIVENESS MEASURES IN INDUSTRY

innovative performance and effectiveness	**number of patents** the average annual number of patents for New Chemical Entities, submitted world-wide with first priority date between 1985 and 1991 (performance), and divided by the annual expenditures on discovery (effectiveness)
	length of development phase length of development phase, the average time span between patenting of the lead compound and the registration of the drug $(years)^{-1}$
industrial performance and effectiveness	**operating profit margin** operating results/revenues: operating results = results after deduction of normal operating charges and before financial income and expenses, taxes etc.; revenues = net turnover including other operating revenues, change in stocks and capitalized costs
	annual growth rate the average annual growth rate of the company from 1985 till 1991, both organic growth and growth through acquisition

Exhibit D.1 FACTOR STRUCTURE OF THE CONTINGENCIES IN UNIVERSITIES, principal components analysis and varimax rotation, n=40

contingencies	factor loading
factor 1: size (eigenvalue 3.08, expl. variance 21%)	
research staff	0.93
total staff	0.93
technological support capacity	0.51
signatory authorization capacity	-0.43
factor 2: project size (1.14, 8%)	
project size	-0.91
factor 3: time-allocation (2.05, 14%)	
research	0.94
clinical practice	-0.94
factor 4: age (2.50, 17%)	
research experience	0.77
management experience[1]	0.84
factor 5: technology (1.02, 10%)	
technological support capacity	0.59
material resources	0.92
factor 6: power (1.10, 11%)	
signatory authorization capacity	-0.41
external funding	0.79
junior to senior scientist rate	0.88

[1] plus attachement to the research unit (0.83), because this item merely overlaps with management experience, it was not distinguished as a separate variable

Exhibit D.2 FACTOR STRUCTURE OF PERFORMANCE AND EFFECTIVENESS IN UNIVERSITIES, principal components analysis and varimax rotation, n=40

performance and effectiveness	factor loading
factor 1: research effectiveness (1.26,13%)	
international scientific publications / reseacher	0.76
PhDs / researcher	0.52
editorial boards / researcher	0.66
peer review / researcher	0.52
factor 2: user effectiveness (3.39, 37%)	
publications in user journals / researcher	0.93
publications in journals for physicians / researcher	0.82
publications in national journals / researcher	0.83
factor 3: citation score (1.77, 18%)	
citation score weighed for journal	0.90
citation score weighed for (sub-)discipline	0.94
factor 4: annual growth rate (1.17, 12%)	
annual growth rate	0.89

Exhibit D.3 FACTOR STRUCTURE OF THE CONTINGENCIES IN INSTITUTES, principal components analysis and varimax rotation, n=17

contingencies	factor loading
factor 1: size (eigenvalue 2.22, expl. variance 20%)	
research staff	0.97
total staff	0.95
project size	-0.69
factor 2: time-allocation (3.57, 32%)	
research	0.69
education	0.81
management	-0.96
factor 3: age and technology (1.71, 16%)	
research experience	0.58
management experience	0.79
technological support capacity	0.84
factor 4: power (1.45, 13%)	
signatory authorization capacity	-0.84
research experience	0.68
project size	0.52

Exhibit D.4 FACTOR STRUCTURE OF PERFORMANCE AND EFFECTIVENESS IN INSTITUTES, principal components analysis and varimax rotation, n=17

performance and effectiveness	factor loading
factor 1: research effectiveness (1.04, 12%)	
international scientific publications / researcher	0.85
PhDs / researcher	0.84
editorial boards / researcher	0.40
peer review / researcher	0.72
factor 2: user effectiveness (3.39, 37%)	
publications in user journals / researcher	0.98
contractor publications / researcher	0.84
editorial boards / researcher	0.86
factor 3: citation score (2.68, 30%)	
citation score weighed for journal	0.86
citation score weighed for (sub-)discipline	0.91
publications in journals for physicians / researcher	0.75

Exhibit D.5 FACTOR STRUCTURE OF THE CONTINGENCIES, PERFORMANCE AND EFFECTIVENESS IN COMPANIES, principal components analysis and varimax rotation, n=14

contingencies	factor loading
factor 1: size (eigenvalue 4.19, expl. variance 60%)	
sales	0.96
R&D budget	0.98
R&D staff	0.97
factor 2: technology (1.85, 27%)	
technological support capacity in discovery	0.90
technological support capacity in development	0.86
percentage discovery	0.66

performance and effectiveness	factor loading
factor 1: innovative performance (2.07, 52%)	
number of patents	0.96
length of development	0.79
factor 2: industrial performance (1.11, 28%)	
operating profit margin	0.86
annual growth rate	0.76

Exhibit E.1 COMPARISON OF THE CONTINGENCIES IN BIOMEDICAL RESEARCH UNITS IN UNIVERSITIES AND INSTITUTES, mean and (s.d.)

contingencies	universities		institutes n-17	F-value
	pre/paraclinical n=24	clinical n=16		
size				
research staff (fte)	10.7 (5.8)	12.8 (6.1)	11.3 (6.7)	0.57
total staff (fte)	18.0 (11.5)	23.5 (15.4)	19.5 (11.5)	0.96
project size (%)	53.0 (23.0)	63.0 (28.0)	32.0 (13.0)	6.60***
time-allocation				
research (%)	74 (14)	38 (7)	78 (5)	na
education (%)	17 (12)	13 (9)	6 (5)	na
management and acquisition (%)	8 (5)	8 (9)	14 (7)	na
clinical practice (%)	4 (6)	43 (11)	2 (4)	na
age				
research experience (years)	19.6 (5.0)	18.4 (2.7)	16.9 (5.2)	1.01
management experience (years)	11.4 (6.0)	10.3 (6.1)	13.4 (6.8)	1.34
technology				
technological support capacity (%)	39.0 (12.0)	36.0 (11.0)	41.0 (9.0)[1]	0.54
material resources (US$ 1,000 /fte researcher . year)	12.9 (11.8)	8.7 (7.6)	19.6 (7.3)[1]	1.91
power				
signatory authorization capacity (US$ 1,000)	8.6 (9.3)	4.5 (4.4)	5.7 (7.0)[1]	1.37
external funding (%)	36.0 (21.0)	43.0 (22.0)	36.6 (14.0)[1]	0.52
junior to senior scientist rate	1.55 (0.65)	0.94 (0.49)	1.17 (1.43)	1.34

*** $p < 0.01$; [1] n=5; na = not applicable

Exhibit E.2 COMPARISON OF MANAGEMENT CONTROL OF RESEARCH UNITS IN UNIVERSITIES AND INSTITUTES, mean and (s.d.)

management control[1]	universitities		institutes n-17	F-value
	pre/paraclinical n=24	clinical n=16		
system control				
effectiveness	2.40 (0.79)	2.59 (0.60)	3.27 (0.90)	6.87 ***
adequacy	2.57 (0.76)	2.41 (0.92)	3.04 (0.81)	2.70 *
administrative control	2.12 (0.79)	2.14 (0.98)	2.70 (0.87)	2.58 *
process control				
planning	3.53 (1.35)	3.72 (1.05)	4.00 (1.08)	0.69
frequency	4.43 (0.57)	4.14 (1.04)	4.62 (0.63)	1.81
attendancy mix	2.81 (0.44)	2.76 (0.41)	2.80 (0.65)	0.08
external control				
international communication[2]	2.74 (0.86)	2.27 (1.00)	2.97 (1.00)	2.39
contractor communication	3.02 (0.98)	2.61 (1.07)	2.55 (1.27)	1.18

[1] Likert 5-point scales, higher values indicate a more positive judgement

[2] number of presentations on international congresses: universities 2.87 (2.83) and institutes 1.45 (1.63) F=3.27*

* $p < 0.1$; *** $p < 0.01$

Exhibit E.3 COMPARISON OF EFFECTIVENESS OF RESEARCH UNITS IN UNIVERSITIES AND INSTITUTES, mean and (s.d.)

effectiveness	universitities		institutes n-17	F-value
	pre/paraclinical n=24	clinical n=16		
research effectiveness				
scientific publication / fte researcher . year	1.22 (0.71)	1.18 (0.44)	0.87 (0.43)	6.25 ***
PhDs / fte researcher . year	0.10 (0.07)	0.11 (0.09)	0.05 (0.05)	3.90 **
citation score (journal weighed)	1.08 (0.39)	1.16 (0.26)	1.26 (0.44)	1.30
citation score (weighed for discipline)	1.16 (0.55)	1.17 (0.39)	1.57 (0.73)	3.37 **
user effectiveness				
user publications / fte researcher . year	0.30 (0.21)	0.96 (0.38)	0.65 (0.42)	3.69 **
general effectiveness				
annual growth rate (%)	9.60 (1.00)	8.40 (4.30)	9.50 (1.10)[1]	0.63

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

[1] n=5

Exhibit F.1 THE SPEARMAN RANK CORRELATIONS OF THE CONTINGENCIES WITH EFFECTIVENESS IN PRECLINICAL AND PARA-CLINICAL UNITS COMPARED TO CLINICAL UNITS

contingencies	preclinical and paraclinical units				clinical units			
	effectiveness		citation score	growth rate	effectiveness		citation score	growth rate
	research n=24	user n=24	n=24	n=19	research n=16	user n=16	n=16	n=12
size								
research staff	-0.15	0.14	0.37*	0.52	-0.20	0.10	0.02	-0.41
project size	0.01	-0.39*	-0.42**	-0.29**	0.50*	0.55**	-0.03	0.13
time-allocation								
research	0.31	-0.36*	0.04	0.30	0.35	-0.37	-0.66**	0.62**
education	0.10	-0.05	0.03	-0.32	-0.51**	0.06	0.03	0.18
management and acquisition	0.09	0.04	0.17	-0.17	0.34	-0.41	-0.14	-0.24
clinical practice	-0.32	0.36*	-0.04	0.03	-0.12	0.43*	0.70***	-0.59**
organizational age								
research experience	-0.07	0.48**	0.13	-0.55**	0.09	0.25	0.24	-0.50*
management experience	-0.18	0.30	-0.04	-0.29	0.13	-0.05	-0.10	-0.48
technology								
technological support capacity[1]	0.12	-0.09	-0.17	-0.17	-0.28	-0.15	-0.49*	-0.29
material resources	-0.09	0.26	0.16	-0.04	-0.23	-0.54**	-0.33	0.35
power								
signatory authorization capacity	0.07	0.01	-0.11	-0.30	0.33	0.46*	0.30	-0.37
external funding	0.22	0.13	0.16	0.35	0.11	0.09	-0.32	0.11
junior to senior scientist rate	0.27	-0.26	0.15	0.10	0.29	-0.39	0.12	0.52*

Exhibit F.2 THE SPEARMAN RANK CORRELATIONS OF MANAGEMENT CONTROL WITH EFFECTIVENESS IN PRECLINICAL AND PARA-CLINICAL UNITS COMPARED TO CLINICAL UNITS

management control	preclinical and paraclinical units				clinical units			
	effectiveness		citation score	growth rate	effectiveness		citation score	growth rate
	research n=24	user n=24	n=24	n=19	research n=16	user n=16	n=16	n=12
system control								
effectiveness	0.36*	0.01	0.40*	0.38*	0.30	0.15	0.31	0.32
adequacy	-0.08	-0.25	-0.07	0.41*	0.63**	0.01	-0.54**	0.11
administrative control	0.22	0.12	0.16	0.11	0.27	0.17	0.13	0.16
process control								
planning	0.18	0.11	0.07	0.41*	0.10	0.10	-0.07	0.33
frequency	0.06	-0.21	-0.17	0.61***	0.33	-0.12	-.005	0.08
attendancy mix	0.14	0.49**	0.14	0.27	0.21	-0.38	0.24	0.22
external control								
international communication	0.24	0.26	0.37*	0.10	0.27	-0.45*	-0.32	0.51*
contractor communication	0.39**	0.05	0.33	0.16	0.17	-0.36	0.12	0.06

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$; 2-tailed significance

[1] the size of the research staff is significantly correlated with the technological support capacity in clinical units, r=0.71***

Exhibit F.3 THE SPEARMAN RANK CORRELATIONS OF THE CONTINGENCIES WITH EFFECTIVENESS IN UNIVERSITIES AND INSTITUTES

contingencies	universities				institutes			
	effectiveness		citation score	growth rate	effectiveness		citation score	growth rate
	research n=40	user n=40	n=40	n=31	research n=17	user n=17	n=17	n=5
size								
research staff	-0.21	0.14	0.23	0.18	-0.38	0.38	0.17	0.85
project size	0.14	-0.19	-0.30*	-0.16	0.50**	-0.39	-0.31	-0.32
time-allocation								
research	0.23	-0.45***	-0.20	0.32*	0.24	-0.17	-0.17	0.22
education	-0.15	-0.09	0.03	-0.16	-0.10	-0.18	-0.18	0.19
management and acquisition	0.21	-0.07	0.05	-0.16	-0.34	0.47*	0.43*	0.50
clinical practice	-0.13	0.47***	0.21	-0.12	nm	nm	nm	nm
age								
research experience	0.05	0.32**	0.17	-0.54***	-0.18	0.19	0.19	0.13
management experience	-0.06	0.24	-0.07	-0.33*	0.25	0.27	0.27	0.16
technology								
technological support capacity	-0.01	-0.13	-0.29*	-0.19	0.16	-0.07	0.30	0.07
material resources	-0.14	-0.08	-0.06	0.10	0.63[1]	-0.22[1]	0.81[1]	0.84
power								
signatory authorization capacity	0.10	0.21	0.02	-0.33*	-0.25	0.04	0.53**	0.13
external funding	0.21	0.11	-0.03	0.25	-0.08[1]	0.67[1]	0.25[1]	0.50
junior to senior scientist rate	0.05	-0.18	0.27*	0.35*	0.06	-0.25	-0.07	-0.07

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$; 2-tailed significance

[1] based on n=5

nm = not measured

Exhibit F.4 THE SPEARMAN RANK CORRELATIONS OF MANAGEMENT CONTROL WITH EFFECTIVENESS IN UNIVERSITIES AND INSTITUTES

management control	universities				institutes			
	effectiveness		citation score	growth rate	effectiveness		citation score	growth rate
	research n=40	user n=40	n=40	n=31	research n=17	user n=17	n=17	n=5
system control								
effectiveness	0.27*	0.07	0.35**	0.16	0.32	0.43*	0.41*	0.90*
adequacy	0.17	-0.18	-0.30*	0.31*	0.08	-0.25	-0.15	0.04
administrative control	0.21	-0.12	0.24	0.26	0.29	0.58**	0.21	0.84
process control								
planning	0.12	0.07	0.05	0.38**	0.04	0.28	0.29	0.84
frequency	0.14	-0.15	-0.13	0.41**	-0.23	0.38	0.01	0.40
attendancy mix	0.16	0.22	0.17	0.24	-0.20	0.26	0.15	0.56
external control								
international communication	0.24	-0.03	0.13	0.27	0.09	0.34	0.32	0.83
contractor communication	0.32**	0.13	0.22	0.14	0.16	0.76***	0.42*	0.46

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$; 2-tailed significance

Exhibit G.1 COMPARISON OF THE CONTINGENCIES IN THE DIFFERENT UNIVERSITIES AND INSTITUTES

contingencies	universities								institutes				
	1	2	3	4	5	6	7	8	1	2	3	4	5
size													
research staff			+	-	-	+	-		-	+	-	+	+
project size		+	+	+	+		+		-	-	-	-	-
time-allocation													
research		-			-		-						
education		+	+					+					
management and acquisition	+	+			-	+	-	-	+		-	-	+
clinical practice					+								
age													
research experience	+	+	+	-	+			-	-	-	-	+	
management experience	+		+	-	+	-	-	-	+			+	-
technology													
technological support capacity	+	+			-	-	-	-	+		+	+	-
power													
signatory authorization capacity		+	+	-	+	+		-	+	-	-		-
external funding	-			+	-	+	+	+	-	-		-	+

+ = the five organizations with the highest scores
- = the five organizations with the lowest scores

Exhibit G.2 COMPARISON OF MANAGEMENT CONTROL IN THE DIFFERENT UNIVERSITIES AND INSTITUTES

management control	universities								institutes				
	1	2	3	4	5	6	7	8	1	2	3	4	5
system control													
effectiveness		-	+	-	-	+	-	-	+		+	+	
adequacy	-			-	-	+		-	+	-	+	+	+
administrative control	-		+	+	-		-	-	+	+	+		-
process control													
planning	+	-			+	+	-	-	+		-	-	+
frequency	+	-	-	+			-	-	+	+		+	-
attendancy mix	+		-	+	+	-	+		-	-	-	+	
external control													
international communication	-	+	+		-		-	-	+	-	+	+	
contractor communication	-	-		+	+	+		+	-	-		-	+

\+ = the five organizations with the highest scores
\- = the five organizations with the lowest scores

Exhibit G.3 COMPARISON OF RESEARCH EFFECTIVENESS IN THE DIFFERENT UNIVERSITIES AND INSTITUTES

effectiveness	universities								institutes				
	1	2	3	4	5	6	7	8	1	2	3	4	5
research effectiveness													
international scientific publications		+	+			+	-	-	+	-	+	-	-
number of PhDs		-	+	+	+	+			-	-	+	-	-
recognition													
editorial boards	+	-	+	-		+		-		-	+	+	-
peer review		-	+		-		+	-	+	-	+	+	-
citation score													
citation score (weighed by journal)	+	-	-	-	-	-	+				+	+	+
citation score (discipline weighed)	-		-	-		-	+	-		+	+	+	+
user effectiveness													
national journals	-	-		+	+		+		-	-	+	-	+
physician journals		-	+	+			+	+	-	-	+	-	-
general effectiveness													
annual growth rate	+	-		+			-	+	-	-	-	+	+

+ = the five organizations with the highest scores
- = the five organizations with the lowest scores

Exhibit H.1 COMPARISON OF SIZE AND MANAGEMENT CONTROL WITH THE NUMBER OF PATENTS PER R&D INVESTMENT AND THE DEVELOPMENT LENGTH, group means and F-value

size and management control	patents / US$ 10 million		F-value	development length		F-value
	low	high		long	short	
size						
sales (US$ billion)	2.20	3.80	3.82 *	2.20	4.50	7.53 **
R&D-expenditure (US$ million)	342	537	3.48 *	315	635	10.92 ***
personnel control						
effectiveness	2.50	3.93	4.98 *	2.13	3.13	5.01 *
resources control						
adequacy	2.33	3.30	2.30	2.60	4.05	4.43 *
administrative control	3.40	2.91	0.40	2.33	3.59	2.48
process control						
planning	3.45	4.60	2.58	3.25	4.75	4.76 *
frequency	3.85	4.37	3.52 *	4.18	4.07	0.09
attendancy mix	4.33	4.50	0.08	2.12	3.28	5.56 **
external control						
international communication	3.85	4.00	0.05	3.85	4.00	0.04

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

low number of patents per US$ 10 million per year: < 5 (mean = 4.4, standard deviation = 1.5, $n_{size} = 8$, $n_{man.\ control} = 5$
high number of patents per US$ 10 million per year: > 7 (mean = 11.5, standard deviation = 2.7, $n_{size} = 6$, $n_{man.\ control} = 5$)
long duration of the development process: > 8 years (mean = 10.6, standard deviation 1.4, $n_{size} = 7$, $n_{man.\ control} = 5$)
short duration of the development process: ≤ 8 years (mean = 7.25, standard deviation = 0.96, $n_{size} = 7$, $n_{man.\ control} = 5$)

Exhibit H.2 COMPARISON OF SIZE AND MANAGEMENT CONTROL WITH OPERATING PROFIT MARGIN AND ANNUAL GROWTH RATE, group means and F-value

size and management control	operating profit margin		F-value	annual growth rate		F-value
	low	high		low	high	
size						
sales (US$ billion)	2.40	4.10	3.45	2.60	3.60	0.94
R&D expenditure (US$ 10 million)	377	570	2.33	361	553	2.27
personnel control						
effectiveness	2.33	3.87	6.13*	2.67	3.56	1.53
resources control						
adequacy	3.22	3.62	0.36	3.43	3.46	0.28
administrative control	2.42	3.67	1.90	2.87	3.56	0.68
process control						
planning	3.70	3.82	0.02	4.06	3.80	0.09
frequency	3.06	3.08	0.00	3.80	4.38	3.52*
attendancy mix	2.34	2.37	0.01	2.32	3.27	3.10
external control						
international communication	3.08	4.06	6.98*	3.80	4.06	0.13

* $p < 0.1$

low operating profit margin: < 17% (mean = 11.1%, standard deviation = 4.5%, $n_{size} = 6$, $n_{man.\ control} = 4$)
high operating profit margin: > 28% (mean = 31.9%, standard deviation = 2.9%, $n_{size} = 8$, $n_{man.\ control} = 6$)
low annual growth rate: < 10% per year (mean = 7.25%, standard deviation = 2.36, $n_{size} = 7$, $n_{man.\ control} = 5$)
short annual growth rate: > 12% per year (mean = 14.5%, standard deviation = 2.59, $n_{size} = 7$, $n_{man.\ control} = 5$)

Exhibit H.3 RADICAL STRATEGY COMPARED TO INCREMENTAL STRATEGY, median split of percentage discovery, mean and F-value

	innovative strategy		F-value
	radical n=5	incremental n=5	
size			
sales (US$ million)	2,635	3,420	0.7
R&D-expenditure (US$ million)	415	625	0.7
technology			
percentage discovery (%)	31.8	19.3	6.3**
percentage scientists (%)	34.2	20.3	4.8*
process control			
R&D process communication	2.8	3.7	5.0*
external control			
international communication	4.4	3.7	4.4*
industrial performance			
annual growth rate (%)	7.4	13.8	20.4***

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

comparison of size and the statistically significant management control and performance and effectiveness measures

Exhibit H.4 COMPARISON OF PURE PLAY PHARMACEUTICALS WITH PHARMACEUTICAL DIVISIONS OF CONGLOMERATES AND ANGLO-AMERICAN WITH CONTINENTAL EUROPEAN COMPANIES, mean and F-value

	pure play pharma-ceuticals	conglom-erate divisions	F-value		anglo american	continental european	F-value
size							
sales (US$ million)[1]	4,195	2,905	1.50		5,305	2,405	10.30 **
R&D-expenditure (US$ million)	610	445	1.50		705	392	7.30 **
personnel control							
career planning	4.33	2.30	15.10 ***		4.17	2.00	24.30 ***
reorganization	3.47	2.17	5.20 *		2.87	2.77	0.02
external control							
international communication	4.25	3.70	0.70		4.60	3.25	9.20 **
industrial performance and effectiveness							
operating profit margin (%)	32.3	17.8	6.50 *		31.90	13.60	36.70 ***
$n_{size,\ performance\ and\ effectiveness}$	7	7			6	8	
$n_{management\ control}$	5	5			4	6	

* $p < 0.1$; ** $p < 0.05$; *** $p < 0.01$

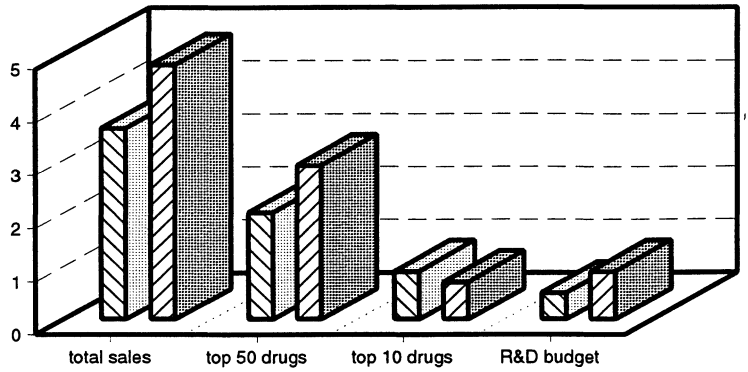
comparison of size and statistically significant management control and performance and effectiveness measures

[1] sales is significantly correlated with career planning (2.15 in small versus 4.04 in large companies, F-value 10.0**)

APPENDIX I

Base-line description of the industrial study sample

ETHICAL DRUGS SALES AND R&D BUDGET (US$ billions 1991)

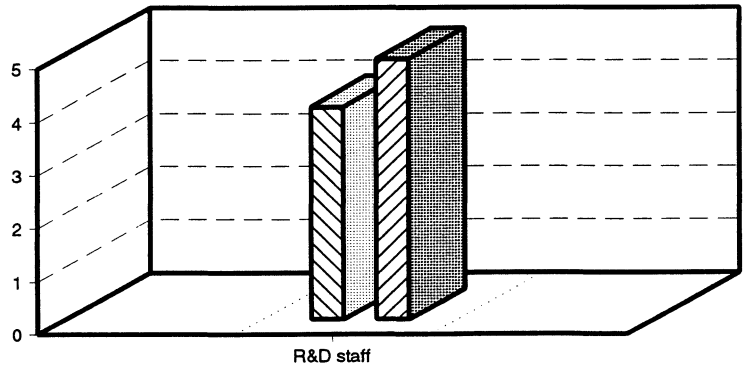


mean	3.6	2.0	0.9	0.5
your comp.	4.8	2.9	0.7	0.9
st. dev.	2.0	1.8	0.9	0.3

mean
your comp.

total sales = *total sales of ethical drugs world-wide, in 1991*
top 50 drugs = *the sales in the highest market segment, i.e. the top 50 drugs in 1991*
top 10 drugs = *idem, but now in the segment of the top 10 drugs in 1991*

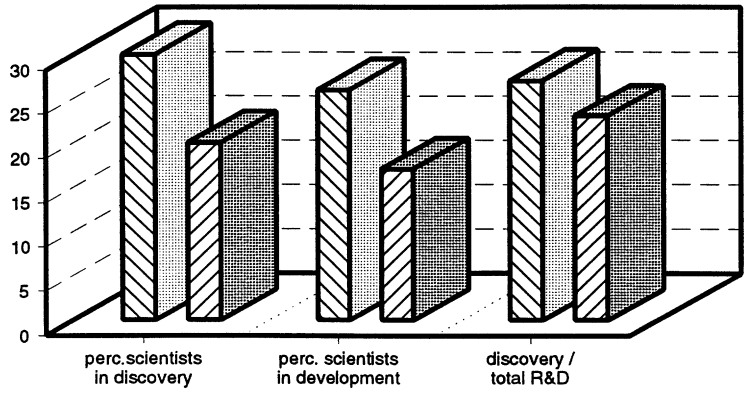
TOTAL R&D STAFF WORLD-WIDE (x thousand)



mean	4.0
your comp.	4.9
st. dev.	1.0

mean
your comp.

PERCENTAGE SCIENTISTS IN R&D AND PERCENTAGE DISCOVERY IN TOTAL R&D



mean	30%	26%	27%
your comp.	17%	17%	23%
st. dev.	11%	12%	9%

mean
your comp.

discovery / total R&D = percentage of the R&D budget which is spent on discovery

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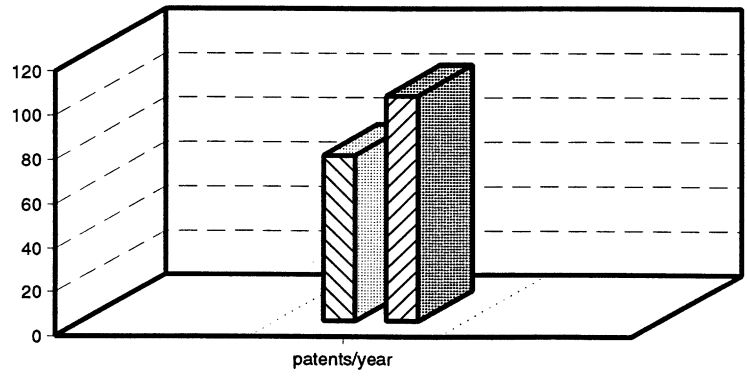
NUMBER OF PATENTS FOR NCEs (average 1986-1991)

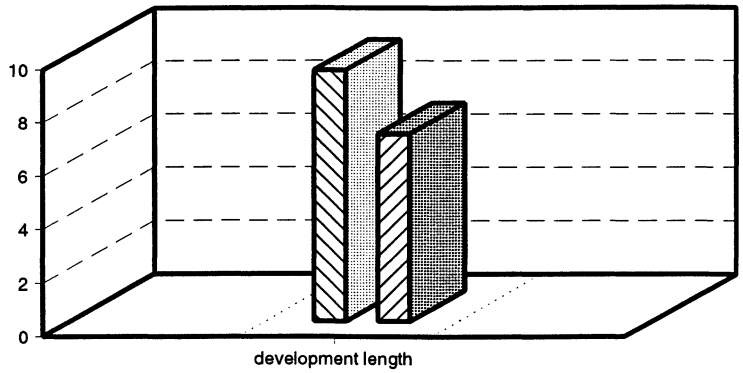


mean	75
your comp.	102
st. dev.	65

mean
your comp.

patents/year = annual number of patents for new chemical entities submitted world-wide between 1986 and 1991 (Derwent data base)

LENGTH OF PHARMACEUTICAL AND CLINICAL DEVELOPMENT (years)

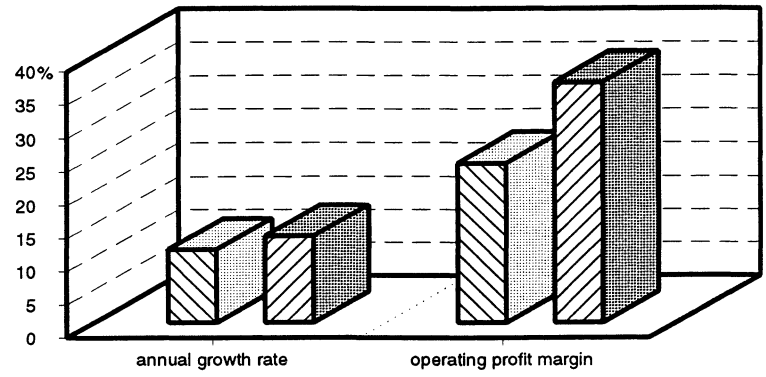


mean	9.4
your company	7.0
standard deviation	2.1

mean
your company

length of pharmaceutical and clinical development = the average development time of a new drug, not including drugs with a relatively short development time (such as antibiotics) nor with a relatively long development time (such as anti-psychotics)

ANNUAL GROWTH RATE AND OPERATING PROFIT MARGIN



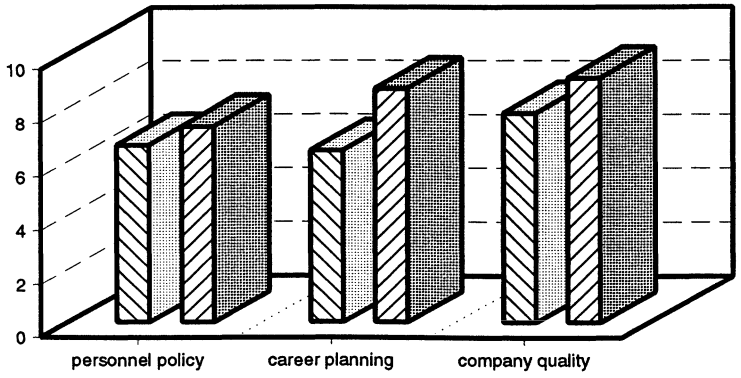
mean	11%	24%
your company	13%	36%
standard deviation	4%	11%

mean
your company

annual growth rate = annual growth rate of the company, both organic growth and growth by acquisition between 1986 and 1991

operating profit margin = pretax profit to turnover rate in 1991

PERSONNEL POLICY AND COMPANY QUALITY (max. score = 10)

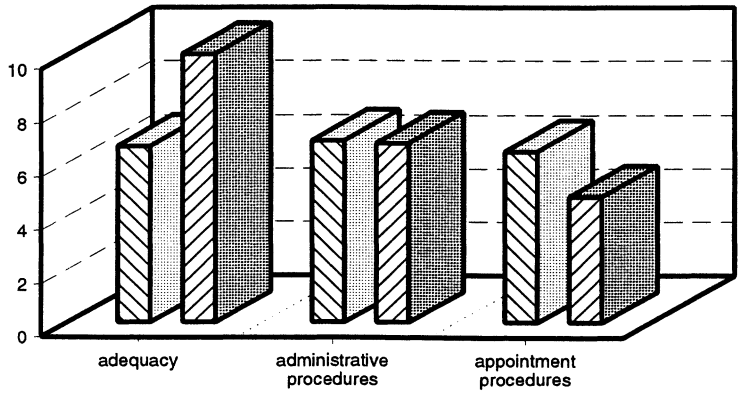


mean	6.6	6.4	7.8
your comp.	7.3	8.7	9.1
st. dev.	2.0	2.6	1.6

▨ mean
▨ your comp.

personnel policy and company quality = judgement on a 10-point scale of different aspects of personnel policy, i.e. opportunities for career planning and overall quality of the company in comparison to competitors (0 = very negative, 10 = very positive)

JUDGEMENT OF ADMINISTRATIVE PROCEDURES AND RESOURCES (max. score = 10)



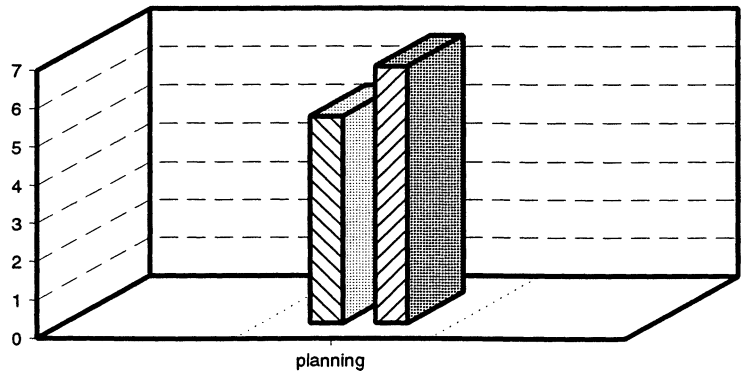
mean	6.6	6.8	6.4
your company	10.0	6.7	4.7
standard deviation	2.3	0.8	2.4

▨ mean
▨ your company

administrative andappointment procedures = the pace of administrative procedures regarding travelling, procurement of expensive equipment and the pace of appointment procedures

adequacy = the judgement of the adequacy of the personnel and material resources, and the technical level of the laboratory equipment

PLANNING (max. score = 10)



mean	5.4
your company	6.7
standard deviation	1.6

mean
your company

planning = the importance of short-term, middle-term, and long-term planning by higher management as a direction for the everyday research work

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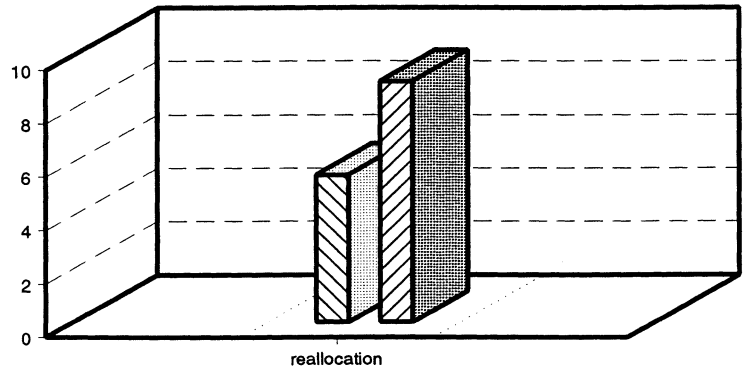
SPEED OF REALLOCATION (months)

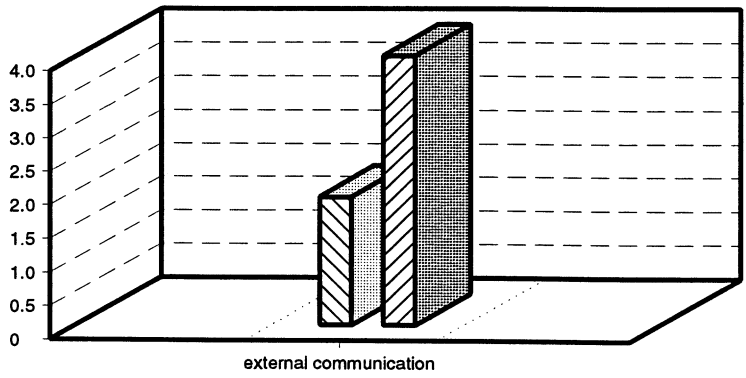


mean	5.5
your company	9.0
standard deviation	2.5

mean
your company

speed of reallocation = the speed of reallocation of a high percentage (> 20%) of the personnel and material resources of the laboratory to a new field of research (discovery only)

EXTERNAL COMMUNICATION (times per quarter)



mean	1.9
your company	4.0
standard deviation	1.8

mean
your company

external communication = rate of external communication with colleagues from other companies and with scientists and physicians at congresses and workshops

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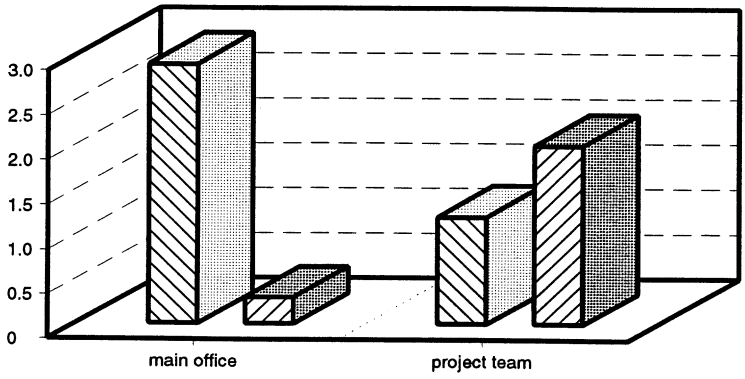
R&D PROCESS COMMUNICATION (times per month)

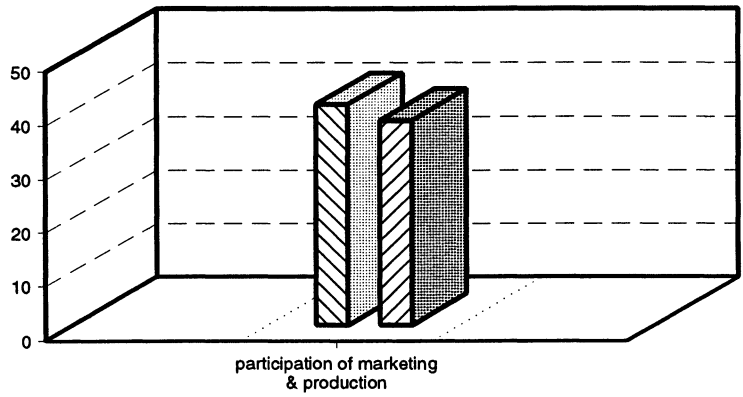


mean	2.9	1.2
your company	0.3	2.0
standard deviation	1.7	0.6

mean
your company

R&D process communication = number of contacts with the main office (times per month), discussing subjects regarding the R&D process, the number of project teams meetings and the level of lateral and cross-functional communication via electronic mail

MULTI-FUNCTIONAL COMPOSITION OF PROJECT TEAMS



mean	41%
your company	38%
standard deviation	11%

multi-functional composition of project teams = percentage of lateral and cross-functional composition of project team meetings; this is 100% if representatives of marketing and production are included in the project teams, together with scientists of different parts of the R&D process (discovery, pharmaceutical development, toxiology and clinical development)