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Managing industrial pharmaceutical R&D. A comparative study of management control and innovative effectiveness in European and Anglo-American companies

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Abstract

Drug regulation and pricing have put strong pressure on the cost-benefit ratio of the innovative pharmaceutical industry. Therefore a study has been conducted in fourteen large and medium sized companies to determine some important organisational and managerial factors influencing success in pharmaceutical innovation. The study consists of structured interviews with Research Directors and questionnaires, submitted to the heads of the different research departments. The following conclusions are tentatively drawn. Firstly, the data suggest that a threshold investment of approximately $150–200 million is needed to maintain the innovative potential. Above approximately $750 million, 'economies of scale' seem to appear in pharmaceutical innovation. Secondly, an incremental strategy aimed at reducing the duration of the development process seems to be more successful than a radical strategy which lays more emphasis on discovery. Thirdly, pure play pharmaceuticals seem to be more successful than the pharmaceutical divisions of conglomerates. Management control, especially the way in which reorganisations are performed, is assessed more positively in pure play pharmaceuticals. Fourthly, the greater emphasis on human resources management in Anglo-American companies, in comparison to continental European companies, seems to be an important explanatory factor for their greater success on the pharmaceutical market.

INTRODUCTION

In a 'science based' industry [Pavitt, 1984], such as pharmaceuticals, innovation has become essential for the profitability and ultimately, for the long term survival of the companies. The necessity to innovate has led to the development of gradually safer and more effective drugs. Increasing innovative effort is being put into complex therapeutic areas (like cancer and multiple sclerosis), requiring a degree of sophistication in methodology and basic scientific knowledge, which is without precedent in the pharmaceutical industry. However, the increasingly strict regulations, regarding the effectiveness and safety of drugs, has reduced the time to recoup past research expenditures considerably. In the 1960s, the period between the finding of the lead compound (a chemical compound with assumed therapeutic effectiveness), and the introduction on the prescription drug market, was about five years. Presently, it takes more than ten years, to introduce a lead compound into the market place. Because a patent is submitted on the lead, while earnings start only ten years later, the effective patent protection time fell back from an average of thirteen years in around 1965, to eight to ten years in the middle of the 1980s [Redwood, 1987]. Taking into account, the policy of most national governments to reduce medical costs by influencing the cost of medication,

for instance, by stimulating the prescription of less costly generic medications, pharmaceutical innovation has gradually become a high risk investment area. Pharmaceutical companies have developed different strategies to cope with these problems. This has led to larger changes in the industrial structure, especially on the level of concentration and diversification. It is the aim of this paper to analyse these changes from the perspective of innovative effectiveness, as related to management control.

Concentration, diversification and innovative effectiveness

In recent years, larger mergers occurred in order to attain cost leadership and profit by economies of scale in marketing and production. This paper analyse whether this tendency towards concentration is also valuable from the perspective of efficiency in pharmaceutical innovation. Taggart [1993] concluded on the basis of different studies, that a minimum investment in R&D is needed, beneath which it is difficult to achieve satisfactory returns on investment. Above this level the picture is not quite clear. A number of researchers [e.g. Angilley, 1973 and Shrieves, 1978] conclude that above this threshold increasing returns on investment are reached in pharmaceutical innovation. Contrary to this, Soete [1979] concluded, on the basis of a more detailed database, a tendency to decreasing returns on investment. In a recent paper Graves and Langowitz [1993] also showed diminishing returns to increasing size of R&D-expenditures. In their study, however, biotechnological firms were compared with pharmaceutical firms. The large differences in size and markets (mostly diagnostics in biotechnology) make it difficult to compare them. For this reason in the present study only pharmaceutical firms were included.

One of the main factors influencing innovative effectiveness is the strategy chosen by the management. Roussel et al. (1991) distinguishes three innovative strategies: a fundamental (only emphasis on basic and applied research); a radical (more emphasis on basic and applied research than on development) and an incremental (more emphasis on development than on basic and applied research). Only radical and incremental strategies are conducted within the pharmaceutical industries. In recent years, innovative pharmaceutical companies are supposed to have moved gradually from a more radical to a more incremental strategy. This is done to in order to increase the life cycle of their products, by implementing smaller improvements (for instance in drug delivery), on a regular basis [Taggart, 1993]. These recent changes and their influence on effectiveness in innovation, will be analysed in this paper.

Over the years, pharmaceutical companies have gradually diversified into related and non-related markets, such as over-the counter drugs, diagnostics, veterinary products, specialised chemicals, and cosmetics and toiletries. In addition, conglomerate diversification occurred, such as in the case of pharmaceutical companies entering consumer products and services. On the other hand, large, mostly chemical corporations, obtained interests in pharmaceutical companies. Taggart [1993] predicts from the cost perspective, that only the large chemical conglomerations will have the financial strength to survive, and will attain more independent pharmaceutical companies in the years to come. Contrary to this is the supposition that independent companies generally are better adapted to the situation on their specific market [e.g. Allen, 1977]. The recent divestments of non-drug interests by some pharmaceutical companies, and the demerger of a pharmaceutical division by a chemical conglomerate, seem to support this supposition. In this paper, pharmaceutical divisions of chemical conglomerates will be compared with independent pharmaceutical companies (the pure play pharmaceuticals).

In the study sample, the conglomerates had predominantly a continental European background, while the pure play pharmaceuticals were generally Anglo-American. Larger differences in organization, management and work-related values, influencing the innovative climate of a company, have been observed between Anglo-American and continental European companies [e.g. Hofstede, 1980]. To get an idea of these differences, in the present paper companies with an Anglo-American are compared with those with a continental head office.

METHOD

Definition of variables

In the context of this paper, pharmaceutical innovation is taken to mean the whole R&D-process, starting with the discovery of the lead (the discovery phase), and the succeeding developmental process (including pharmacokinetics, toxicological and clinical testing), aiming to bring this lead to the market (the pharmacological and clinical developmental phase). Various researchers have used different methods to quantify the innovative effectiveness, but there is no general agreement on this respect. The measures most generally used are: the percentage of sales spent on R&D, the number of patents granted per R&D-investment, and the number of new products launched. All measures individually have their advantages and disadvantages. However, if all measures combined are pointing in the same direction, this can be considered as strong evidence for the existence of innovative effectiveness. Therefore, in the present study all three measurements are used. In addition, the length of the developmental process is added as a measure for innovative effectiveness, because it is considered to be one of the most important performance measures, influencing the profitability of a pharmaceutical company. Although the recent developments in biomedical and pharmacological research have enlarged the knowledge about the bimolecular background of diseases tremendously, and molecular modelling have made the searching for the lead compound less fortuitous, the pace of the finding of the lead, and therewith the length of the discovery phase is still highly unpredictable. On the other hand, the toxicological and clinical testing in the developmental phase is well defined, and can be planned according to strict schedules. The better a company succeeds in reducing this length, the more successful it will be.

In order to obtain comparable data, the Research Directors were asked to give an estimation of the maximum time span between the patenting of the lead compound and the introduction of the registrated drug on the prescription drug market, for anti-hypertensive and anti-ulcer drugs. These drugs were chosen because the developmental process is neither relatively short (antibiotics) nor very long (anti-psychotics). In five companies the reported length was checked for ten drugs which were launched after 1987. In all cases the findings proved to concord, the period between patent submission and launch being 1 to 2 years shorter than the reported maximum length of the developmental process. The finding of the lead proceeds patent submission. As a result, the time span of patent submission to launch a product will always be somewhat shorter. The expenditures for development include those for the clinical phase IV studies, the post marketing surveillance on long term side effects of drugs.

Because the primary interest of this paper is to establish a better understanding of the work of the proprietary innovative efforts of a company, joint development of a drug by two or more companies and in- and out-licencing (to buy the right to use a patent from or to sell this right to a competitor) have not been studied. For the same reason, 'biotechnological' patents (immune-diagnostics, oligo- and polypeptides and DNA- and RNA-sequences) have not been taken into consideration. Also, patents for pharmaceutical and therapeutical extensions (improved versions of the original drug) and patents on process technologies are not included.

Innovation although essential is not enough to reach the goal of attaining long term profitability for the company. It is obvious that without an adequate marketing and sales structure an innovative drug would never reach its full profit potential. Therefore, the measures of industrial efficiency are also used in the present study: the annual growth rate, and the operating profit margin. The innovative strategy, chosen by the company, is reflected in the structure parameters. Companies conducting a radical strategy will spend a larger part of the R&D-expenditures on the discovery phase. They are expected to appoint a higher percentage of scientists in R&D and their scientists will pay more attention to international communication, being more eager to get new innovative ideas. On the other hand, companies conducting an incremental

strategy will pay more attention to the planning and organization of the developmental process, so are expected to show more frequent R&D-process communication.

'Management control is the process by which managers assure that resources are obtained and used effectively and efficiently in the accomplishment of the organization's objectives' [Anthony, 1965, p. 27]. Anthony conceives management control as the planning and control level between strategic planning (goal formulation) and operational control (assuring that specific tasks are carried out). Management control is divided into system, process and external control. System control refers to the control over the personnel and material resources of the system (the research laboratory). Personnel control is measured by the assessed effectiveness of the human resources management, and resources control by the estimated pace of the administrative procedures. Process control describes the control over the research process, and is assessed by planning and research process communication. External control refers to the control over the environment [Pfeffer and Salancik 1978], and is assessed by international communication. For a more detailed description of the variables, the reader is referred to table 1.

Table 1 The definition of size, structure, management control, and performance

Size	
Sales	World wide sales of ethical drugs in 1991 in US $billion
R&D-expenditures	Worldwide R&D-expenditures in 1991 in US $million (also divided into' expenditures for drug discovery, and expenditures for pharmacological and clinical development, and post marketing surveillance (phase IV clinical trials, no patent and registration costs)
Structure	
Percentage discovery	Percentage of the total R&D-expenditures allocated to the discovery phase
Percentage scientists	Percentage scientists in the total R&D-staff (scientific staff plus technical and analytical support staff
System control	
Personnel control	Subjective assessment of the efficacy of staffing policy, appointment, promotion, career planning, and the effects of reorganisation
Resources control	Rapidity of administrative procedures, regarding appointment and procurement of equipment
Process control	
Planning	Subjective assessment of the importance of short and middle range planning by higher management
R&D-process communication	Frequency of discussion meetings with colleagues of the own laboratory, with researchers of other phases of the R&D-process and with marketing, and production
External control	
International comm.	Frequency of contacts with colleagues, scientists and physicians on congresses and workshops
Innovative performance	
Number of patents	The average annual number of patents for new synthetic chemical compounds, submitted world wide with first priority date from 1985 till 1991, absolute and divided by the annual expenditures for discovery (Pharmdoc section of the World Patents Index, DERWENT Publ.)
Length of development	Length of the development phase, the average time span between patenting of the lead and the registration of the drug (in $years^{-1}$)
Industrial performance	
Growth rate	The annual growth rate of the company, both organic growth and growth through acquisition
Operating profit margin	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 capitalised costs.

Study analyses

For the assessment of the management control variables, Likert's 5-point scales were used. Examples of the questions are provided in the appendix. After the data-collection a factor analysis was performed, which revealed that the individual sub-scales corresponded with the variables as defined in table 1. Cronbach's α [1970] was sufficiently high (>0.75), to warrant confidence in the internal consistency of the items, intended to measure a single concept. The effectiveness variables were measured by use of bibliometric methods (patents) and public information (sales, operating profit margin), and checked by the management of the company concerned. The parameters measured at ratio level are analysed with Oneway Anova, those measured at interval and ordinal level with non-parametric statistical methods. However, in order to get uniformity of presentation, all variables are presented using Oneway Anova. In order to discuss the individual variables in more detail, the results of the univariate analyses are presented in this report. In a forthcoming paper by the authors the results, of a multivariate analysis, using the neural network method [Hoptroff, 1991], will be presented.

Data collection and response rate

In 1992, twenty large and medium sized pharmaceutical companies with major research laboratories in the EC were approached. Fourteen agreed to take part (a response rate of 70%). Ten of them are among the top 20 companies ranked according to the worldwide ethical drug sales in 1991. Patent analysis revealed that 25% of the pharmaceutical patents submitted with a European priority from 1985 till 1991, originated from the companies in the present study. 22 structured interviews were held with the Directors of Discovery, and Pharmacological and Clinical Development (1 to 2 interviews per company). In 10 companies, questionnaires concerning personnel, budgetary and research policies were submitted to the head of the different research departments. In total 59 questionnaires were sent, of which 38 were returned (3 to 4 questionnaires per company laboratory, an individual response rate of 64%).

RESULTS

In Fig. 1 the relationship between the R&D-expenditures and the sales of ethical drugs in 1991 is presented. The curve rises almost in a linear aspect, until the sales of ethical drugs approaches approximately \$4 billion. Thereafter, the R&D-expenditures rise only moderately, from about \$700 million to a maximum of about \$875 million, while the sales of ethical drugs rise to approximately \$7 billion. Independent of scale the average R&D-expenditures of the companies amounted to 15.6% (s.d. 3.2%) of the ethical drug sales.

In order to examine the effectiveness of the discovery phase, the average annual expenditures for discovery of 1988 till 1991 are plotted against the average annual number of pharmaceutical patents submitted in the same period. The curve in Fig. 2 begins at around \$50 million, and increases to approximately \$200 million, while the average number of patents rises from 10 to 175 patents submitted annually.

A t-test was performed in order to examine whether a difference in effectiveness could be established between larger and smaller companies. Calculated per \$10 million investment in discovery, the larger companies submitted 9.6 patents, while the smaller ones submitted only 2.7 patents* per year. In addition, the number of therapeutic areas in which the pharmaceutical companies execute research increased with the size of the R&D-expenditures from 5–6 therapeutic areas in the smaller companies to 8–9 in the larger ones.

In Fig. 3 the length of the development phase is plotted against the expenditures spent on development. There proves to be a significant correlation, the higher the expenditures, the shorter the duration of the developmental phase. Initially, the period drops steeply, from 12 years at about \$120 million until 9 to 10 years at \$250 million. Then it remains constant until around \$450 million, and drops again to a period of around 6 to 7 years above \$600 million.

In all companies a considerable number

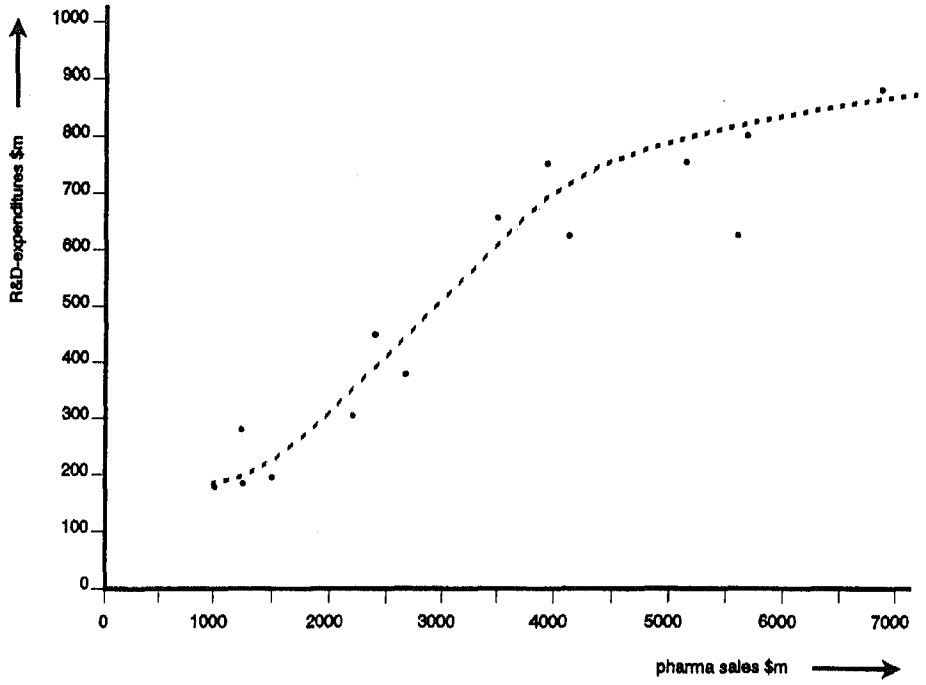

Figure 1 Sales of ethical drugs versus the R&D-expenditure per company in 1991 both in $m)
Sources: Annual reports of the pharmaceutical companies and the present study

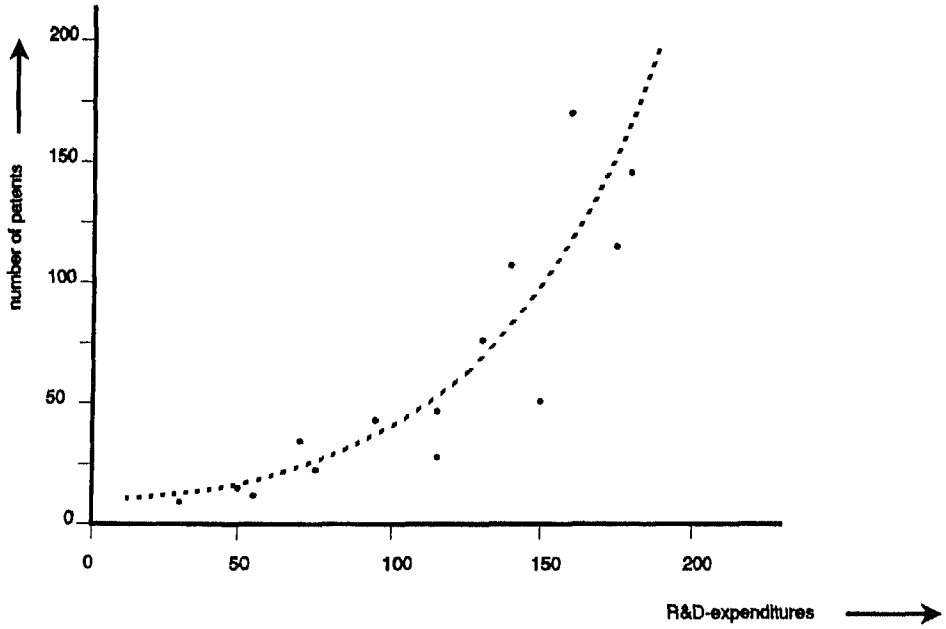

Figure 2 Average annual number of patents for new chemical compounds submitted worldwide versus the average annual expenditure for discovery per company from 1988 till 1991 (in $m)
Sources: World Patent Index and annual reports

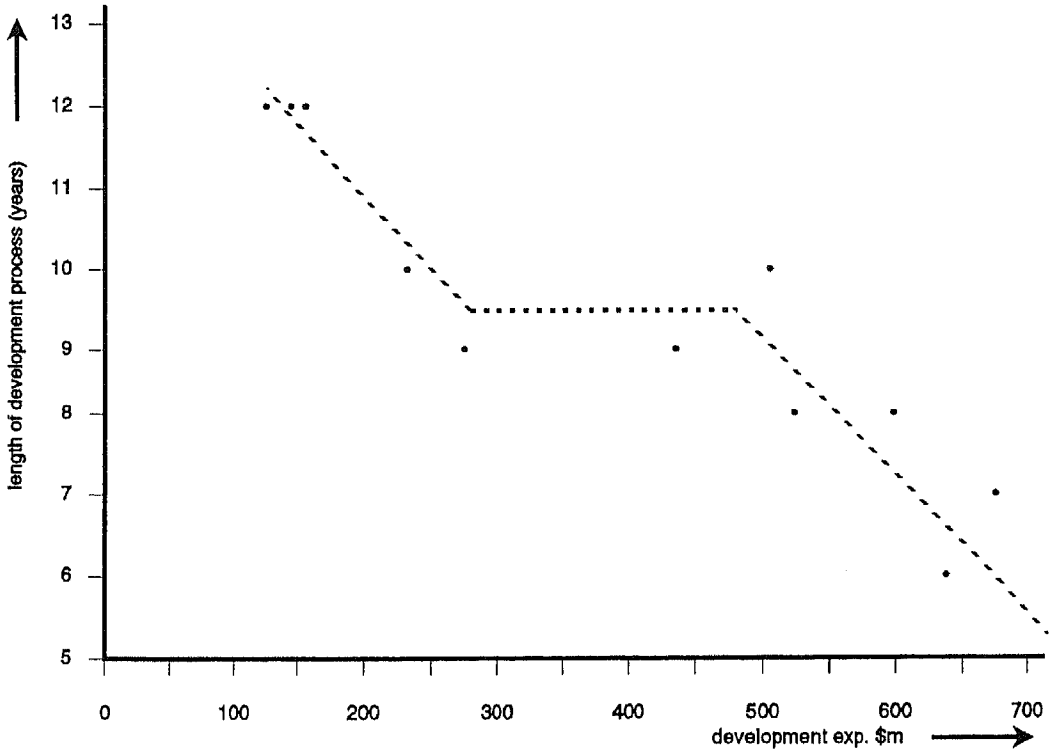

Figure 3 Length of the developmental process (in years) versus the R&D-expenditure spent on development (in $m) per company in 1991
Sources: see Fig. 1

of launches of innovative products was claimed. However, most of them proved to be therapeutic or pharmaceutics extensions of earlier innovations. Although these extensions can be of major therapeutic importance, they were not considered to be a valid measurement of innovative potential. In fact, only six of the larger companies launched innovative drugs in the 1980s. However, these innovative drugs accounted for a large part of the companies profitability. Ten to fifty percent (on average 32%) of the total pharmaceutical sales revenues of 1991 came from these innovative drugs.

Before reliable comparisons can be made between a radical and incremental strategy, pure play pharmaceuticals and conglomerates, and Anglo-American and continental European companies, the influence of size must be first taken into consideration. The only management control variable, which was (weakly) correlated with the volume of sales was personnel control ($r^2 = 0.33$, $p < .1$). Sales was also (indirect via the R&D-expenditures) significantly correlated with the innovative performance variables. However, sales was not significantly correlated with either of the industrial performance variables. Little difference in growth rate was found between smaller and larger companies (9.4% versus 11.9%), and a larger difference in the operating profit margin (16.6% versus 28.2%).

Table 2 shows that a more radical and a more incremental strategy can be distinguished. On the one hand, '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. On the other hand, 'incremental' companies, spending on average less than 20% on discovery, and employ 20% or less scientists in R&D. The total R&D-expenditures of the companies conducting an incremental

Table 2 The structure parameters, as indicators for a radical (n = 5) or an incremental (n = 5) strategy (median split of percentage discovery). Also size, and the statistically significant management control and performance variables are given (mean and F-values)

	Innovative strategy		
	Radical	Incremental	F-value
Size			
Sales	2,635 $m	3,420 $m	0.7
R&D-expenditures	415 $m	625 $m	0.7
Structures			
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 commuinication	4.4	3.7	4.4*
Industrial performance			
Growth rate	7.4 %	13.8 %	20.4***

Statistically significant: *$p < 0.1$; **$p < 0.05$, ***$p < 0.01$
R&D process and international communication: Likert 5-point scales, higher scores indicating a more intensive communication.

strategy were somewhat, but not significantly, larger than those conducting a radical strategy. As expected, a radical strategy was significantly correlated with international communication, and an incremental strategy with research process communication. However, no significant correlation was found between a more radical strategy, and the (absolute or relative) number of patents. In addition, no significant correlation was found between a more incremental strategy and the length of the developmental process (data not shown). Contrary to this, a very significant correlation was found with growth rate. The companies conducting an incremental strategy were growing nearly twice as fast as those conducting a more radical strategy.

Table 3 shows a comparison of pure play pharmaceuticals versus pharmaceutical divisions of conglomerates, and of Anglo-American versus continental European companies. The differences in size, personnel and external control, and industrial performance proved to be statistically significant in both of the comparisons. The results are presented in table 3. The pure play pharmaceuticals are somewhat, but not significantly, larger than the divisions of the conglomerates. Comparatively, the differences between Anglo-American and continental European companies are much greater. The average sales volume and the R&D-expenditures are both more than twice as high in Anglo-American companies. In both comparisons the difference in personnel control was significant. Personnel control is constructed from four items. They were analysed separately in order to gain an impression of which item had the largest impact. It proved that the emphasis on career planning, and, although to a lesser extent, the way reorganisations were performed, had the largest impact. It is interesting to note that both were assessed very negatively in the pharmaceutical divisions of conglomerates. In both cases, the average values on a Likert's 5-point scale lay considerably below three. Contrary to this, in pure play pharmaceuticals the assessments were much more positive, the average values laying considerably above three. In the comparison between Anglo-American and continental European companies the difference in the assessment of the possibilities of career planning were even more pronounced. The employees in the Anglo-American companies appeared considerably more positive than their colleagues in the

Table 3 Comparison of pure play pharmaceutical with pharmaceutical divisions of conglomerates and Anglo-American with continental European companies on size, management control and performance (mean and F-values)

	Pure play pharmaceuticals	Conglomerate divisions	F-value	Anglo-American	Continental European	F-value
Size						
Sales	4,195 $m	2,905 $m	1.5	5,305 $m	2,405 $m	10.3***
R&D-expenditures	610 $m	445 $m	1.5	705 $m	392 $m	7.3**
Personnel control						
Career planning	4.33	2.30	15.1***	4.17	2.00	24.3***
Reorganization	3.47	2.17	5.2*	2.87	2.77	0.02
External control						
International communication	4.25	3.70	0.7	4.60	3.25	9.2**
Industrial performance						
Operating profit margin	32.3 %	17.8%	6.5**	31.9 %	13.6 %	36.7***

Statistically significant: *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$

[1] Sales is only significantly correlated with career planning (2.15 in small versus 4.04 in large companies, F-value 10.0**).

Personnel and external control: Likert 5-point scales, higher scores indicating a more positive assessment. Size and industrial performance: pure play pharmaceuticals (n = 7); conglomerates (n = 7); Anglo-American companies (n = 6); Continental European companies (n = 8). Personnel and external control: pure play pharmaceuticals (n = 5); conglomerates (n = 5); Anglo-American companies (n = 4); Continental European companies (n = 6).

continental European companies. A more positive opinion about the possibilities of career planning was also found in the larger companies. However, the difference was smaller than between pure play pharmaceuticals and conglomerates and even much smaller in comparison with Anglo-American and continental European companies. Therefore, it is assumed that the differences in the assessment of career planning, although partly scale dependent, can mainly be contributed to the cultural background of the company. Between Anglo-American and continental European companies, the difference in the assessment of the execution of reorganizations disappeared almost totally. Consequently, it is likely that this difference must mainly be attributed to the concentration or diversification level. International communication is not significantly related to concentration or diversification level. Scientists in Anglo-American companies attend international congresses and workshops at a significantly higher frequency than their colleagues on the continent. The pure play pharmaceuticals perform better than the divisions of conglomerates. However, the difference between Anglo-American and continental European companies is even greater. In Anglo-American companies, the operating profit margin is more than twice that of a company located on the continent.

DISCUSSION AND CONCLUSIONS

For the correct interpretation of the results the following aspects must be first considered. Firstly, because a cross-sectional design has been used no cause-effect relationships can be identified with certainty. Secondly, although the study sample can be considered to be representative for pharmaceutical innovative industry, containing 50% of the top 20 companies, the inevitable limited number of cases may have influenced the conclusions. Thirdly, the data obtained in one research laboratory are considered to reflect the whole innovative process of the pharmaceutical company. However, the different steps in the R&D-process of the large pharmaceutical companies are carried out in a number of laboratories located in different countries. In order to reduce the chance of an accidental deflection, the main research laboratory of the company was examined (in 75% of the cases), or in case of an American company, a major laboratory in Europe. Fourthly, related to the last point is the

question: whether all companies used comparable definitions for the different aspects of R&D and sales. To check this, the annual reports and public information were studied, and additional data were obtained in the structured interviews. Could some of the data, for instance the percentage of scientific versus total R&D-staff, be checked in the laboratory under study, this was not so in all cases. Although much care has been taken to get uniform information it is possible that differences in interpretation occurred between companies. However, on the global level of the analyses there is no reason to assume that the conclusions would be distorted.

In order to evaluate whether economies of scale can be observed in pharmaceutical innovation, the outcome of the different parameters of innovative effectiveness will be discussed separately. Concerning the first indicator: R&D-expenditures as percentage of sales. At lower sales levels, the R&D-expenditures increase almost linearly with size, indicating that the companies in this section increase their innovative potential proportionate to sales. At the highest sales-volumes, however, a saturation level seems to be reached. Apparently there is no further need to invest the extra sales-volume in innovative potential.

Concerning the second indicator: number of patents as percentage of the investment in discovery. The larger firms clearly submit more patents per invested dollar than the smaller ones. This could be a clear indication for their higher innovative effectiveness. However, one could wonder why the larger companies would not invest more in discovery, in order to get a more than equal return in number of patents. An explanation could be that larger companies submit their patents relatively earlier than smaller ones. Basberg [1987] and Pavitt [1988] indicate that some companies play for safety and apply for a patent in an early stage of the innovative process, while others wait longer. The first strategy decreases the risk that a competitor submits 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 advantages and disadvantages. Because for the larger companies the patent fees and the translation costs constitute a smaller part of their R&D-budget, they are more likely to play for safety. In the structured interviews, however, most Research Directors indicated that the chosen patent strategy mostly depended on the therapeutic area. In a highly competitive area, like 'Aids', patenting was done in an early stage of the innovative process. The normal procedure was to wait longer; until about one year before the start of clinical testing. Only two Research Directors stated that their companies executed a restrictive patent policy. In point of fact, in Fig. 2 the data of these companies lay somewhat beneath the curve. The Research Director of a third company with a relative lower number of patents, however, complained of backward innovative potential. A further explanation can be, that not the discovery, but the developmental phase, is the limiting factor in pharmaceutical innovation. Indeed, in the structured interviews many Research Directors indicated that the increasing costs of innovation was mainly due to the continuously rising costs of the developmental process, especially in the large scale clinical trials.

Concerning the third parameter: the number of new products launched. The larger companies in the sample were the only ones who introduced innovative drugs, giving strong support for the thesis of higher innovative strength. This result should be interpreted with some caution. Ethical drugs differ from almost all other consumer goods, in that the buying decision is not made by the final consumer, but by the prescribing physicians. To influence them, frequent face-to-face contact of a highly knowledgeable sales force, combined with direct mail and advertisements in medical journals, and the organisation of medical congresses and other meetings, are necessary. Only the largest companies can finance the huge marketing and sales effort essential influencing the prescribing pattern in the desired direction. Consequently, it is possible that smaller companies had introduced innovative drugs and did not receive the recognition they deserved. Indeed, a Research Director of a smaller company stated that one of their most innovative drugs performed only moderately, until it

was outlicenced to one of the major companies. It proved only then to be a great success in the market.

Concerning the fourth parameter: the length of the developmental process which proves to be shorter in the larger companies. This finding can of course be mainly attributed to the greater size of the developmental budget. In the structured interviews, some Research Directors gave as further explanation that larger companies have more possibilities for parallel development. It is relatively easy to shift R&D-staff between projects. According to the model developed by Grabowski and Vernon [1987]; each year an innovative drug can be launched earlier, counts for three years of additional patent protection. If a drug has been on the market for a longer period of time, the chance that it will be forced out of the market increases.

Although all four measurements can be separately criticised on solid grounds, when combined they point in the same direction. Namely, that economies of scale, in terms of increasing returns on investment, can be observed in pharmaceutical innovation. How can we explain this finding in the light of the conclusion of Soete [1979] of diminishing returns on R&D-investment? Perhaps the main difference with the 1970s is that the governmental regulations have become much more strict. For that reason, the investments needed, especially for the large scale clinical trials, have increased considerably. While the possibilities to recoup these investments have decreased, especially for the smaller companies which cannot afford a huge marketing and sales force.

In order to establish whether the costs in pharmaceutical R&D are still evolving, or if the data might indicate any sign of a steady state, the following, very rough calculation, based upon the information of the Research Directors, was made. For the execution of the whole R&D-process for one new drug, an investment of $150–200 million is needed ($150 million is also mentioned by Ballance et al., 1992, based on data of the early 1980s). Roughly speaking, one in every four drugs is successful on the prescription drug market and once in every four years a pharmaceutical company develops a successful drug. Considering that the successful drugs count for the profitability of a pharmaceutical company, it can be calculated that a minimum annual R&D-expenditure of $200 million is needed to maintain the innovative potential. The curve in Fig. 1 starts at around $180 million, which could indicate the entrance of a steady state. However, further research is needed to confirm these data systematically.

An apparent difference in R&D-strategy is traced between the companies involved in the present study. More scientists are working in companies with a radical strategy, and a greater part of the R&D-budget is allocated to research. The researchers report more international contacts at congresses and workshops. An incremental strategy proves to be related to internal communication. This finding can be explained by the fact that as the R&D-process continues, more and more structured consultations are needed with staff members of marketing, sales and production, in order to speed up the developmental time. In order to get the best integration of R&D, marketing and production most companies work with project teams. To check this conclusion an additional test was performed on the frequency of project team meetings in research in comparison to development. It showed that in development the number of meetings and the duration was significantly higher than in the research phase. In terms of growth rate, the companies executing an incremental strategy prove to be more successful. This could indicate that at the moment speeding up product development could be a more rewarding strategy for pharmaceutical companies than concentrating on discovery. The company may therefore decide to buy 'research in progress', for instance from biotechnological companies. However, companies adopting this strategy will also need to maintain considerable 'in-house' skills in order to be able to evaluate the potential of the biotechnological knowledge offered. In addition, the 'fallacy of composition' should be kept in mind. Although a particular strategy might be very attractive for a limited number of companies, if too many competitors adopt it, its popularity becomes self-defeating.

Although it is possible that, in accordance with Taggart's prediction, in the long run

the conglomerates will become more successful, at present the pure play pharmaceuticals clearly perform better. On the level of management control, the major difference between the pure play pharmaceuticals and the conglomerates proved to be the pace, way and manner reorganizations were performed. These findings are in line with the expectations. The pace is considered to reflect the eagerness of the management of pure play pharmaceuticals to survive on the market. They lack the possibility to fall back on a 'mother'-company in less favourable times. The positive judgment of the way and manner reorganizations were performed, reflecting the knowledge about and the interest in the needs of the research staff and the greater possibilities to meet them. In a conglomerate the directorate of a division must comply with the general rules which may not always supply the best match for the pharmaceutical market.

The respondents from the Anglo-American companies report more incentives and better career possibilities than their colleagues in the continental European companies. In the structured interviews, a number of incentives were reported for extraordinary contributions, such as flexible salary, bonuses, use of a company car and the provision of company shares and options. All Research Directors indicated, however, that there is a driving force, which is even more important for the scientific staff than material incentives. This driving force is getting recognition for scientific merits, externally by the scientific auditorium, and internally by the company management. The opportunity to publish, and to a lesser extent attendance at congresses, are strong incentives for the scientific staff. The R&D-staff in Anglo-American companies report a significantly higher attendance at congresses. Possibly, because of their universal language. Aside from the research results concerning the non-patented leads in the discovery phase, only minor restrictions are placed on publications. Bibliometric research by Koenig [1983] revealed that the research staff of the large pharmaceutical companies in the US published so many articles in top journals, that they could compete with university departments. Although in Europe the companies are less publication-oriented than in America, the scientific production can still be considerable. For instance in 1990 the pharmacologists and clinical research associates of Hoechst-Roussel were author or co-author of 699 articles, congress contributions and abstracts [Hoechst-Roussel 1990]. Several Research Directors of 'continental' companies indicated, that especially the lack of career possibilities in the scientific ranks, was one of their major managerial problems. Existence of a dual ladder system, which can compensate this problem, was only reported in the Anglo-American companies. One of the Research Directors of a Division of a continental European conglomerate noted, that a dual ladder system would be beneficial for his R&D-department, but that the mother-company opposed it. One of the Anglo-American Research Directors characterized the advantages of this system as follows: 'Especially the possibility to get recognition for scientific efforts appears to be an important feature for scientists, because a relatively flat organization like a laboratory, offers only limited possibilities for promotion in terms of responsibility. The dual ladder goes all the way up to 'vice-president' on the managerial and to 'distinguished research scholar' on the scientific ladder'.

MANAGEMENT IMPACT

Given the inherent limitations of a cross-sectional design and a relatively small study population, the results presented in this paper lead to the following tentative conclusions for R&D-management. Firstly, the greater emphasis on human resources management in Anglo-American in comparison to continental European companies seems to be an important explanatory factor for their greater success on the pharmaceutical market. Because in a flat organization like an R&D-laboratory, the possibilities for promotion in terms of responsibility are limited. Promotion on the bases of scientific merits, such as in the case of the dual ladder system, and other incentives for scientific staff, could be considered. Secondly, an incremental strategy, directed to reduce the duration of the developmental process, for

instance by parallel development, seems to be more successful than a radical strategy which places more emphasis on discovery. Thirdly, pure play pharmaceuticals seem to be more successful than pharmaceutical divisions of conglomerates. Especially the pace; way and manner in which reorganizations are performed is assessed negatively in conglomerates and positively in pure play pharmaceuticals. Conglomerates, considering the less favourable times to come, could therefore consider making their pharmaceutical divisions self-dependent. Fourthly, the data suggest that a threshold investment of around $150–200 million is needed to maintain the innovative potential. Above approximately $750 million, 'economies of scale' seem to appear in pharmaceutical innovation.

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