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Scale economies of pharmaceutical patent and blockbuster R&D with possible endogeneity and dynamics

Atsushi, F. [1] **and T. Miyashige** [2]

[1] *Faculty of Economics and Business Administration, The University of Kitakyushu, Fukuoka, Japan*
[2] *Department of International Trade and Transport, Toyama National College of Maritime Technology, Toyama, Japan*
Email: afujii@kitakyu-u.ac.jp

Abstract: The purpose of this paper is to analyze the scale economy of world big pharmaceutical companies' R&D. We focus on the two distinguished sub-processes of pharmaceutical R&D (blockbusters and patents) and define the production functions for each of the sub-processes. The result of GMM estimation of the two sub-processes shows that (i) the blockbuster development sub-process shows weak diseconomies of scale (that is, close to constant returns) while the patent research sub-process shows clearly diseconomies of scale; (ii) the difference between the scale economies of the two sub-processes is widened if we explicitly take into account the dynamic aspect of pharmaceutical R&D; (iii) the linear feedback coefficient is 0.6 which implies 40% of blockbusters become non-blockbusters in the subsequent years, and (iv) the quantitative connection between the patent and the blockbuster measured by elasticity of the blockbusters is smaller than the direct effect of development expense on blockbusters.

Keywords: *Blockbuster, patent, pharmaceutical R&D, count data, linear feedback model*

1. INTRODUCTION

In this article we analyze empirically the scale economy of pharmaceutical R&D processes. Many of the previous studies on the pharmaceutical R&D can be classified in at least four categories on the basis of measurement of R&D performance: Gambardella (1992), Henderson and Cockburn (1996), and Schwartzman (1976) considered the number of pharmaceutical patents; Graves and Langowitz (1993), Jensen (1987), and Odagiri and Murakami (1992) used the number of new chemical entities (NCEs); Comanor (1965), Schwartzman (1976), and Vernon and Gusen (1974) used a combination of the number of NCEs and the sales amount; Cockburn and Henderson (2001) used the number of approved new drugs.

Once we turn to the profitability of pharmaceutical R&D, however, it should be stressed that most of the profit for a pharmaceutical company comes from selling only a few brands of new drugs (called *blockbusters*) as discussed in Miyashige (2008). According to Miyashige et al. (2007), where blockbusters were considered as R&D performance index, the pharmaceutical R&D process can be well divided in two subsequent sub-processes: a research process to produce patents and a development process to raise these patents to approved final product as medical drugs. In this point of view, we can say that the previous studies described above except for Cockburn and Henderson (2001) analyzed the research sub-process, rather than the development sub-process which is essentially important in the management of profit-seeking pharmaceutical companies. Hence, it has certain importance to analyze firm-level blockbuster data as a pharmaceutical R&D performance index.

The analysis of blockbusters requires statistical method for count data, since the number of blockbusters that one pharmaceutical company sells rarely exceeds ten. Miyashige et al. (2007, hereafter abbreviated as MFK) utilized a simple Poisson regression to do so. On the analysis of count data, a lot of studies have been developed so far in the field of econometrics, especially in treating endogenous or predetermined regressors in dynamic count data models: Montalvo (1997), Crépon and Duguet (1997), Blundell et al. (1995), and Blundell et al. (2002), to name but a few. They suggested usable moment conditions to estimate dynamic count data model in the generalized method of moment (GMM) framework. Abdelmoula and Bresson (2005) applied these studies to the series of patents data of European regions with incorporation of the linear feedback model (LFM), which has its foundation in the integer-valued autoregressive (INAR) process proposed by Al-Osh and Alzaid (1987).

This paper reconsiders the pharmaceutical blockbuster R&D analysis developed by MFK following the approach of Abdelmoula and Bresson (2005): We try to identify the difference between the scale economies of patent and blockbuster R&D, by explicitly considering the problem of predetermined regressors and dynamic aspect of blockbuster development and patent research.

2. MODEL AND DATA

Following MFK we formulate the numbers of patents and blockbusters:

$$\mathrm{E}\left(\log PAT_{it} \middle| W_{it}\right) = \alpha_0 + \alpha_R \log R_{it} + \alpha_P \log PAT_{i,t-1}, \tag{1}$$

$$\mathrm{E}\left(BB_{it} \middle| Z_{it}\right) = \beta_0 \exp\left(\beta_R \log R_{it} + \beta_P \log PAT_{i,t-1}\right) + \beta_B BB_{i,t-1}. \tag{2}$$

The symbols are defined as follows: PAT_{it} is the number of patents that is newly acquired by the pharmaceutical company i at time period t; R_{it} is the annual total R&D expense of the company; BB_{it} is the number of blockbuster brands sold by the company; $\alpha_0, \alpha_R, \alpha_P, \beta_0, \beta_R, \beta_P, \beta_B$ are parameters; W_{it} and Z_{it} are sets of instrumental variables to be explained later. Equation (1) states research process that generates patents or NCEs. The first term of equation (2) states the number of blockbusters newly developed is a function of the outcome of the research process in the previous period $\left(PAT_{i,t-1}\right)$ and contemporaneous R&D expense $\left(R_{it}\right)$. The second term of the equation stands for the surviving blockbuster brands from the previous period $\left(BB_{i,t-1}\right)$, and is a characteristic feature of linear feedback model. Since the number of blockbusters is typically a count data (the maximum in our data is 9), the sum of these two terms constitutes the conditional expectation that must be non-negative by definition, while we do not put such restriction on the number of patents whose maximum in our data exceeds 300.

The set of instrumental variables differs depending on whether we assume the regressors are exogenous, predetermined, or endogenous: it consists of the regressors at any periods if they are strictly exogenous; contemporaneous and past values of the regressors if they are predetermined; contemporaneous values only if they are endogenous. As we have limited sample size, we try the following simple settings for instruments: Let $W_{it} = \{\text{constant}, \log PAT_{i,t-1}, \log R_{it}\}$ and $Z_{it} = \{\text{constant}, \log PAT_{i,t-1}, BB_{i,t-1}, \log R_{it}\}$ for endogenous-regressors assumption; $W_{it} = \{\text{constant}, \log PAT_{i,t-1}, \log R_{it}, \log R_{i,t-1}\}$ and $Z_{it} = \{\text{constant}, \log PAT_{i,t-1}, BB_{i,t-1}, \log R_{it}, \log R_{i,t-1}\}$ for predetermined-regressors assumption; $W_{it} = \{\text{constant}, \log PAT_{i,t-1}, \log R_{i,t+1}, \log R_{it}, \log R_{i,t-1}\}$ and $Z_{it} = \{\text{constant}, \log PAT_{i,t-1}, BB_{i,t-1}, \log R_{i,t+1}, \log R_{it}, \log R_{i,t-1}\}$ for strictly exogenous assumption.

Since there are three types of assumptions on the exogeneity of the regressors for an equation, we have nine combinations of the instrumental variables sets (labeled as models (I) through (IX)) depending on the combination of the exogeneity assumptions on each equation if we estimate equations (1) and (2) jointly.

Our data were collected from several sources. For the number of blockbusters, 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 and the number of patents, international classification A61K in Japan) were obtained from DATABOOK (1992-2005) published by Japan Pharmaceutical Manufacturers Association (JPMA). The 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 collecting data, we limited our sample to those pharmaceutical companies that have never been involved in M&A (mergers and acquisitions) in our observation periods, in order to avoid contamination of the sample. The final sample for estimation consists of seven firms and 89 observations in total. The descriptive statistics are

Table **1**. Descriptive statistics.

Company	Variable	Mean	Std. Dev.	Min.	Max.
Bayer	*BB*	1.50	0.67	0	2
	PAT	44.75	19.86	5	78
	R	2865	375	2244	3578
Bristol-Myers Squibb	*BB*	1.92	0.95	1	4
	PAT	51.15	25.61	6	84
	R	1522	521	881	2279
Eli Lilly	*BB*	1.77	1.17	0	4
	PAT	72.38	38.59	14	143
	R	1423	633	703	2350
Merck	*BB*	3.62	1.66	1	7
	PAT	112.69	59.65	52	268
	R	1748	736	854	3178
Pfizer	*BB*	3.54	3.23	0	9
	PAT	111.54	90.73	29	314
	R	2625	2101	640	7131
Roche	*BB*	0.83	1.19	0	4
	PAT	36.75	17.52	12	74
	R	1522	655	726	2657
Schering-Plough	*BB*	1.00	0.91	0	2
	PAT	25.15	11.84	12	53
	R	895	405	380	1469

shown in Table 1.

3. EMPIRICAL RESULTS

In Table 2 we report the results of GMM estimation of equations (1) and (2), for various exogeneity assumptions on the regressors, except for Model (IV) for which we could not achieve convergence in iterative calculation of GMM. The parameter estimates are similar across the models (the difference between the models are less than 10% relative to the average of eight models) except for α_0. The lower Sargan test p-values for models (I), (II), (III), and (VII), all of which are imposed endogeneity regressors assumption, tell that such assumption is suspicious for any of the two equations. Instead, combinations of predetermined and/or exogenous assumptions on regressors seem to fit the data (models (V), (VI), and (IX)). In this sense, the possibility of endogenous regressor problem is limited in the blockbuster R&D.

Table **2**. GMM estimation results for equations (1) and (2).

	Exogeneity assumption on the regressors in:		Parameter estimates								
Model	Eq. (1)	Eq. (2)	α_0	α_R	α_P	β_0	β_R	β_P	β_B	Sargan	d.f.
(I)	Endog.	Endog.	-0.105	0.307	0.487	0.000	0.896	0.445	0.659	46.985	37
			0.069	0.018	0.025	0.000	20.365	0.017	0.290	0.126	
(II)	Endog.	Predet.	-0.056	0.312	0.471	0.000	0.845	0.472	0.614	50.419	44
			0.060	0.017	0.024	0.000	0.035	0.015	0.025	0.235	
(III)	Endog.	Exog.	-0.135	0.323	0.461	0.000	0.849	0.479	0.611	58.130	51
			0.059	0.016	0.023	0.000	0.031	0.016	0.023	0.229	
(IV)	Predet.	Endog.	-	-	-		-	-	-	-	
			-	-	-		-	-	-	-	
(V)	Predet.	Predet.	-0.106	0.313	0.475	0.000	0.847	0.472	0.618	51.535	51
			0.051	0.016	0.024	0.000	0.028	0.013	0.021	0.453	
(VI)	Predet.	Exog.	-0.166	0.326	0.464	0.000	0.857	0.477	0.617	59.406	58
			0.052	0.015	0.021	0.000	0.026	0.013	0.019	0.424	
(VII)	Exog.	Endog.	0.000	0.272	0.536	0.000	0.790	0.468	0.610	58.604	51
			0.068	0.017	0.024	0.000	0.033	0.018	0.029	0.217	
(VIII)	Exog.	Predet.	-0.022	0.278	0.529	0.000	0.792	0.473	0.612	65.383	58
			0.057	0.016	0.022	0.000	0.025	0.012	0.019	0.236	
(IX)	Exog.	Exog.	-0.082	0.295	0.509	0.000	0.808	0.478	0.611	68.150	65
			0.040	0.012	0.016	0.000	0.021	0.009	0.014	0.371	

Note: Standard errors are shown below the parameter estimates. The figures below the Sargan test statistics are corresponding p-values.

On the scale economies of blockbusters R&D, $\hat{\beta}_R$ ranges from 0.8 to 0.9. For the patent research process, the scale economy parameter $\hat{\alpha}_R$ is about 0.3. Thus, the scale economies are quite different between the two R&D outcome indices: the degree of scale diseconomy reduces greatly if we use blockbusters instead of patents as R&D outcome. This finding casts light on the fact that many previous researches concludes pharmaceutical R&D's scale diseconomy while there have been some M&A cases of the world's leading pharmaceutical companies.

On the dynamics of the R&D sub-processes, modeled as linear feedback in blockbuster development and conventional autoregressive process in patent research, $\hat{\alpha}_P$ and $\hat{\beta}_B$ are approximately 0.5 and 0.6, respectively. As in other LFM specifications, $\hat{\beta}_B$ can be easily interpreted that about 40% of blockbuster brands disappear every period, possibly by the reduction in their sales. For both of $\hat{\alpha}_P$ and $\hat{\beta}_B$, they are significantly different from zero, and thus the dynamic aspect of pharmaceutical R&D is implied as main source of intertemporal correlation of the R&D outcomes.

Since our model and MFK are common in the specification of conditional expectation functions except for the lagged dependent variables, we can easily compare the results of the two analyses.

First, our estimate $\hat{\beta}_R$ is quite similar to 0.9 in MFK, while our $\hat{\alpha}_R$ is nearly half of that reported in MFK. It strengthen the result of MFK that the patent research process requires less scale in operation than the blockbuster development process does, since our model is a superset of MFK in the sense that it extends the flexibility of the model to handle the dynamics.

Second, on the relation between $\hat{\beta}_P$ (the elasticity of blockbuster with respect to patent) and $\hat{\beta}_R$, we obtain a result that the former is smaller than the latter, implying limited effect of patents on blockbusters. This result is nearly same as that of MFK, except that our estimate $\hat{\beta}_P$ =0.5 is a bit larger than 0.4 in MFK. Therefore, it implies that for the big pharmaceutical companies the development of blockbusters requires more investment scale of its own than the patent research sub-process does, rather than concentrating on patent research and simply expecting the patents to grow to blockbusters.

4. CONCLUDING REMARKS

Our results of joint estimation of blockbuster and patent equations can be summarized as follows: (i) the blockbuster development sub-process shows weak diseconomies of scale (that is, close to constant returns) while the patent research sub-process shows clearly diseconomies of scale; (ii) the difference between the scale economies of the two sub-processes is widened if we explicitly take into account the dynamic aspect of pharmaceutical R&D; (iii) the linear feedback coefficient is 0.6 which implies 40% of blockbusters become non-blockbusters in the subsequent years, and (iv) the quantitative connection between the patent and the blockbuster measured by elasticity of the blockbusters is smaller than the direct effect of development expense on blockbusters.

These results are well contrasted by the previous studies in the following points: though the previous studies suggested diseconomies of the scale in the pharmaceutical R&D, we come to different conclusion if we replace the R&D outcome index with blockbusters which is directly important to for-profit companies. This finding is very useful in considering series of M&A that has taken place among the world's big pharmaceutical companies.

Future research should enhance the sample to include other pharmaceutical companies which have shorter history of data or has been involved in any M&A, by explicitly incorporate the synergy effect caused by M&A to the model.

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