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Management control, uncertainty, and performance in biomedical research in universities, institutes and companies

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Abstract

This paper surveys the relationships between management control, uncertainty and performance in biomedical research. It starts from the contextual variation, stemming from differences in objectives and goals, profit orientation and level and sources of uncertainty between universities, institutes and companies. The study consists of in-depth interviews and questionnaire surveys of R&D directors, institute directors, biomedical professors and their senior scientific staff. Confirming evidence has been found for the thesis, that a fundamental association exists between management control and performance, dividing high from low performers. Our results indicate that the difference in uncertainty between basic research, applied research and industrial R&D is not as high as generally assumed. It is not primarily the uncertainty of the research process itself, but the uncertainty in relation to the task environment that counts. Developmental research has gradually become more uncertain, because of the high costs of failure. Only the best pharmaceutical companies have adapted their control systems to this level of uncertainty. An incremental strategy seems more successful than a radical one in the short run. However, a company which puts too much emphasis on incrementation may find itself below the critical mass for keeping up the innovative potential in the long run. © 1997 Elsevier Science B.V.

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1. Introduction

In fundamental research especially, the traditional idea of creating excellency by bringing some brilliant people together, providing them with the best facilities, letting

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them work in a 'creative'—possibly remote—environment, waiting for the breakthroughs 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 as well. 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 necessary for success, but is it the only thing that matters? In fact, there is a general feeling that it is not. Many people working in the field of research management have experienced that just bringing some brilliant people together often ends up in an argument. All the 'How to manage, how to organize' literature starts from the underlying assumption that management control does make a difference between success and failure in research. However, up to now, only few studies are available to test this assumption at the empirical evidence.

A lot of academic papers have been published on different aspects of the management of research. A proportion of the literature covers the managerial aspects of industrial R&D (for a selected overview, see Tushman and Moore, 1988). These studies mainly concentrate at 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; Zeldenrust, 1989), on academic research management in general (e.g., Mason, 1979; Latour, 1987) and on individual laboratories (e.g., Latour and Woolgar, 1979; Knorr-Cetina, 1981). Gilley et al. (1986) and Birnbaum (1988) concentrate at individual leadership, and Spangenberg (1989) on management and culture in relation to performance. Concerning 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 at only one type of research organization. Up to now, only two large European surveys have been conducted that include universities, institutes and companies in the study population (Andrews, 1979; Franklin, 1988). However, in these studies, the large contextual variation between R&D-settings and technology fields (such as electronics, information technology and pharmaceutics), was disregarded.

This paper takes the contextual variation between different R&D-settings as the starting point of the research. The strata universities, institutes and industrial R&D were investigated because of their great contextual variation, in terms of objectives and goals, profit orientation and level and sources of uncertainty. The present study focuses at the following questions: Can management control (control exerted by the research management, the professors and their scientific staff in universities, and the department heads with their staff in institutes and company laboratories) enhance the performance of a research organization by mediating the level of uncertainty? And if so, 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 and its level and sources of uncertainty on this relationship? In order to answer these questions, a European survey of the main R&D laboratories of innovative pharmaceutical companies

has been conducted. This was combined with a comparative study of the Dutch biomedical research laboratories in Academic Hospitals, Medical Faculties and Large Health Research Institutes.

2. Theoretical framework and research hypotheses

2.1. Management control and performance

In management practice, control is often narrowly defined, embracing only monitoring and correcting, often used in financial terms to mean budget control. However, the concept of control used in the present study 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.

Modern definitions of performance, such as the one suggested by Kearney in Byrne and Markham (1991), are highly customer focused: using the combined resources of all the participants in the supply chain in the most efficient way to provide high quality, cost-effective customer service. This means that first, organizations must ensure they provide the customers with what they want (effectiveness, doing the right things, at the right time, with the right quality, etc...). Then, they should seek ways to improve the efficiency of doing so (doing the right things right). So, performance relates the output to the invested input and to the apparent use of the output by the customer. In this study the output of knowledge institutions (universities and institutes) is divided into output directed to the scientific community (research performance) and output directed to industrial and governmental contractors (user performance). In industry, performance is assessed at the research process level (innovative performance), and at the company level (industrial performance).

$$P = f(\mathrm{MC}) + \mu \tag{1}$$

where P = Performance, MC = Management Control, μ = residual variation.

Eq. (1) shows, in a mathematical form, the basic assumption that performance can be considered as a function of management control. The parameter μ reflects the residual variation, for instance caused by the omission of parameters influencing performance, the natural response variability in the study sample, and errors in the measurements as a result of the imperfect correspondence between concepts and operationalizations.

$$\mathrm{MC} = f(\mathrm{OF},\mathrm{CC}) + \mu_1 \tag{2}$$

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

According to Volberda (1992), management control can be considered to be a function of organizational flexibility and control capacity (see Eq. (2)). 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 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 Section 3.6, the operationalization of the different variables of management control will be discussed in more detail.

2.2. *Uncertainty*

Agreement on the conceptualization of uncertainty is still lacking (Allen, 1977; Withey et al., 1983; Daft, 1992). This study starts from the basic definition of uncertainty given by Galbraith (1973): "Uncertainty is the gap between the amount of information required to perform the task and the amount of information already possessed by the organization". This definition starts from the assumption that, in situations of high uncertainty there is lack of clarity about cause–effect relationships, lack of agreement among involved parties and it is difficult to identify appropriate sources of information to reduce uncertainty. To maintain equivalent levels of performance, managers of high uncertainty projects should, therefore, process more information than those of projects of low uncertainty (Tushman and Nadler, 1980).

Uncertainty may stem from three dimensions, in general—the environment, the technology or task, and the strategy and goals (De Leeuw, 1990). The first two dimensions are closely related to the third dimension. 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) were among the first to observe that organizations adapt to their tasks and environment, which may be more stable or more turbulent. Some organizations may live in a rather homogeneous and stable 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. Galbraith (1973) divides task uncertainty according to the different stages of transformation of the task, into uncertainty in task input (the number of input resources), conduct and outcome (diversity of output and level of goal difficulty).

Woodward (1965) found that the effectiveness of an organization depends on the 'goodness of fit' of the organizational structure and the technology used by the organization to transform inputs into outputs. It can differ in terms of complexity (the number of elements an organization must simultaneously deal with), 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).

Where clarity of project requirements is low, or constraints are confusing and variable, research managers are more likely to believe that the probability of success is comparatively low.

2.3. Uncertainty and context

Tushman (1979) found that task related and environmental uncertainty were positively associated with information processing activity, but only among high-performance R&D projects. Among low-performance projects, Tushman found no significant relationship between information processing activity and either source of uncertainty. Based on these findings, Tushman concluded that information processing moderate the normally negative uncertainty-performance relationship.

In short, to achieve equivalent levels of performance, laboratories facing turbulent or complex environments, using advanced technologies, and exhibiting extensive interdependencies require more information processing than do laboratories facing placid or simple environments, using routine technologies, and exhibiting minimal interdependencies (Galbraith, 1973; Tushman and Nadler, 1980; Daft, 1992).

But in contrast to this general view, more communication may not always be of value. The very act of linking with others may create uncertainty (Pfeffer and Salancik, 1978). Williamson (1981) suggests that opportunity costs and actual financial costs are associated with the time and energy required to nurture any linkage. Too much interaction and too much information may overload developers. The requisite amount of information transfer should, therefore, vary with respect to the innovational context (e.g., Allen, 1977).

The present paper takes the large contextual variation between the organizational settings of universities, institutes and companies as the starting point of the research. The study design is based on the concept of 'context-comparison'. If, for a certain phenomenon (management control) in one overall context (biomedical research) but in three different sub-contexts (the strata—universities, institutes and industrial R&D) consistent relationships with outcome are found, this phenomenon is considered fundamental for these relationships and may, therefore, be generalized to related contexts in other technology fields.

2.4. Sources of contextual differentiation

Three main sources of contextual differentiation are distinguished in this study. There are differences originating from the objectives and goals, the profit orientation and the level and sources of uncertainty. In the following paragraphs these sources of differentiation and their expected influence on the relative strength of management control in the three strata will be discussed.

2.5. Objectives and goals

In order to provide for standardized measures, the Organization for Economic Cooperation and Development (OECD, 1980) issued the *Frascati Manual*, in which

generally accepted definitions for science and technology are given. In the *Frascati Manual*, research and experimental development is defined as follows: 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 breaks the term research and experimental development into three parts by distinguishing between basic research, applied research and experimental development. Basic (fundamental) research is defined as 'experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts without any particular application or use in view'. The day-to-day practice of basic research 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 defined as 'original investigation undertaken in order to acquire new knowledge directed primarily towards a specific practical area or objective'. 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. Whereas basic and applied research concentrate at 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, finally, is 'systematic work drawing on existing knowledge gained from research or practical experience directed towards producing new materials, products and devices, to installing new processes, systems and services and towards substantially improving those already produced and installed'.

Although universities, institutes and companies all span activities covering basic research to 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 industrial laboratories is to perform R&D. [1] It is more accurate say that the main objective of universities is to produce and disseminate scientific and technical knowl-

[1] That this also applies for the US show the figures of the division of basic research over universities, institutes and industrial laboratories. In 1993, universities, colleges, and national research centres in universities account for about two-third, whereas institutes and industry each account for about one-sixth of the total basic research conducted in the US (National Science Board, cited in Leonard-Barton, 1995).

edge. This objective is met by doing basic 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. 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, contributes more to the advancement of his discipline than his colleague who writes a paper for a scientific journal. Patients are also more interested in the medical skills of the physician than in his scientific prestige. The reader should keep in mind that a department which performs poorly in research might well be leading in surgery or education. 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 an industrial R&D laboratory 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.

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

H1A: Robust and similar positive relationships across the strata with those performance measures which reflect the primary goals and objectives of the organization.

H1B: Weak and different relationships across the strata with those performance measures which reflect secondary goals and objectives of the organization.

2.6. *Profit orientation*

The present study includes profit, not-for-profit and non-profit organizations. At the profit side, we find the industrial laboratories and at the non-profit side, we find the university departments. In between are the not-for-profit institute laboratories. 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). In recent years the, boundaries between profit and non-profit organizations have shifted gradually. Budget retrenchments have pushed university and institute departments into contract research for industrial and governmental contractors. For a good understanding of the Dutch situation, it must be remembered that the large variation in quality, funding and orientation of knowledge institutions, which can be found in the USA, does not exist in the Netherlands. All Dutch universities and part of the institutes are publicly financed, operate under the same conditions, and have, within boundaries, the same access to funding. They are 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. 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. 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.

The accountability, the relationship between objectives and performance, is most clear in profit organizations. As Besse (1973) 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 laboratories 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.

H2: The assessment of system control will be most positive in industry, and least positive in universities, with the institutes taking up an intermediate position.

2.7. Level and sources of uncertainty

The level of uncertainty is generally assumed to decrease as activities pass through the sequence basic research, applied research and experimental development (Cohen and March, 1974; Weick, 1979; Spangenberg, 1989; Zeldenrust, 1989). Activities in basic research are thought to be rather uncertain in the sense that task outcomes are not repetitive and predictable. Therefore, scientific research is generally said to be conducted in a sea of unforseen contingencies. To lower the level of 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 laboratories 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).

H3: The level of research process communication and international communication

will be highest in universities and lowest in industrial laboratories, with institutes taking up an intermediate position.

2.8. Uncertainty differences in industry

According to literature, industry differences in the level of uncertainty may be encountered dependent on the phase of the R&D process (i.e., drug discovery vs. pharmaceutical and clinical development) and the R&D strategy chosen by the company (radical vs. an incremental strategy). In the following two paragraphs, these possible sources of uncertainty will be discussed in more detail.

2.9. Comparison of discovery and development

Although the use of new techniques (such as computer added drug design and high capacity screening) has made the searching for NCEs less fortuitous, the research activities in the drug discovery phase are still highly unpredictable. The scientific staff may try to reduce 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. Gambardella (1992) concludes, based on 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". This leads to the following hypothesis:

H4: High performing discovery departments will show a higher level of research process communication and international communication than low performers.

Mainstream literature on the subject suggests that uncertainty is greatest during the early phases of the R&D process, and should decrease towards full development. The R&D process starts with broadly defined goals and objectives that become narrowed and focused as the project progresses. Therefore, the largest number of knowledge gapsx are likely to exist early in the R&D process. In contrast to this dominant view, Gales et al. (1992) suggest that the impact of uncertainty will not decrease but will increase as R&D projects progress. In early innovation stages, uncertainty may be high but it is often not problematic, because you may stop an unsuccessful project with only limited loss of R&D resources. As projects progress into development, consequences of continued unresolved uncertainty rise, because of higher sunk costs and growing constraints (March and Shapira, 1987; Steele, 1989). For instance, huge amounts of R&D-investments may be lost if unexpected negative side-effects are encountered in clinical development. In a study of 44 innovation projects, Gales and Mansour-Cole (1995) found that involvement of users increased from idea generation to commercialization. It is, therefore, expected that intensive cross-functional communication with marketing and production and international communication is essential to improve the

time-to-market. The primary goal of international communication 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 the new product.

Most research activities in pharmaceutical and clinical development are of a more repetitive and predictable nature compared to the discovery phase, and can be planned according to strict schedules. It is, therefore, expected that in the most successful development departments the scientific staff is more committed to the necessities of planning and will react more positively to planning directives by higher management. This leads to the following hypothesis:

H5: 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 will be higher, and (3) the international communication will be more frequent.

2.10. Radical vs. incremental orientation

The amount and the advancement of technology a company needs also depends on the orientation of the company (Roussel et al., 1991). A company conducting a radical strategy emphasizes discovery, whereas a company conducting an incremental strategy is primarily directed towards speeding-up development in order to introduce drugs with small improvements on a regular basis (Taggart, 1993). The importance of such incremental improvements is sometimes neglected. For example, whether a drug has to be injected or can be taken orally can make a large difference to the patients concerned. As Gross (1983) 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".

Radical innovation projects may lack standardization and information may not be readily available. These projects are expected to require more extensive information processing than incremental projects which rely on standard procedures and readily available information (e.g., Steele, 1989). More radical oriented pharmaceutical companies are therefore expected to put considerable effort into gathering innovative ideas, and implementing joint research projects with universities, institutes or biotechnological or other pharmaceutical companies.

H6: 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.

3. Research design and measures

3.1. Study domain

Biomedical research has been chosen as the domain of the study, because in the three strata a large study population is available; it provides a good example of research in an

applicational context and ethical (prescription) drug pharmaceutics is the most technology driven of all industries. A study of Capron (1994), including 135 companies in the chemical, (tele)communication, computer and aviation industries, under which 22 branded ethical drug firms, revealed the pharmaceutical industry as one of the most technology driven. In pharmaceutical industry, even more than in other high-tech industries, the competitive power is based on the innovative capacity.

Biomedical research is defined as concerned with medical biological studies, for instance into cell and tissue cultures and animals (RAWB, 1983). 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. The pharmaceutical R&D-process takes a decade in general, and is carried out in a number of laboratories located in different countries. It includes the laborious searching for NCE's (New Chemical Entities with assumed therapeutic efficacy) in drug discovery, drug targeting and toxicology testing in pharmaceutical development and the succeeding clinical testing on healthy volunteers and patients (Omta, 1995).

3.2. Sample

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 pharmaceutical 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. Twenty large and innovative pharmaceutical companies were approached for this study. The companies were selected at the basis of their (world-wide and European) sales volume of ethical drugs, and their innovative capacity, measured by the number of R&D-staff and the number of patents submitted with an European priority. In order to prevent a selection bias based on the use of only quantitative data, 14 leading Dutch clinicians in universities and health research institutes were asked to name the most innovative drugs introduced to their specific therapeutic areas. The information obtained in this inquiry generally supported the quantitative selection. Only one company was added on the basis of the qualitative judgment.

Fourteen companies agreed to participate, including the company selected on qualitative grounds (a response rate of 70%). They have large discovery and/or development laboratories in Great Britain, Germany, France, Belgium or the Netherlands. Ten 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. Nine companies are among the top 20 companies ranked according to world-wide branded ethical drug sales. The other five are top 50 pharmaceutical companies. Patent analysis revealed that 3874 licensees submitted pharmaceutical patents to the European authorities in the five years preceding the study. The strong innovative capacity was illustrated by the fact that the 14 companies together submitted 25% of all the pharmaceutical patents in this period.

There are 13 universities in the Netherlands. In these universities, the scientific staff spends in total nearly 14,000 full-time equivalents (ftes) on research. A substantial

portion of this research, more than 3000 ftes, is carried out on medical research. In this study, only the eight universities in which biomedical research is carried out are analyzed. The chaired professors of all 82 Dutch biomedical laboratories and 20 biomedical laboratories of five large health research institutes were invited to participate in the study. Two institutes are closely linked to universities (para-university institutes), with annual budgets of US$2.5 and 3 million. 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. Three medical institutes are analyzed, with research budgets of US$12, 22 and 30 million (RGO, 1994).

3.3. Instruments of data collection

The study consisted of two parts. In the first part, in each pharmaceutical company, structured interviews were held with one or two of the Directors of the Research, Development and Clinical Research Divisions (mostly members of the Board) about research management in general. In addition, one or two of the Directors of the Health Research Institutes and a selected sample of experienced professors were interviewed. To avoid misinterpretation, the interviews were taped and the protocols were sent to the interviewees for approval.

Two standardized survey questionnaires, consisting of 126 precoded questions were sent to the research staff of the participating laboratories (Research Questionnaires, ReQuest 1 and 2, see Appendix B for an excerpt of the questions). Before the data collection started the questionnaires were tested on a sample of 12 biomedical researchers from the Faculty of Science, and four retired staff members of pharmaceutical and chemical industry. Their comments were incorporated into the questionnaires. In order to ensure uniform interpretation, definitions of the variables were included in the questionnaires. ReQuest 1 consists 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 (annual reports, bibliometric measures) did not correspond with the answers on ReQuest 1, this was checked by the research management concerned. In institutes, for each laboratory a ReQuest 1 was filled out at the institute level. In universities one respondent per laboratory filled out ReQuest 1 (mostly by the chaired professor). Because only a few questions in ReQuest 1 regard the company situation, these were included in the structured interviews (see Appendix A).

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 laboratories and their senior scientific staff in universities and institutes and 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 were used, and a limited number of items were assessed with 2 and 3-point response formats.

3.4. Data collection

Twenty-two R&D directors, nine institute directors and 16 chaired professors were interviewed. Ten companies agreed to distribute research questionnaires to the heads of the different R&D laboratories. Fifty-nine questionnaires were distributed, of which 38 were returned (three to four questionnaires per company laboratory, a response rate of 64%).

Questionnaires were sent to the 47 chaired biomedical professors, who had accepted the invitation, and their 218 senior scientific staff members. The professors returned 44 questionnaires (a response rate of 58% of the eligible population of 76, because six professors were abroad at the time of the study) and the senior scientific staff returned 105 questionnaires (a response rate of 52% of the eligible population of 202). Seven questionnaires could not be used, so 142 questionnaires stemming from 40 biomedical laboratories could be analyzed, i.e., three to four questionnaires per laboratory. In institutes, questionnaires were sent to the 20 laboratory heads and 52 to their senior scientific staff. Seventeen questionnaires were returned by the laboratory heads (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 the laboratory feels more obliged to participate, because of the commitment of the institute directorate to the study.

3.5. Research measures

3.5.1. Management control

Management control is divided into system, process and external control. System control refers to the control over the personnel and material resources of the laboratory. 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 (Badawy, 1988; 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 laboratory resources. It refers to the subjective assessment by the scientific staff of the adequacy of personnel and material resources, laboratory equipment, devices and space to conduct the goals and objectives of the laboratory. 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. The assessment of the importance of strategic, tactical and operational planning by the top management for day-to-day research relates to the goal setting/accounting relationship between the research management and the top management. 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 laboratory, 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).

External control refers to the position of the laboratory in the international scientific network and for knowledge institutions also to the network with industrial and governmental contractors. 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 (see Table 1).

3.5.2. Performance

3.5.2.1. Publication count. The performance of the university and institute laboratories was measured by the Centre for Science and Technology Studies (CWTS) in Leiden. For a thorough description of the methodology used, 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 laboratories 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 the laboratory 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 laboratory was a (co-)author, which were published in international scientific journalswhich were entered in the Science Citation Index, the Social Science Citation Index or the Arts and the Humanities Citation Index.

The number of publications found in the ISI database was on average 20% lower than

the report of the research management concerned. 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 laboratories 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 to notice that an output measure, which

Table 1
Operationalization of management control

System control

Personnel control (12 items)

Subjective assessment of the performance of personnel policy {3 and 5-point response formats, higher values indicate a more positive assessment, for instance: How much emphasis is laid on career planning in your organization? No emphasis at all (1-2-3-4-5) Very much emphasis} regarding:
- Pace and manner in which reorganizations are executed.
- Cases concerning appointment, promotion and dismissal.

Material incentives:
- Primary and secondary working conditions, for instance average salary level in comparison to management functions and competitors.
- Stocks, options and use of company car etc.
- Extra payment for extraordinary research efforts.

Immaterial incentives:
- Career planning and training facilities.
- Good reputation of the organization.
- Career possibilities in the organization or as a step-up towards other organizations.
- Recognition, e.g., possibilities for scientific publishing and presentation, or a dual ladder system and fellowships.

Adequacy (Resources control, 4 items)

Subjective assessment of the adequacy {5-point response formats, for instance: How long would it take to reallocate a larger part (e.g., 20%) of the personnel and material means to a new field of research? (1) (less than) one month; (2) 1 to 3 months; (3) 3 to 6 months; (4) 6 to 12 months; (5) (more than) a year} of:
- Personnel and material resources.
- Advanced laboratory equipment, devices and space.

Administrative control (Resources control, 4 items)

Subjective assessment of the speed of the administrative procedures (5-point response formats, 1 = (more than) a year; 5 = (less than) a month}:
- Appointment and procurement of equipment (US$50,000).
- Reallocation of a larger part (20%) of the personnel and material resources to a new research field or therapeutic area.

Process control

Planning (3 items)

Subjective assessment of the importance of short and middle range planning by higher management on the every day research work {5-point response formats, for instance: the annual research plan drawn up by the laboratory directorate serves as an important guideline for the planning and monitoring of the research group program. Disagree entirely (1-2-3-4-5) Agree entirely}.

Frequency (Research process communication, 1 item)

Frequency of research meetings {5-point response format: 1 = (less than) once in six months; 5 = (more than) once a week}.

Table 1 (continued)

Attendancy mix (Research process communication, 4 items)
General attendancy of research meetings: only researchers of the own R&D-phase or also staff members of other R&D-phases and/or marketing and production (5-point response formats, higher values indicate a higher level of lateral and cross-functional communication).
External control
International communication (3 items)
Frequency of international contacts with scientists and physicians and colleagues of other companies, for instance on congresses and workshops {5-point response format, 1 = (less than) once a year; 5 = (more than) once a month}.
Contractor Communication (2 items)
Frequency of contacts with industrial and governmental contractors.

plays such an important role in Dutch research policy, is treated so casually by some of the laboratory heads.

3.5.2.2. 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 chemical compounds (NCEs) with first priority date submitted world-wide 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 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 whose CAS number indicated that they were new at the time of patenting were selected.

A notable problem in patent statistics 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 order to check for this, the research management was asked for their patent strategy.

3.5.2.3. Length of development. 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

Table 2
Operationalization of performance

Research performance (universities and institutes) The average number of papers published annually by scientists of the laboratory, in international scientific journals per scientist.
User performance (universities and institutes) The average number of reports published annually per scientist of the laboratory for industrial or governmental contractors.
Number of patents (industry: innovative performance) The average annual number of patents for New Chemical Compounds, submitted world wide with first priority date per US$ 10 million R&D-expenditures in discovery.
Length of development (industry: innovative performance) The average time span between patenting of the lead compound and the launch of the registered drug on the prescription drug market (years^{-1}).
Operating profit margin (industry: industrial performance) Operating result/revenues. Operating result: result 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.

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 length of the developmental process. The finding of an NCE precedes patent submission; therefore, the time-span between patent submission and launch will always be shorter. For the operationalization of the different performance indicators, the reader is referred to Table 2.

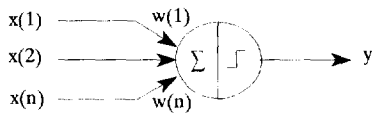
3.6. Data analysis

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 modelling. 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 one-way ANOVA. Non-parametric analysis of group means, using the Kruskal–Wallis test, did not alter the conclusions. The multivariate associations acquired by 4Thought, a multilayer feedforward neural network, are presented. Neural models are based on pattern recognition and are therefore essentially non-parametric. This enables the multi-variate comparison of variables operationalized at different measurement levels (see Kappert and Omta, 1997 and the box for a more detailed description of neural modelling).

Box

Neural networks are based upon the functioning of the human brain. The basic element is the artificial neuron (called node), which can be considered a functional abstraction of the biological neuron. The human central nervous system consists of more than 100 billion of interconnected neurons. The information of one neuron is passed though to thousands of others. Learning in the human brain consists of the continuous readjusting of the synaptic strength, the relative strength of the signals send between the different neurons.

Typically, an artificial neural network consists of three or four layers of nodes, working in parallel, an input layer, one or two hidden layer(s) and an output layer.



Adding more than two hidden layers to the neural network architecture gives no advantage, in general. The network uses the input (independent) variables to build a model of the output (dependent) variable(s) (White, 1990 and Anderson, 1995). In a feedforward network, such as 4-Thought, the information flows in one direction, only. In a recurrent network, also connections within one layer and with the nodes in the preceding layers of the network, occur. Inside a node the weighted (w_{i-n}) input signals (x_{i-n}) are summed (Σ), and a 'learning' algorithm is used to calculate the node's output signal (y) to the next layer (in 4-Thought an exponential sum formula based upon series expansion, Hoptroff et al., 1991). The actual 'training' process consists of continuously readjusting the synaptic strengths, the relative weights of the connections between the nodes in the various layers.

Neural modelling can lead to 'overfitting'. An 'overfit' model ignores the natural variability (the 'noise') in the data. It performs well within the boundaries of the existing dataset, but produces nonsensical generalizations over new data. With a procedure called 'parallel cross-validation', this risk can be reduced. To this, the dataset is split into a 'training' set and a 'test' set. In 4-Thought the training set consists of 80% and the test set of the remaining 20% of the data. The 'training' 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 again, while the error in the training set continues to fall. At this point, the resulting model is presented.

A neural network provides powerful analytic capabilities. Firstly, it can cope with multi-collinearity. By combining inputs in a specific node, covariation can be modelled and analyzed. Secondly, neural modelling provides a nonparametric approach to multivariate data analysis, because it is based upon pattern recognition. It is not surprising, therefore, that neural networks are used in quite different areas such as: design support, process management, (medical) diagnostics, marketing (data base mining), speech and visual memory and predicting of exchange rates, prices of shares and options.

The α of Cronbach (1970) was calculated for the individual subscales in order to find out whether they correspond with the variables defined, and to check the internal consistency of the items, which are supposed to measure a single concept. Table 3 shows that in all cases Cronbach's α is sufficiently high (> 0.62) to warrant confidence in the internal consistency of the scales (Van de Ven and Ferry, 1980). It must be remarked that contractor communication and international communication can be considered as one variable in knowledge institutions. Apparently, universty and institute laboratories, which have much contacts with contractors, put more effort in contacts

Table 3
Internal consistency of the variables of management control (Cronbach's α)

Management control	Number of items	Universities $n = 142$	Institutes $n = 44$	Companies $n = 38$
System Control				
Personnel control	12	0.77	0.87	0.85
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
Frequency	1	–	–	–
Attendancy mix	3	0.69	0.63	0.79
External Control				
External Communication	5/3[a]	0.63	0.68	0.79

[a]International and contractor communication in knowledge institutions and international communication in industry.

with the outside scientific world, as well. For clarity reasons, the two variables are treated separately in the results.

4. Results

4.1. Descriptive statistics

Table 4 shows that the average sales volume of branded ethical drugs amounted to US$3.4 billion, with an 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. About 25% of the total R&D-expenditures was spent on discovery, which resulted in about five patents per US$10 million annually. The development phase has a long duration. It took the companies on average more than nine years to bring an NCE to the market.

Table 5 shows that about 20 staff members work in a university or institute laboratory. The running costs in biomedical research, being part of 'big science'

Table 4
Descriptive statistics of pharmaceutical companies ($n = 14$)

	Mean	Standard deviation
Annual sales of ethical drugs (US$ million)	3372	1913
R&D-expenditures (US$ million)	540	248
- Discovery (US$ million)	126	70
- Development (US$ million)	390	209
Number of patents (per US$10 million)	5.3	2.6
Length of development (years)	9.3	2.1
Operating profit margin (%)	23.6	11.2

Table 5
Descriptive statistics of laboratories in universities ($n = 40$) and institutes ($n = 17$; mean and F-value)

	Universities	Institutes	F-value
Staff (fte)	19.9	19.5	0.01
Material resources (US$/fte)	11,330	19,630	2.53
External funding (%)	39	37	0.14
Research performance (sc. papers/fte)	1.22	0.87	6.25***
User performance (reports/fte)	0.30	0.65	3.37**

$F_{\text{oneway anova}}$ ** $p < 0.05$, *** $p < 0.01$.

(Spiegel-Rösing and De Solla Price, 1977), are rather high. The material costs per researcher amount from more than US$10,000 in universities to nearly US$20,000 in institutes. The percentage external funding of the research laboratories in this study doubled in the preceding five years from around 20% to nearly 40%. It has often been argued that if more than one-third of the resources of a laboratory stems from external funding the (programmatic) continuity would be at risk. For most of the laboratories, this is already the normal situation. As expected, the research performance is higher in universities, whereas the user performance is twice as high in institutes. The scientists publish (and supervise) more than one scientific paper per year. Calculated per PhD student, this is approximately 2–2.5 papers.

4.2. Comparison of the strata

Table 6 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 performance of personnel policy than their colleagues in universities and institutes. Although large differences could be established between

Table 6
A comparison of management control in universities, institutes and pharmaceutical companies (mean and F-value)

Management control	Universities $n = 142$	Institutes $n = 44$	Companies $n = 38$	F-value
System Control				
Personnel control	2.52	3.09	3.33	6.96***
Adequacy	2.54	2.89	3.56	3.65**
Administrative control	2.00	2.41	3.48	8.96***
Process Control				
Planning	3.62	3.64	3.78	0.06
Frequency	4.25	4.49	3.07	10.50***
Attendancy Mix	2.81	2.80	2.37	3.37**
External Control				
International Communication	2.54	3.06	3.46	3.64**
Contractor Communication	2.84	2.59	na	0.09

na = not applicable; $F_{\text{oneway anova}}$ ** $p < 0.05$, *** $p < 0.01$.

scientists in the different companies, their average judgement of renumeration, career possibilities and recognition was clearly more positive. In universities especially, the average assessment of the personnel policy situation and the adequacy of resources is judged negatively (the average assessment is below three on the Likert 5-point scale).

The other variables of system control, adequacy of resources and administrative control, are judged more positively in companies, as well. The estimated pace of the administrative procedures is nearly twice as high than in universities. The monitoring of the scientific network is also more intensive and the participation in international conferences is significantly higher. The researchers in institutes take up an intermediate position between universities and companies on all the variables of system and external control. In contrast to this, 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.

4.3. Performance

Table 7 shows the multivariate associations of management control and performance. Concerning universities and institutes, the best models are found for research perfor-

Table 7
Percentage explained variance of performance by management control

	Universities		Institutes		Companies		
	res. perf. %	user perf. %	res. perf. %	user perf. %	pat. nr. %	dev. l. %	op. pr. m. %
System Control							
Personnel control	10	–	13	22	32	9	30
Adequacy	–	–	–	–	–	–	–
Administrative control	8	–	–	16	–	–	19
Process Control							
Planning	–	–	–	–	–	4	–
Frequency	–	–	–	–	25	–	–
Attendancy mix	–	–	–	–	–	10	–
External Control							
International communication	4	–	–	11	–	–	18
Contractor communication	15	–	–	14	na	na	na
Total	37	–	13	63	57	23	67
Training set	38	–	23	65	59	22	66
Test set	28	–	6	52	44	30	68

res. perf. = research performance.
user perf. = user performance.
pat. nr. = patent number.
dev. l. = development length.
op. pr. m. = operating profit margin.
– variable does not associate significantly with the performance indicator at issue.
na = not applicable.

mance in universities and user performance in institutes, with a total explained variance of 37% and 63%, and comparable test set fits of 28 and 52%, respectively. In both cases personnel control, administrative control and international communication count for the total of the explained variance. No model was found for user performance in universities and a very weak one for research performance in institutes with a total explained variance of 13% and a test set fit of only 6%. It is interesting to notice that the same three variables of management control also explain (in strictly statistical sense) most of the variance of the industrial performance measure, the operating profit margin. The fact that process control does not add explained variance to all the performance measures in universities and institutes and to the industrial performance measure in industry, is also worth mentioning. The neural network models of the innovative performance indicators show that the frequency of project team meetings is higher in the case of high performance in the discovery phase. A short development phase is positively associated with the adequacy of resources, the importance of short-term, middle-term and long-term planning and the attendancy mix, indicating a high level of lateral and cross-functional communication.

4.3.1. Radical vs. incremental orientation

Table 8 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% 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 NCEs for further

Table 8
Radical strategy compared to incremental strategy (median split of percentage discovery). Comparison of size and the statistically significant management control and performance measures (mean and *F*-values)

	Radical	Incremental	*F*-value
Size			
Sales (US$ million)	2635	3420	0.7
R&D-expenditures (US$ million)	415	625	0.7
Structure			
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			
Growth rate (%)	7.4	13.8	20.4***

Statistically significant: $^{*}p < 0.1$; $^{**}p < 0.05$; $^{***}p < 0.01$.

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 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 grew nearly twice as fast than those conducting a more radical strategy.

5. Discussion and implications

5.1. High vs. Low performers

Table 7 shows that personnel control, administrative control, and external control associate strongly with research performance in universities and user performance in institutes. Management control is not, or only weakly, associated with user performance in universities and research performance in institutes. Together, these results provide confirming evidence for *H1*. Robust and similar associations are found between management control and those performance measures which reflect the primary goals and objectives of the research organization, which are conducting basic research in universities and applied research in institutes (*H1A*). While weak and different associations are found with the performance measures which reflect the secondary management goals and objectives (*H1B*).

Interestingly, personnel control, administrative control and external control separate the above-average from the below-average performers for the indicator for industrial performance, the operating profit margin. In the companies with the greatest 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. 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, as well. However, because of the large size of the companies at issue it may be expected that spending budgets will not be so much of a bottleneck for procurement, appointment and international travelling. Possibly, the operating profits not only reflect 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.

The most important management control variable turned out to be personnel control, which explains part of the variance of all of the performance indicators, except user performance, reflecting a secondary management goal of universities. The best universities, institutes and companies use career systems which lead to an inspiring work environment. Several research directors of low-performance laboratories registered loss of commitment of their R&D staff (*A Nine to Five Mentality*). They indicated, that lack of career opportunities 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, was only used on a wider scale in the better companies. These companies also provide more opportunities for attaining recognition. They stimulate publishing, give visible rewards, such as fellowships, and bring their staff in contact with professional networks, for instance, via a company-wide professional society dealing with technical issues, including both corporate and professional peers. This is a clear confirmation for the central thesis in socio-dynamic literature that stimulating and rewarding environments, which enhance the motivation of the scientific personnel, are needed for high performance.

Another interesting observation derived from Table 7 is that process control is relatively unimportant in discriminating between high and low performers in universities and institutes and to the operating profit margin in industry. For the latter parameter, this is not astonishing. The operating profits of a pharmaceutical company can depend on only one or two major products, but also on a variety of products. Thus a direct relationship between profit performance and R&D process organization is very unlikely. For universities and institutes, one can say, that although large differences were established in the way and manner in which research is supervised, these differences were not found in the neural network analysis. 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) may lead to high performance, provided that the fundamental requirements of system and external control are met.

5.2. Profit orientation

Table 6 shows great differences in the average assessment of the factors of management control across the three strata. In most cases the laboratories in universities are found at one end of the scale and the industrial laboratories at the other end, with the laboratories 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 are confirmed by the empirical findings. In confirmation with *H2*, the respondents in companies are clearly more positive in their judgement of the variables of system control than those in universities and institutes. For instance, according to the scientific staff in more than 50% of the university laboratories, 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 control may indicate that, despite the recent policy to improve market orientation, the fundamental differences between profit, not-for-profit and non-profit organizations still exist in the Netherlands.

5.3. Levels and sources of uncertainty

In accordance with *H3*, that the informational need is higher in knowledge institutions than in industrial laboratories, Table 6 shows that both the frequency of research meetings and the attendancy mix are significantly higher in universities and institutes. In contrast to *H3*, however, international communication 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.

We want to point at an additional explanation, namely that the difference in uncertainty between basic research, applied research and industrial R&D is not as high (any more) as generally assumed. Mayntz (1985) considers the external environment of institutes even as more hostile than that of universities. The fact that outside contractors expect value for money in terms of applicable concepts and artifacts, puts a lot of pressure on the institute's management. In institutes and companies uncertainty is also relatively high. In recent years, uncertainty in pharmaceutical discovery has grown considerably, because of the shift from random screening to basic research.

Our point is, that it is not important that there is uncertainty pur sang, but the question is, whether this uncertainty is 'relevant' or not. It is not primarily the uncertainty of the research process itself, but the uncertainty in relation to the task environment that counts. The primary process of basic research is directed towards publication in international scientific journals. Not the uncertainty in conducting the research, but the accessibility of the scientific audience counts for the uncertainty which is encountered. 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 (Kuhn, 1970).

The fact that basic research results are unpredictable is only then 'relevant' if the scientific journals ('the customers') are not willing to publish negative results. 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. This bias towards 'good news', fortified by the lay press, may have caused the too optimistic view of the progress of medicine by the general public.

5.4. Discovery vs. development

Table 7 shows that the innovative performance indicators relate more closely to process control than the industrial performance indicator. In accordance with *H4*. part of the variance of the performance indicator for the discovery phase, the patent number, is

explained by the frequency of project team communication. In the structured interviews, it became apparent that the best performing companies shift their attention from the screening of thousands of chemical compounds to the understanding of the biochemical and physiological background of diseases. The screening process itself is becoming increasingly automatized. According to theory, the growing task uncertainty which derives from this shift from systematic screening to fundamental research, will lead to a higher informational need which is met by a higher frequency of project team meetings. In contrast to *H4*, however, more intensive international communication did not add explained variance, probably due to the danger of leaking out of confidential information. A pharmaceutical company will try to screen off the information about a promising NCE, for which a patent has not been submitted, yet, in order to avoid putting a competitor on the trail. An example of the risk of insufficient information blocking is given by Lynn (1991) for the anti-ulcer drugs Zantac and Tagamet.

H5 is confirmed by the data. A positive correlation is found of shorter development length with the assessed importance of strategic, tactical and operational planning by the top management, and the attendancy mix. This indicates the prominent role that concurrent engineering (parallel development with intensive lateral and cross-functional communication in project teams) takes in modern development. Concurrent engineering practices have so fundamentally changed the pharmaceutical R&D-process, that the current R&D process in the most innovative pharmaceutical companies can best be described as a chain of integrated learning loops (Janszen, 1994). Interestingly, the close monitoring of the developmental process did 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. A high frequency of meetings would mean a lot of travelling. Mutual adjustment was therefore attained mainly by telecommunication (e-mail and video conferences). In case of too frequent project team meetings a tendency towards ineffectiveness was observed.

The comparison of the discovery and the development phase in industrial R&D also indicates that it is too simple to state that uncertainty is higher in discovery. It is more correct to say that the uncertainties are different. It can even be argued that developmental research has gradually become more uncertain, because of the synchronic nature of the developmental process, combined with the high costs of failure. It is interesting to note that only the best pharmaceutical companies have adapted their monitoring devices and control systems to this level of uncertainty by highly decentralizing the decision-making process. In the best companies, every project team manager is empowered to provisionally stop the process if one of the parameters is negative. In the conventional pharmaceutical companies with a strict hierarchical planning it could take up to three months before the go/no go decision was taken.

5.5. Radical vs. incremental orientation

Table 8 shows that apparent differences in innovative strategy can be traced between the companies in this study. In accordance with *H6*, companies conducting a more radical strategy employ a higher percentage of R&D staff, which 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 workshops than in companies adopting a more incremental strategy. An incremental strategy turns out to be related to lateral and cross-functional communication. In terms of annual growth rate, the companies conducting a more incremental strategy turn out to be more successful. That is to say, that speeding-up development, in order to introduce drugs with small improvements on a regular basis (Taggart, 1993), is currently more rewarding 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.

6. Limitations and directions for future research

6.1. Limitations

The first limitation of the present study stems from the cross-sectional nature of the design. 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. For instance, it is found that an outstanding laboratory 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 laboratories 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. Contractors are also more interested in contracting the best researchers (note that Cronbach's α indicated that the amount of international communication and contractor communication are closely related, see Table 3). Or is it cause and effect simultaneously? The latter could very well be the case. In many places in this paper 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..., are encountered. If it were possible to provide clear-cut relationships, then management would become a formalistic system, which would eliminate the need for scientific enquiry. The fact that it is not points at the potential danger of a set of 'rules for success'. At the very moment these rules 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.

The second limitation refers to the fact that a survey approach has been used. 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 above-average from the below-average performers. 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.

The third limitation concerns the industrial sample. Data obtained in one R&D laboratory are considered to reflect the whole innovative process. However, the different steps in the innovative process of 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. Some of the data, for instance the percentage of scientific vs. 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.

Other criticisms may focus on the obvious defects of any empirical management study, such as the relatively small study population leading to an unfavorable variable/observation ratio. Moreover, there are probably more factors related to performance 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.

6.2. Research directions

Despite these limitations, the results of this study give rise to some interesting generalizations. One of the most striking results of this study is that the high performers clearly differed from their low performing competitors. If the assumption is correct, that operating profits also reflect, to a certain extent, the contribution of the R&D function, then in all three strata the same management control variables: personnel, administrative and external control, closely associate with performance. This would provide confirming evidence for the main hypothesis, that there is a fundamental association between management control and performance, dividing the above-average from the below-average performers, regardless of the organizational setting.

The most important management control variable turned out to be personnel control, which explains part of the variance of all but one of the performance indicators. This is a clear confirmation for a central thesis in socio-dynamic literature that stimulating and rewarding environments, which enhance the motivation of the scientific personnel, are needed for high performance.

Probably just as interesting is the observation that process control did not come out as an important factor discriminating between high and low performers in universities and institutes. 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) may lead to high performance. There are many ways for good research managers to reach their goals, but what they cannot change is the inflexibility of the organization. Research management and management consultants may profit from this knowledge, by concentrating their efforts on organizational flexibility.

Seen in the light of the great differences in levels and sources of uncertainty between university and industrial R&D which emerges from literature, it was remarkable that the differences found were not so large. Probably, the difference in uncertainty between

basic research, applied research and industrial R&D is not as high (any more) as generally assumed. It was stated that it is not primarily the uncertainty of the research process itself, but the uncertainty in relation to the task environment that counts. The primary process of basic research is directed towards publication in international scientific journals. Not the uncertainty in conducting the research, but the accessibility of the scientific audience counts for the uncertainty.

The comparison of the discovery and the development phase in industrial R&D also indicates that it is too simple to state that uncertainty is higher in discovery. It is more correct to say that the uncertainties are different. It can even be argued that developmental research has gradually become more uncertain, because of the synchronic nature of the developmental process, combined with the high costs of failure. It is interesting to note that only the best pharmaceutical companies have adapted their monitoring devices and control systems to this level of uncertainty by highly decentralizing the decision-making process.

A 'certain' incremental strategy seems more successful than a more 'uncertain' radical one. Companies, finding themselves under increasing pressure 'to-do-more-with-less', may be tempted to shop for NCEs at biotechnological research 'boutiques', and simultaneously reducing their discovery staff. However, if too much emphasis is placed on incrementation, 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 will need to maintain considerable 'in-house' skills in order to evaluate the potential of the NCEs on offer. Therefore, such a strategy, which may seem sensible in the short-run, may prove to be the opposite in the long-run.

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Appendix A. Excerpt of general questions about R&D management

A.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]?

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 laboratories in the discovery phase and laboratories for pharmaceutical and clinical development (e.g., concerning size and hierarchy)?

A.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? And where in the R&D process are the most important milestones?

A.3. Innovation

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?

A.4. Human resources

What incentives are being given to scientific staff (both material and immaterial)?

What is the company policy on scientific publishing?

A.5. Management

Budget responsibility—at which level in the organization?

How are investments decided upon?

A.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 five 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?

Appendix B. Excerpt of the questions of ReQuest 1 and 2

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

	1985	1990	1995
Personnel means	..... ftes	..... ftes	..... ftes
Material means	..... US$	..... US$	..... US$
Basic funding	..... %	.....	..... %
External funding	..... %	..... %	..... %

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

3. How many working hours has the scientific staff of your laboratory spent, in the last year, on joint projects with:

other laboratories within your organization? .....

laboratories outside your organization but within the country? .....

laboratories abroad? .....

4. How many editorial boards do you sit on?

International journals .....

National journals .....

5. How many articles of which a member of your laboratory 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

6. 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.

7. '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)

8. 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.

9. If an (internal or external) evaluation shows 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.

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

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

11. What is your opinion with the respect to positive or negative consequences for your laboratory of such reorganizations?
Very positive - 1 2 3 4 5 - very negative
12. How often do you have meetings (concerning work content) with:
Colleagues within your laboratory? 1 2 3 4 5
Colleagues from other laboratories 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.
13. How often do you have meetings (concerning work content) with:
Colleagues outside the research organization but within the country? 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.
14. Please indicate the degree of the limitations imposed on the laboratory by administrative regulations (e.g., regarding travelling, budget, etc...).
Very large - 1 2 3 4 5 - very slight
15. 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$
16. 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.
17. How many scientific staff members of your laboratory 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)?

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