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The Scale Effect in Blockbuster Drug Development

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Blockbusters have become internal resource of pharmaceutical companies for competitive advantage. This article divides the pharmaceutical R&D into two processes: The research process and the development process. Based on the RBV theory with VRIO framework, we argue that it is better to analyze the performance of the development process rather than the research outcome in order to determine the relation between innovation and the proprietary firms' activity. As an outcome index of the drug development process, the number of blockbusters is utilized. As a result of regression analysis, it is determined that scale effect does exist in the pharmaceutical blockbuster development process.

Field of Research: Management

1. Introduction

Since 1989, the pharmaceutical industry has experienced the continued giant mergers of companies. It is often said that the purpose of M&A is larger scale for larger profit. Given the fact that major source of profit is blockbusters (big sale new drugs), it is interesting to investigate the scale effect of blockbuster production.

In this article, we will empirically analyze whether scale effect exists in the process of the development of blockbusters. To quantify the outcome of the development process, we will use the VRIO framework based on the RBV theory, which is frequently used in the field of the management science.
This article is organized as follows: In Section 2, we will describe the VRIO framework based on the RBV theory and show that a blockbuster is a resource for the competitive advantage of pharmaceutical companies. In Section 3, we will

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review previous studies on the scale effect in pharmaceutical R&D. In Section 4, we will separate the R&D process into two sub-processes, and describe they are affected by different factors. In Section 5, we will describe factors affecting the total number of blockbusters in detail so as to determine the explanatory variables in our regression analysis. Finally, in Section 6, the results of our regression analysis will be reported, and the existence of scale effect shall be discussed.

2. Pharmaceutical R&D Performance Index

Here we will describe the ‘resource based view’ theory (RBV theory) and show that a blockbuster is a resource for the competitive advantage.Since the 1980’s, RBV theory, which claims each company’s internal resource contributes to its competitive advantage, has come to the forefront (Barney, 1991; Nelson, 1991; Wernerfelt, 1984). Barney (1991) noted such internal resource should have economic value, rareness and inimitability jointly. The method to analyze the internal resources based on this theory is referred to as ‘VRIO (value-rareness-inimitability-organization) framework’.

Kranzler et al. (1995) and Boulton (2000) suggested the use of blockbuster as a measure of effective internal resource for pharmaceutical companies, because it enables business organizations to satisfy VRIO criteria. Their suggestion seems to emphasize proprietary firms’ profit motivation in the analysis of pharmaceutical R&D, and to reveal that previous studies have shortcomings in the selection of target variable. We thus employ the number of blockbusters as a good measure of R&D final output. By reviewing previous studies in the next section, we will illustrate the merit of using this measure.

3. Literature Review

In this section, we will review previous studies which analyzed whether the scale effect exists or not in the R&D process of a pharmaceutical companies, including studies by Comanor (1965), Gambardella (1992), Graves and Langowitz (1993), Henderson and Cockburn (1996), Jensen (1987), Odagiri and Murakami (1992), Schwartzman (1976), and Vernon and Gusen (1974). Among these, Schwartzman (1976) is the only study that shows positive evidence for scale

effect existence. These previous studies may be categorized into three groups in principle, depending on the selection of internal resource as outcome of R&D process.The first group is the empirical studies by Gambardella (1992), Henderson and Cockburn (1996), and Schwartzman (1976), which measured the internal resources by the number of patents. The second group is by Graves and Langowitz (1993), Jensen (1987), and Odagiri and Murakami (1992), which used the number of NCEs. These variables in the first and the second groups lack rareness and economic value except for inimitability. The third group is by Comanor (1965), Schwartzman (1976), and Vernon and Gusen (1974), which used a combination of the number of NCEs and the sales amount. The explained variables in this group have both inimitability and economic value, but not rareness. Therefore, according to analysis of the VRIO framework based on RBV theory, it is acknowledged that the explained variables used in these previous studies cannot be regarded as internal resources for competitive advantage. We may point out on this matter that R&D should be separated into two distinctive sub-processes: Research and development. In this light, the explained variables in these studies are only the results of the research process, not of the R&D processes.

Cockburn and Henderson (2001) is the only study so far to focus on the development process, separating the pharmaceutical R&D into the two processes. In their study, the internal resources were quantified by the number of approved new drugs. This explained variable has inimitability and limited economic value, but it lacks rareness.Hence, previous studies may be characterized by incomplete satisfaction of VRIO criteria. Moreover, except for Cockburn and Henderson (2001), they analyzed pharmaceutical research process which is only the beginning part of whole R&D. Thus in this article, we analyze empirically whether scale effect exists in the development process, focusing only on this process of blockbusters that are regarded as resources of a pharmaceutical companies for competitive advantage.

4. Research Process and Development Process of Drug

In this section, we divide pharmaceutical R&D into the research and the development processes, explaining the determinant factors of the latter are different from those of the former. The research process is the process to

determine a NCE candidate for development. This process goes from the lead generation, to lead optimization, and then to the selection of a candidate for development. Thus a NCE and a pharmaceutical patent result from the research process. And, the result of the research process often depends on serendipity, so a large investment, such as that seen in the development process, is not required.

The development process takes the NCE obtained from the research process and develops it into product to be used in medical supplies. This process goes from the preclinical trial, to the clinical trial, and then to the post marketing surveillance (PMS) after approval and release. In the development process, especially at the stage of the clinical trial and PMS, a vast amount of development investment and many largely organized activities are required. After the approval of the new drug and subsequent release by the pharmaceutical company, a PMS is conducted by the same company. If the safety and effectiveness of the medicinal product cannot be confirmed during PMS, the approval for such medicinal product will be canceled. Therefore, a new drug that remains approved is regarded as a result of the development process.
On the difference between the two processes, JPMA (2006) report the following characteristics: Success rates at research process and development process are 0.05% and 20%, respectively; 20-25% of the R&D investment is spent in the research process and the remaining 75-80% is spent in the development process. In addition, according to Kuwashima and Takahashi (2001), the main characters involved in the problem solving of these two processes are different: It is the researcher in the research process, while it is pharmaceutical company in the development process. That is to say generally, during the development process, multiple teams or sectors within a pharmaceutical company cooperate with each other in various activities, and a decision maker in a superior position solves the problem by coordinating with the company.

This qualitative difference between the processes is well consistent with the above-mentioned numerical difference. Hence the development process in the pharmaceutical R&D should be considered essentially different from the research one. Further, the fruit of development process benefits the management of the company more directly than that of research process. This implies the adoption of big seller products as a target of analysis is suitable to

the scale effect analysis of pharmaceutical development.

5. Variables and Data

5.1 Selection of Variables

It is therefore natural to focus on the development process for given research outcome if we are to analyze the scale effect in the development process of a blockbuster. In order to do so, the regression model is used to explain the distribution of the number of blockbusters of each corporation by the following two variables: The first variable is the development investment of each pharmaceutical company, and is the most important variable in the development process; The second variable is the number of patents as a result of the research process. Each variable is described below.

Development Investment

As described in previous section, an NCE that has been issued a substance patent is developed to be approved as a pharmaceutical product. Fortunately, the amount of investment into the R&D of pharmaceutical products by major pharmaceutical companies has been reported. Thus this investment amount is incorporated as an explanatory variable in the regression model as the most important input in the development process of the pharmaceutical products. In connection with the adoption of the development investment as an explanatory variable in the regression model, there are several points which should be discussed in detail.

First, as described above and in previous studies, we found many empirical studies where the amount of R&D investment can not sufficiently explain the number of patents or NCEs (Gambardella, 1992; Graves and Langowitz, 1993; Henderson and Cockburn, 1996; Jensen, 1987; Odagiri and Murakami, 1992). As explained in the previous section, the results in the research process rely on serendipity to a certain extent. The results in previous studies are attributable to this characteristic in the research process. On the other hand, the development process of a pharmaceutical product requires a large amount of development investment.

Second, Cockburn and Henderson (2001) discussed the relationship between the result index of the development process and development investment, and concluded that the amount of development investment does not necessarily increase the result index. The result index in their study involved individual product projects of pharmaceutical companies. The investment amount that should be linked to the success or failure of a project is the investment amount for each project, not the aggregate amount of investment at the corporate level. Cockburn and Henderson noted that the aggregated amount of development investment at corporate level is relevant to the number of projects operated within the company. Since the result index of the development process in our study is the number of blockbusters aggregated at corporate level, their view is applicable even in our study.

Despite the above-mentioned appropriateness, when the amount of development investment is used as an explanatory variable for the number of blockbusters, it is necessary to interpret the results considering the following point: The data of the amount we use includes not just development specific investment. The total amount of whole R&D investment is used due to limits in data availability. However, fortunately, as indicated by JPMA (2006), it may be estimated that the ratio of investment amount of the development process to the total amount of the R&D investment falls within a certain narrow range. Seen in this light, this problem may be alleviated to a certain extent by interpreting the estimation result carefully.

Patent

As described in Section 4, after the research process is successfully completed and a patent for the NCE is obtained, a pharmaceutical company begins to develop the NCE into the product. Thus patents are indispensable to the development process. A positive correlation between the result of the research process and the result of the development process (the number of blockbusters) can be assumed. For this reason, the number of patents is used as an explanatory variable. If the research outcome index is given like this, it may be said that the estimated coefficient of the amount of R&D investment for the development process extracts the pure scale effect specific to the development process.

5.2 Data

Our dataset was obtained by combining several sources. The source of blockbusters (BB) is as follows: Data for 1990 to 1995 were from various issues of *Scrip Magazine* between 1991 and 1996, published by Informa, Ltd., in U.K.; Data for 1996 was from *Pharma Future Magazine* (1996) published by UTO-BRAIN, a pharmaceutical market research company in Japan; Data for 1998 was from *Pharma Japan Handbook* (1998, *Yakuji Handbook* in Japanese) published by Yakugyo Jihosha in Japan; Data for 1999 and 2000 were from a press release dated May 28, 2001, by Yoshikawa Pharma Institute (Yoshikawa Iyaku Kenkyujo, in Japanese), also available at the institute's website; Data for 2001 to 2003 were from various issues of *Monthly Mix Magazine* between 2003 and 2004, published by Elsevier Japan. No data could be obtained for 1997. Data for 1998 was available for U.S. firms only. Blockbusters with an annual sale exceeding one billion U.S. dollars were examined.

Data on the amount of R&D investment (RD) and the number of patents (PATENT) were obtained from *DATABOOK* (1992-2005) published by JPMA (Japan Pharmaceutical Manufacturers Association). This data book summarizes the annual reports issued by pharmaceutical companies. The amounts of R&D investment for top 20 pharmaceutical companies in annual sales are listed in this data book. The figures in currencies other than U.S. dollars were converted to U.S. dollars by the Purchasing Power Parity (PPP), published by the Organization for Economic Co-operation and Development (OECD). Thus the amount of the R&D investment in our data is described in millions of U.S. dollars for uniformity.

The result of the research process is measured by the number of patents belonging to the A61K of international classification recognized by the government of Japan. International classification A61K is the classification of patents relating to pharmaceutical products, including patents of any kind that may complement a substance patent in the manufacturing process of a pharmaceutical product (e.g. process patent, formulation patent). Therefore, our result index of the research process includes various research results as required for the development process of a new drug, in addition to the NCE. In

this sense, our result index of the research process is appropriate for the analysis of the scale effect in the development process.

The descriptive statistics of the data described above are shown in Table 1.

Table 1: Descripitive statistics of variables

Variable	Minimum	Maximum	Mean	Std. Dev.
BB (number of blockbusters)	0	10	1.6487	1.8855
RD (R&D expenses in mil. US$)	423	8488	1794.2703	1220.7129
PATENT (number of patent)	0	749	63.3892	80.7161
Number of observations	185			

6. Estimation Result

In this section, in order to investigate the existence of the scale effect in the development process, the results estimated by the ordinary least squares (OLS) to explain the number of blockbusters are discussed. TSP version 4.1 was used for this estimation. The estimation result is shown in Table 2. All the explanatory variables are subtracted by their own sample means before entered into regression, so the estimated constant term equals theoretically to the sample mean of the number of blockbusters.

Table 2: OLS regression result for successful blockbuster developments

Explanatory variable	Estimated coefficient	Std. err.	P-Value
Constant	1.6487	0.0954	P<0.001
RD	0.0007	0.0001	P<0.001
PATENT	0.0088	0.0013	P<0.001
adj R2	0.5267		
Sample size	185		

The adjusted R-squared is 0.5267, which seems moderate fit compared to the previous studies. The coefficient of RD, which is our main concern in this study, represents the increase in the number of blockbusters that occurs when a pharmaceutical company raises development expenses by one million U.S. dollars. The estimated coefficient of RD is 0.0007, which, together with its standard error being 0.0001, implies that the coefficient is significantly greater than zero and thus the scale effect does exist. For example, let us consider two companies operating at our sample mean levels, that is, each of two companies

having on average 63.4 patents and investing 1794 million U.S. dollars to obtain 1.65 blockbusters. Our estimated result tells that, if these two companies are merged, the expected number of blockbusters to be developed is 3.46, which is 4.92% greater than 3.30, the sum of pre-merger blockbusters by two individual productions. Hence, the development process of new drug exhibits large degree of scale effect and can be a good incentive for M&A.

The coefficient of a patent, which is entered into the regression equation to control variation in research process results between firms, is shown as 0.0088, a significantly positive estimate. This result means that, by rough estimate, approximately 110 new patents will lead to one additional blockbuster. It therefore suggests that most patents have very little influence on emerging new blockbusters. It also suggests the analysis of development process rather than the research process from the proprietary aspect of pharmaceutical companies. This result implies the serendipity in research process does not add much uncertainty in development process. It should be stressed that, unlike previous studies, weak serendipity in the development process could be identified in our analysis of the number of firm-level blockbusters.

7. Conclusion

In this article, we have empirically investigated the existence of the scale effect in the development process of new drugs with big sales, called blockbusters.
In Section 2, we described VRIO framework based on the RBV theory and showed that a blockbuster is a resource for the competitive advantage of a pharmaceutical company.

In section 3, we reviewed previous studies on the scale effect in the R&D process of a pharmaceutical company. The explained variables of the previous studies (the number of patents, the number of NCEs, the number of approved new drugs) were inappropriate as effective internal resources in view of VRIO framework based on the RBV theory.

In Section 4, the decomposition of pharmaceutical R&D was presented in detail. For these two processes, we explained that while the research process relies on

serendipity, the development process, given the outcome of the research process, relies on the scale, not serendipity. Many previous studies reported no evident scale effect in the entire R&D process. In fact, however, these studies mainly analyze simply research process rather than the entire R&D. Thus, no empirical studies have analyzed the scale effect in the development process at the corporate level. We have therefore analyzed whether the scale effect exists in the development process of blockbuster. This was the main objective of this article.

In Section 5, variables and samples were explained. The appropriateness of using the amount of R&D investment and the number of patents as explanatory variables was discussed.

In Section 6, results of the empirical analysis were described. The scale effect in the development process of blockbusters was found to exist. Serendipity incidental to the development process is not as large, unlike in the research process. Although these results have been mentioned informally, this is the first time to be empirically demonstrated.

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