Are Research and Development Processes Independent in the Pharmaceutical R&D?

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EXTENDED ABSTRACT

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. Our result of simultaneous estimation of patent and blockbuster equations are summarized as follows: (i) The development process is much more affected by the company scale than the research process is; (ii) The empirical effect of patents on the number of blockbuster is small compared to the scale elasticity on the development output.

1. INTRODUCTION

In this article, we will empirically analyze whether the research and the development processes are independent in the pharmaceutical R&D. By 'independent' we mean that the outcome of the research process does not affect empirically the outcome of the following development process.

To quantify the outcome of the R&D process, we will use the 'value-rareness-inimitability-organization (VRIO)' framework based on the 'resource based view (RBV)' theory, which is frequently used in the field of the management science.

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; Wernerfelt, 1984). Barney (1991) noted such internal resource should have economic value, rareness and inimitability jointly. These three criteria constitute VRIO framework.

Kranzler et al. (1995) and Boulton (2000) suggested the use of 'blockbuster' (a new drug with big sale) as a measure of effective internal resource, because it enables business organizations to satisfy VRIO criteria. Their suggestion emphasizes proprietary firms' profit motivation, and reveals that previous studies have shortcomings in the selection of target variable as described below.

Using this suggested concept, we categorize previous pharmaceutical R&D studies into four groups as follows.

The first group is the empirical studies by Gambardella (1992), Henderson and Cockburn (1996), and Schwartzman (1976), which measured internal resource by the number of pharmaceutical patents. The second group is those by Graves and Langowitz (1993), Jensen (1987), and Odagiri and Murakami (1992), which used the number of new chemical entities (NCEs). These variables 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. Explained variables in this group have both inimitability and economic value, but lack rareness.

The fourth group is by Cockburn and Henderson (2001), which used the number of approved new drugs. The explained variable has inimitability and limited economic value, but it lacks rareness.

Therefore, by introducing blockbuster as an output measure, we are able to overcome these shortcomings. Moreover, if we take blockbuster as final output measure, the patents and NCEs should be treated simply as intermediate inputs to the whole R&D process. These two improvements can be made by estimating patent equation and subsequent blockbuster equation simultaneously, and are our main concern. Before presenting the estimation model, we propose dividing the R&D into two sub-processes in the next section.

2. RESEARCH AND DEVELOPMENT PROCESSES OF BLOCKBUSTER

In this section, we explain that pharmaceutical R&D can be divided into the research and the development processes, as well as the peculiar determinant of each process.

The research process is the process to determine a NCE candidate for development. Thus a NCE and a pharmaceutical patent result from the research process. Each research project is carried out by a small unit of individual researchers, and these units seek different NCEs independently. The success of each individual research project depends highly on serendipity, rather than large scale financial investment. Further, the percentage of useful NCEs and patents that shows immediate applicability to blockbuster is quite small.

The development process makes up one of the NCEs into a medicinal product. 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 clinical trial and PMS, a vast amount of development investment and many large organized activities are required. If the safety and effectiveness of the medicinal product cannot be confirmed during PMS, the approval for such medicinal product will be cancelled. Therefore, a blockbuster that remains approved can be seen as a result of the development process.

By this argument, although the outputs of research process (patents and NCEs) are inputs to the development process, we expect in our empirical study that (i) the development process is affected by the organizational scale of R&D to a higher degree than the research process is; (ii) the effect of research process on the development process is limited. The empirical model to analyze this relation is presented in the following section.

3. MODEL AND DATA

A simultaneous equation model for pooled data with a count data equation is used to estimate the relation between R&D expense, patents, and blockbusters. The model is:

$$\log PAT_{i,t-1} \mid \mu_{i,t-1} \sim N(\mu_{i,t-1}, \sigma^2), \quad (1)$$

$$\mu_{i,t-1} = \alpha_0 + \alpha_R \log RD_{i,t-1}, \quad (2)$$

$$\Pr(BB_{i,t} = b \mid \lambda_{i,t}) = \frac{\exp(-\lambda_{i,t}) \cdot \lambda_{i,t}^{\ b}}{b!}, \quad (3)$$

$$\log \lambda_{i,t} = \beta_0 + \beta_P \cdot \log PAT_{i,t-1} + \beta_R \cdot \log RD_{i,t}, \quad (4)$$

where PAT is the number of patents newly acquired by the company; BB is the number of blockbusters sold by the same company; RD is the annual total R&D expense of the company. The subscripts i and t denote firm and period respectively. We assume BB has a Poisson distribution with mean λ (equation (3)). Given the data for PAT , BB , and RD , the parameters (α_0 , α_R , β_0 , β_P , β_R , σ) are estimated by the maximum likelihood estimation (MLE) method.

For equation (1), we assume PAT has a log-normal distribution. Though PAT is a count data by nature, the maximum value of PAT is 495 so that it is too large to apply a conventional count data model such as a Poisson regression. Instead, we adopt a normal distribution for $\log PAT$.

For equation (2), we employ $\log RD$ as its explanatory variable which is a proxy variable for the firm size as well. In many previous studies the lagged values of RD are jointly taken as explanatory variables. Unfortunately, our data has relatively short time-series for many firms and thus we instead focus on the scale aspect of the firm at the corresponding time period when the explained variable is observed.

Equation (3) depicts the count data nature of the number of blockbusters, with the mean given in equation (4). As explanatory variables of BB, we employ both the log of the number of patent ($\log PAT$) at the previous period and $\log RD$ at the current period, as indicated in equation (4). As is clear by the argument in the previous section, the pharmaceutical companies seek to turn their foregoing patents into profitable products. Therefore we take the lagged value of $\log PAT$ as explanatory variable together with the firm scale proxy $\log RD$ at the observed time period.

Our data were collected from several sources. For the number of blockbusters (BB), the source is as follows: Data for years 1990 to 1995 were from various issues of *Scrip Magazine* (Informa in U.K., 1990 to 1995); Data for 1996 was from *Pharma Future Magazine* (UTO-BRAIN in Japan, 1996); No data could be obtained for 1997; Data for 1998 was from *Pharma Japan Handbook* (Yakugyo Jihosha in Japan, 1998) and were available for U.S. firms only; Data for 1999 and 2000 were from a press release by Yoshikawa Pharma Institute in Japan (dated May 28, 2001); Data for years 2001 to 2003 were from *Monthly Mix Magazine* (Elsevier Japan , issues in 2003 and 2004). Blockbusters with an annual sale exceeding one billion U.S. dollars were examined.

The R&D investment (RD) and the number of patents (PAT , international classification A61K in Japan) were obtained from *DATABOOK* (1992-2005) published by Japan Pharmaceutical Manufacturers Association (JPMA). The RD data were converted to U.S. dollars by the Purchasing Power Parity (PPP) issued by Organisation for Economic Co-operation and Development (OECD), and is expressed in million U.S. dollars.

After eliminating observations which lack necessary data, we obtained 136 observations for 29 pharmaceutical companies. Sample years range from 1992 to 2003 except for 1997. The descriptive statistics of the data described above are shown in Table 1.

Table 1. Descriptive statistics.

Variable	Mean	Std. Dev.	Min	Max
BB	1.926	1.961	0.000	10.000
log *PAT*	3.717	0.861	1.609	6.205
log *RD*	7.337	0.596	6.122	8.872

*Number of Observation is 136.

4. ESTIMATION RESULT

Table 2 shows the estimation result of the equations (1) through (4). The scale effect parameter in the blockbuster equation, β_R , is estimated to be 0.903

with the standard error 0.184. These figures show no evidence of increasing or decreasing returns to scale in the production of BB. On the other hand, α_R, the scale effect parameter in the patent equation, is clearly less than unity. This result emphasizes the productivity of pharmaceutical research process is quite different from that of development process in terms of company scale.

The parameter β_P reflects how much the development process is affected by the output of research process. The estimate is 0.361, which means 1% increase in the number of patents brings 0.361% increase in the number of blockbusters. This elasticity is definitely less than the scale elasticity β_R. Using the sample means of $\log PAT$ and BB (3.717 and 1.926 respectively), we roughly calculate in numerical term, 59 (=exp(3.717)/1.926/0.361) newly approved patents are required to issue one additional blockbuster. Thus the serendipity in each individual research process may have limited effect on the development process.

The small effect of patents on the blockbuster, together with the great difference between the scale effects on patents and blockbusters, implies the essential difference in the research and the development processes in the pharmaceutical R&D. Therefore it is consistent with the independence of the two processes as discussed in the previous sections.

Table 2. Result of MLE of blockbuster and patent.

Parameter	Estimate	Std. Err.	t-statistic	P-value
α_0	-1.119	0.888	-1.260	0.208
α_R	0.667	0.119	5.597	0.000
β_0	-7.591	1.283	-5.919	0.000
β_P	0.361	0.123	2.944	0.003
β_R	0.903	0.184	4.897	0.000
σ^{-1}	1.321	0.087	15.269	0.000.
Log likelihood	-343.715			

5. CONCLUSION

Our result of simultaneous estimation of patent and blockbuster equations are summarized as follows: (i) The development process is much more affected by the company scale than the research process is; (ii) The empirical effect of patents on the number of blockbuster is small compared to the scale elasticity on the development output.

Therefore our result supports the empirical independence of development process and the research process due to the qualitative difference in the characteristics between the two sub-processes, as discussed in detail in Section 2.

This seems to have two important implications. First, the productivity or the production structure of pharmaceutical R&D should be analyzed not only with technological focus but also the proprietary view on the pharmaceutical companies' behavior, since the blockbuster brings much more profit to the company than the patent which is just an intellectual asset unless it is developed to a selling product. Second, in the pharmaceutical industrial organization, M&A for the larger scale to enable efficient blockbuster development may still occur, if the search for NCE is more specialized by the relatively small ventures.

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