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ORIGINAL PAPER

Measuring the efficiency of large pharmaceutical companies: an industry analysis

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Abstract This paper evaluates the relative efficiency of a sample of 37 large pharmaceutical laboratories in the period 2008–2013 using a data envelopment analysis (DEA) approach. We describe in detail the procedure followed to select and construct relevant inputs and outputs that characterize the production and innovation activity of these pharmaceutical firms. Models are estimated with financial information from Datastream, including R&D investment, and the number of new drugs authorized by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) considering the time effect. The relative performances of these firms—taking into consideration the strategic importance of R&D—suggest that the pharmaceutical industry is a highly competitive sector given that there are many laboratories at the efficient frontier and many inefficient laboratories close to this border. Additionally, we use data from S&P Capital IQ to analyze 2071 financial transactions announced by our sample of laboratories as an alternative way to gain access to new drugs, and we link these transactions with R&D investment and DEA efficiency. We find that efficient laboratories make on average more financial transactions, and the relative size of each transaction is larger. However, pharmaceutical companies that simultaneously are more efficient and invest more internally in R&D announce smaller transactions relative to total assets.

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Introduction

Managing a research and development (R&D) portfolio of new drugs in the pipeline is a challenging task that involves an active selection and reallocation of resources. In order to be efficient, pharmaceutical laboratories should decide upon strategic issues regarding the laboratory size, internal and external growth options and synergies, and diversity of innovative drugs in each therapeutic area. This decision making should take into consideration the R&D strategies of their competitors.

In this regard, large pharmaceutical laboratories have two nonexclusive alternatives for managing their portfolio of new drugs in an efficient way. They may develop new drugs internally, but simultaneously they may also engage in mergers and acquisitions (M&As)—or other financial transactions—to obtain new drugs or to change the composition of their portfolio of promising drugs (sometimes simultaneously selling new drugs and buying other types of new drugs); see Fig. 1.

Thus, the market for technology is a way to both acquire and sell knowledge [3] either through collaboration (co-research, co-development, or other collaborations), licensing or (and) trough financial transactions. Nishimura and Okada [47] examine how R&D portfolios of Japanese pharma labs affect licensing decisions (license out and inward licensing). They observe drug pipelines quite accurately due to the rigorous regulatory process of clinical

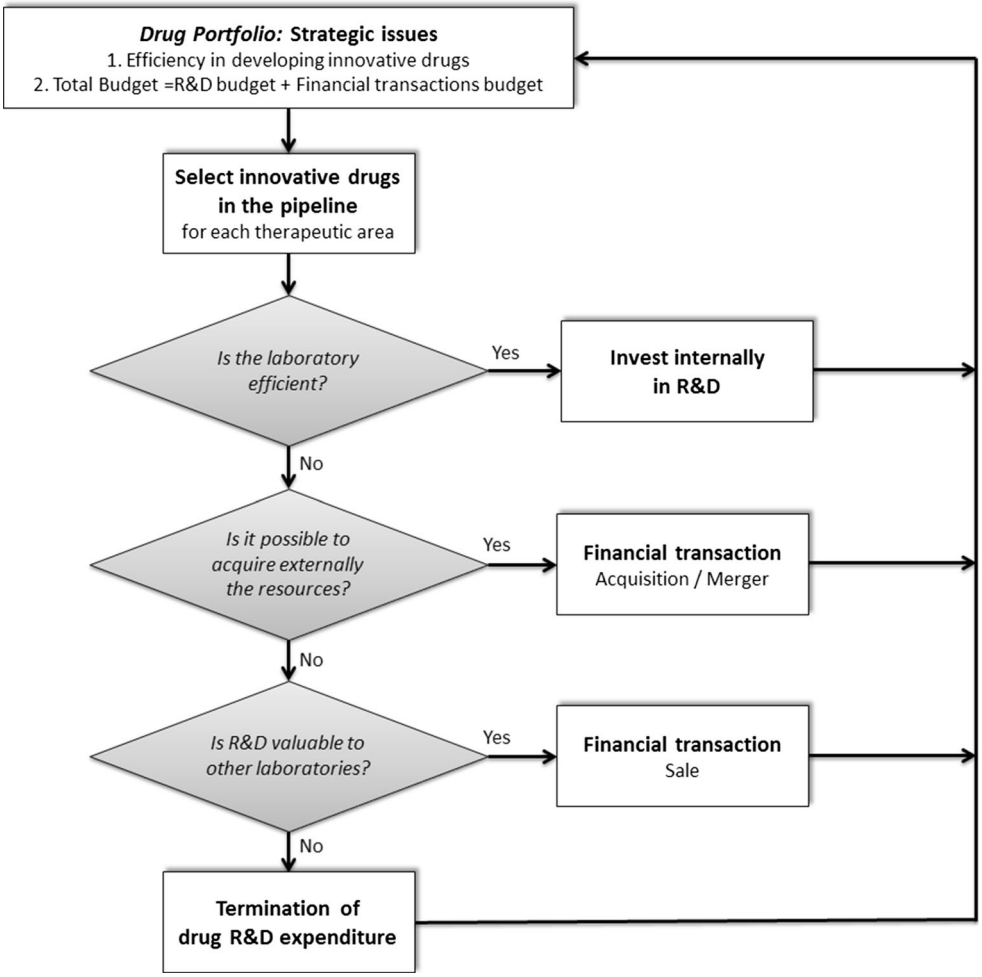

Fig. 1 Internal and external R&D management of drug portfolio

testing. They conclude that drug pipelines may dictate a licensing decision as a result of portfolio adjustment across different stages.

A second alternative to buy (and also sell) knowledge is through financial transactions. In this paper, we measure relative efficiency of pharmaceutical labs and then perform several regressions to test whether efficient labs announce more or less financial transactions than inefficient labs in order to realign their R&D portfolios.

To the best of our knowledge, regarding the measurement of efficiency of pharma labs, the only contribution similar to this paper is the one by Shimura et al. [52], where large pharmaceutical firms are categorized into four groups (on the basis of their respective R&D efficiency) and two dimensions (one based on DEA efficiency scores and the other based on effectiveness scores) in order to analyze R&D productivity. They consider new molecular entities from 21 global pharmaceutical companies in the period 2002–2007 from a database provided by Barclays capital. However, many new drugs in the pipeline do not reach Phase III and some drugs reach it faster than others, so the R&D activity of a pharmaceutical laboratory is composed of both successful and unsuccessful drugs. These authors account for this by considering R&D expenditure and net present value.

The DEA efficient frontier in our output-oriented model comprises laboratories that perform better than others. A laboratory in the sample is efficient, given its inputs, if it is not possible to find a linear combination of laboratories in the sample having the same inputs and yielding higher outputs. In our case, we use information about successful new drugs from medicines authorized by the EMA and the FDA but in our models we also consider financial information from Datastream, aiming to take into consideration both short-term and long-term indicators of the success of R&D activity. So, accounting information, market information, and data about new authorized drugs are combined in our DEA efficiency models. In the case of new authorized drugs, we take the time effect into account in a more precise manner. We focus exclusively on DEA efficiency scores, and our objective is to extract as much information as possible from them.

Regarding internal and external R&D activity, Comanor and Scherer [16] indicate that, in response to lagging innovation, some companies have sought refuge in M&As. Shimura et al. [52] in their 2002–2007 sample, showed that companies with lower R&D relative to efficiency were more likely to engage in consolidation.

Higgins and Rodriguez [32] focus on the acquisition of knowledge by examining the performance of 160 pharmaceutical acquisitions from 1994 to 2001 and find that on average acquirers realize significant positive returns. These returns are positively correlated with prior acquirer access to information about the R&D activities at target firms and a superior negotiating position. They also find that firms experiencing declines in internal productivity or which are more desperate are more likely to engage in an outsourcing-type acquisition in an effort to replenish their research pipelines.

Girotra et al. [26] indicate that value of an R&D project depends not only on its properties but also on the other R&D projects being developed by the pharma lab. They conduct an event study around the failure of phase III clinical trials and their effect on the market valuation of the lab. They find that the presence of other R&D projects targeting the same market and a build-up of projects that require the same development resources reduce the value of an R&D project.

Hagedoorn and Wang [31], using a panel sample of 83 incumbent pharmaceutical firms during the period 1986–2000, find that internal R&D and external R&D, through either R&D alliances or R&D acquisitions are complementary innovation activities at higher levels of in-house R&D investments, whereas at lower levels of in-house R&D efforts, internal and external R&D turn out to be substitutive strategic options. Kang et al. [38] show that external technology acquisition has an inverted U-shaped relationship with subsequent technology innovation performance, and that is not complementary to internal R&D activities.

Bena and Li [7], using a large sample of acquirers with patents and targets with patents over the period 1984–2006, focus on corporate innovation activity as a source of synergy. They find that firms with large patent portfolios and low R&D expenses are more likely to be acquirers, while R&D-intensive firms with slow growth in patent output are more likely to be acquired. Also, technological overlap between firms' innovation activities has a positive and significant effect on the likelihood of a merger pair formation. The likelihood of a merger is reduced for firm pairs that also overlap in product markets. Finally, they show a positive treatment effect of a merger on post-merger innovation output when there is premerger technological overlap between merging firms. They conclude that synergies obtained from combining innovation capabilities are an important motivation for corporate acquisitions. The findings of their paper suggest several new directions for future research and they mention first that their paper highlights that many merger transactions are driven by efficiency motives.

Our paper tries to contribute to previous literature relating lab efficiency as a whole to internal and external R&D strategies. The novelty of our approach is that we consider large laboratories from different countries and, simultaneously, we combine in a novel way alternative sources of data—Datastream, the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA)—to select and construct relevant inputs and outputs that characterize the production and innovation activity of large pharmaceutical companies. Previous papers have estimated either DEA efficiency or DEA total factor productivity of pharmaceutical laboratories, but most of them consider laboratories from a single country [27, 33, 43] or consider innovation in several countries but the unit analyzed is not the pharmaceutical laboratory but the country itself [29, 50].

In addition, when measuring R&D efficiency of either countries or pharmaceutical firms, most previous papers consider the number of patents as a proxy for R&D output [19, 30, 37]. In our study, as a proxy for R&D output we consider not only the number of new chemical entities (excluding generics) approved by the EMA and the FDA for each laboratory, but also we adjust this figure considering the specific date of authorization of each approved medicine. Although studies considering patents adjust for the quality of patents by considering the number of times that a patent has been cited, in our case only the most successful new drugs in the pharmaceutical pipeline (after a successful Phase III evaluation) are approved by the EMA and/or the FDA, so we consider this measure to be a better proxy for successful R&D than patents.

We consider a common efficiency frontier for large pharmaceutical firms irrespective of their country of origin given that they compete with each other when trying to obtain new drug authorizations from the EMA and/or the FDA. Also, firms with authorized medicines sell the same chemical entities in many different countries, and global investors in the pharmaceutical sector analyze the big laboratories' returns and risks when deciding on portfolio weight and diversification issues. So pharmaceutical companies are global in several dimensions.

After dropping laboratories with any missing values, we end up with a final sample of 37 large firms. If these are compared with the Datastream sample of 241 companies, our sample accounts for more than 80 % of market value, net sales and net income. Thus, we believe that our 37-laboratory sample is significantly representative of the pharmaceutical industry.

This article aims to measure first the relative efficiency of a sample of 37 large pharmaceutical laboratories from different countries, which can be considered representative of this industry, in the period 2008–2013 using a Data Envelopment Analysis (DEA) non-parametric approach. Our results suggest that the pharmaceutical industry is a competitive sector with many laboratories at the efficient frontier and many inefficient laboratories close to the frontier. Then, we split our sample into efficient labs and inefficient labs and we analyze in detail financial transactions announced by efficient and inefficient labs.

The paper proceeds as follows. "Efficiency measurement in pharmaceutical firms" describes efficiency measurement in pharma labs, "DEA efficiency: Results and discussion" discusses DEA efficiency results, and "M&A activity and other financial transactions by pharmaceutical laboratories" analyzes M&A as well as other announced transactions by efficient and inefficient pharmaceutical laboratories. Conclusions are drawn and suggestions for future research are given in "Conclusions".

Efficiency measurement in pharmaceutical firms

The development of a globalized economy has led to a new environment, in which international competitiveness has become fierce and where the concept of 'efficiency' has become strategically important. The pharmaceutical sector, in which R&D is key, is no exception and competition in it has increased dramatically. So, given the importance of this industry from both the political-economic and the ethical-healthcare points of view, this paper aims, as a first step, to measure the efficiency of large pharmaceutical firms.

The pharmaceutical industry is very important not only in health terms but also in economic terms, so it is relevant to study its internal and external R&D activity at both industry and laboratory level, and from the perspectives of public [9] and private funding of R&D. In addition, pharmaceutical companies have engaged in R&D collaboration not only with other laboratories but also with other firms and universities [45]. According to the IMS Institute [35], spending on medicines will reach nearly 1.3 trillion USD in 2018. This would mean an average annual growth of 6 % over the period 2009–2018. The pharmaceutical industry is therefore a key sector. Few other industries can match its contribution to investment in R&D, trade balance, and creation of skilled employment.

Nonetheless, this sector faces major challenges in the current context. In addition to regulatory hurdles and escalating R&D costs, it has been severely hit by the impact of fiscal austerity measures. How pharmaceutical companies –and related stakeholders—approach these problems may impact both the worldwide economy and the future health of the world population.

In this concentrated industry, the ten largest pharmaceutical laboratories represent approximately one-third of the global market. Six of them are from the US, while the remaining four are from Europe. A study by the IMS Institute [34] highlights that, although there has been rapid growth in emerging economies (such as Brazil, China, and India), North America and Europe currently account for more than 50 % of global spending, which justifies the use of the EMA and the FDA in this study.

Regarding the analysis of efficiency in the pharmaceutical sector, most of the literature has centered on Asian countries. One of the earliest studies was by Honjo and Haneda [33], who analyzed the efficiency of 14 Japanese pharmaceutical firms over the period 1977–1991 with a DEA model comprising one input and two outputs.

You et al. [59] measured the efficiency of pharmaceutical firms and identified their determinants using Korean and American samples. They used four different types of efficiency (cost, allocative, technical and scale) based on DEA and, by means of regression techniques, studied the impact of ownership structure, R&D investment, and scale economies. Mao et al. [43] evaluated the business performance of thirty-four Chinese pharmaceutical companies using DEA. They considered three inputs (size of the workforce, administrative expenses, and gross assets), and one output (operating revenue). This study concluded that the overall efficiency of this sector in China was not high. Other studies have used this methodology to rate pharmaceutical firms in India [44] and Iran [36].

In this sector, innovation is of special importance from a health perspective, so the importance of R&D should be considered in the analysis. Wang and Huang [56] evaluated the relative efficiency of R&D activities across countries. These authors used patents and academic publications as outputs. Hashimoto and Haneda [30] focused on the R&D efficiency of pharmaceutical companies in Japan and considered that the efficiency frontier shifted over time. As an input, they used R&D expenditure and considered three outputs: patents (as a proxy of invention), pharmaceutical sales (as a proxy of product innovation), and operating profit (as a proxy of process innovation). Shimura et al. [52] used one input (R&D expenditure) and three outputs (sales, operating profit, and the accumulated number of weighted new molecular entities approved by the Japanese Ministry of Health) to measure R&D productivity. Cruz-Cáceres et al. [19] discussed the relationship between innovation and performance and proposed a new approach to tackle it, using R&D capital stock and highly skilled staff as innovation inputs, and new products and patents as innovation outputs.

DEA optimization technique

A company's business efficiency can be defined as the relation between the value created and the resources used for creating it [6]. It is a broad term that can be assessed by considering a single ratio or by means of several inputs to consider resources employed and outputs to express value creation.

When measuring the efficiency of a company, the literature offers a wide variety of alternatives for inputs and outputs depending on the authors' approach. A general pattern does exist, however. Input variables tend to represent investment metrics, both tangible—such as number of employees, number of branches, and administrative expenses [58]—and intangible—like product and process knowledge [2]. On the other hand, output variables are generally key performance indicators, both in absolute—such as profit, market share, and market value [55]—and in relative terms—like profit ratio, return on assets, and B/M ratio [57].

Under these circumstances, DEA is a common approach for studying business efficiency. Cooper et al. [18] define DEA as a "data-oriented approach for evaluating the performance of a set of peer entities that convert multiple inputs into multiple outputs". For this reason, this technique has been used to measure relative efficiency in different kinds of entities, such as hospitals [11, 41], universities [51], retail stores [55], banks [58], airports [48], holdings [57], and sport teams [24].

Figure 2 outlines the approach followed for assessing the efficiency of pharmaceutical companies. It is mainly based on a four-step process. The first one is the study of strategic issues—the pharmaceutical sector (and its distinctive features) and DEA-based techniques. The second one aims to determine how efficiency must be measured in this environment. Note that DEA allows the efficiency of companies to be measured from a multidimensional perspective, so several inputs and outputs are defined. The third one is the construction of the DEA model under two different assumptions: constant returns-to-scale (CRS) and variable returns-to-scale (VRS). In the last step, results are analyzed from a double perspective. On the one hand, the efficiency of a relevant sample of the world's leading pharmaceutical companies is evaluated, which is the main goal of the paper. On the other hand, the peers, i.e., references at the frontier for inefficient firms, are discussed.

Additionally, and as intermediate steps in the evaluation process, data, results, and consistency must be checked. Data are checked to verify that the DEA model can operate with the defined combination of inputs and outputs (e.g., with non-negative values, or with constraints in the available data), while results are checked to study the representativeness of the solutions. Finally, consistency is checked to ensure that the results are sufficient to draw conclusions, so a number of models are created. For reasons of space, in this paper we only discuss the three final models. The whole process was carried out during 5 months, with weekly meetings of an interdisciplinary group of five people, some of them experts in the methodology and others with proven knowledge of this sector.

In the original study by Charnes et al. [13], DEA is described as a "mathematical programming model applied to observational data that provides a new way of obtaining empirical estimates of relations—such as the production functions and/or efficient production possibility surfaces—that are cornerstones of modern economics."

DEA is a non-parametric frontier-efficiency method using a linear programming technique for measuring performance. It assesses the relative efficiency of a set of decision making units (DMUs), pharmaceutical laboratories in this study, that are engaged in performing a similar function using a set of inputs (related to investment by the firms) to produce a set of outputs (indicators of their performance). When a DMU maximizes the relationship between outputs and inputs, it is located on the frontier, and is regarded as an efficient unit (100 %). If not, the relative efficiency of the DMU is measured in the interval (0, 100 %) subject to the absolute efficiency of the DMUs on the frontier, which reveals that this efficiency could be improved by changing the proportion among inputs. Subsequently, the DMUs can summarize the quantitative index of overall efficiency and hence can be ranked by scale.

DEA has been widely used by researchers in a number of fields for modeling operational processes for performance evaluations, in governmental and nonprofit sectors and in regulated and private sectors. These multiple applications were supported by further development by Zhu [60], who tested a number of DEA models that can be used in performance evaluation and frontier estimation.

DEA can be carried out under the assumption of CRS or VRS—i.e., by introducing a scale constraint in the model, hence DMUs are not penalized for operating at a non-optimal scale [4].

Under the VRS approach, the CCR model (from the CRS approach) [13] becomes the BCC model if the convexity constraint is added. This classic DEA-based model in its output-oriented form to measure efficiency is formulated by (1), where n is the number of DMUs (general index i, while l is the index of the specific DMU whose efficiency is being assessed), m is the number of inputs (general index j), p is the number of outputs (general index k), λ_i are the multipliers used for computing linear combinations of the DMU's inputs and outputs (i.e., the model's decision variables), x_{ij} is the observed amount of input

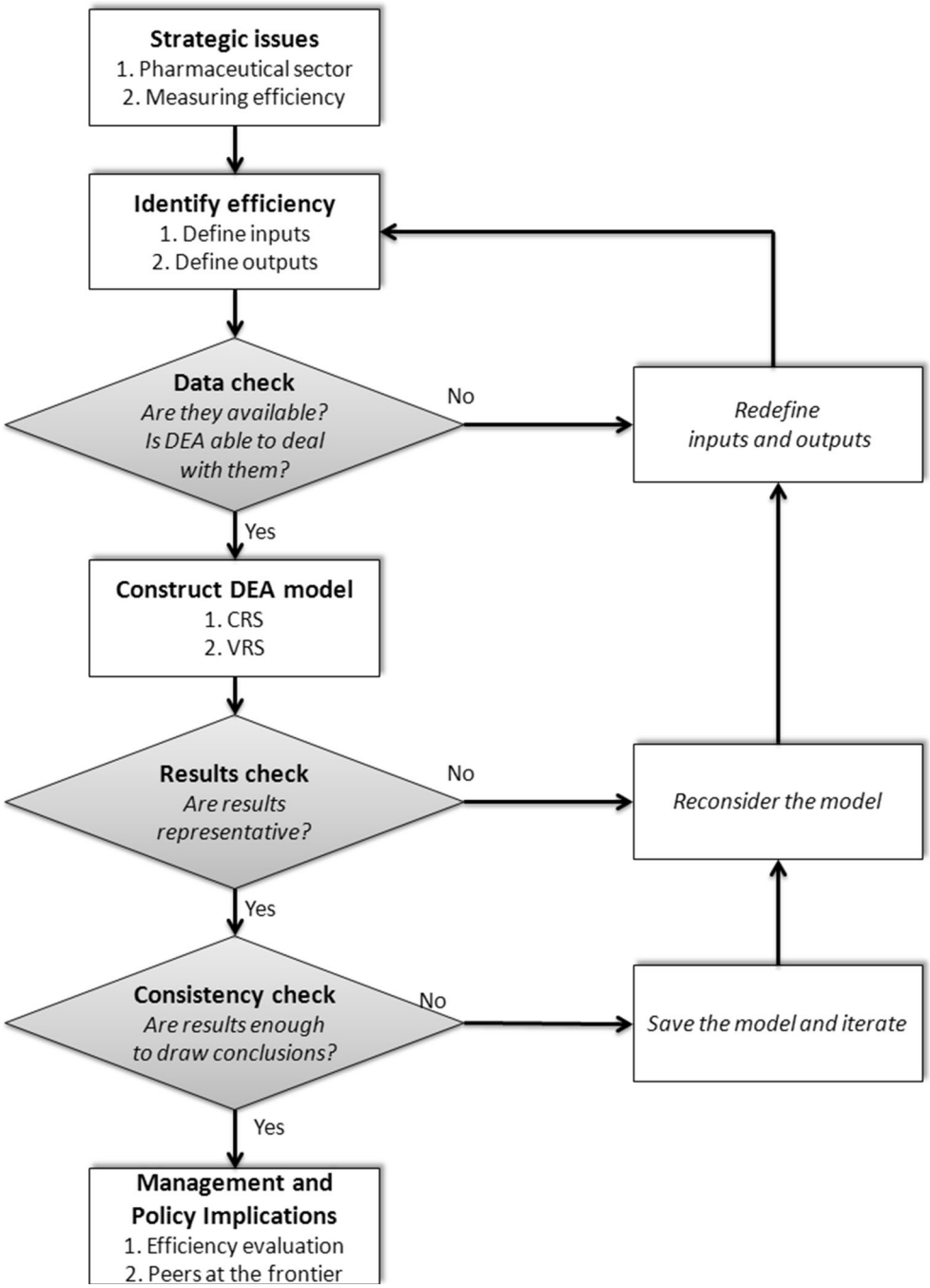

Fig. 2 Evaluation process of the laboratories' efficiency

j of DMU i, and y_{ik} is the observed amount of output k of DMU i. Note that φ^* refers to the optimal efficiency score of a DMU. That is, if $\varphi^* = 1$, DMU l is technically efficient. Note that both the CCR and the BCC models are radial projection constructs for characterizing efficiency, unlike other models such as non-radial ADD [14]. Finally, both models are invariant to the units of measurement. Maximize:

$$\varphi^* = \max\varphi$$

Subject to:

$$\begin{aligned}
&\sum_{i=1}^{n} \lambda_i x_{ij} \leq x_{lj}; \quad \text{for } j = 1, 2, \ldots, m \\
&\sum_{i=1}^{n} \lambda_i y_{ik} \geq \varphi y_{lk}; \quad \text{for } k = 1, 2, \ldots, p \\
&\sum_{i=1}^{n} \lambda_i = 1; \quad \text{for } i = 1, 2, \ldots, n \\
&\lambda_i \geq 0; \quad \text{for } i = 1, 2, \ldots, n.
\end{aligned} \tag{1}$$

The work by Barr [5] can be consulted to decide between the technological choices that are currently available to implement DEA. In order to estimate relative

efficiencies under the standard CRS and VRS models we used the DEAP software developed by Professor Tim Coelli. In particular, to solve the linear programming problems this study used DEAP 2.1 software [15], which is also valid for computing Malmquist DEA, i.e., for calculating indices of total factor productivity (TFP).

Some studies estimate Malmquist productivity indexes (TFP indexes) using DEA and break them down into sources of productivity change. We did not calculate TFP given that a data set with no missing values is needed in all the relevant years (from 2008 to 2013 in our case). The Malmquist productivity index was introduced by Caves et al. [12] as the ratio of two distance functions pertaining to distinct time periods. There are several alternative ways to compute TFP. For a discussion and for an empirical example applied to pharmaceutical laboratories in Spain, see [27]. For a study on the dynamics of technological innovation, see [1].

Data selection and DMUs

This research uses data within the 2008–2013 time period obtained from three main sources: the FDA, the EMA, and Datastream. The FDA and the EMA are responsible for protecting and promoting public health in the US (the former) and the EU (the latter) through the regulation and supervision of medicines. They require that each new medicine is evaluated through various phases of clinical trials. Both agencies maintain a historical database with all medicines approved.[1] Data was also taken from Datastream, a global financial and macroeconomic database.

Initially, we focused on a list of 241 large pharmaceutical laboratories taken from Datastream (TR GLOBAL PHARMA list) and generated on June 4, 2014. All financial information from large laboratories from different countries was generated in USD.

We then identified the Datastream constituents with financial information in the study period 2008–2013 and computed an average for each of the financial variables considered over the study period. We chose an average in order to deal with possible missing values in any given year for specific laboratories. We also considered the sum of all values for each variable (instead of the average) with no significant changes in efficiency estimates.

Subsequently, we searched for Datastream laboratories with new chemical entities approved by the EMA and FDA during the study period (at least one drug authorized in the period 2008–2013 by EMA or FDA). Our final sample is made up of 37 pharmaceutical laboratories, which are the DMUs in our research, with full Datastream information and also with new drugs approved by the EMA and/or FDA in the period 2008–2013.

Given that there were 241 pharmaceutical laboratories in the original Datastream list and that a balanced data set with no missing values in any of the variables is needed in order to estimate DEA relative efficiencies, two important issues must be taken into account in order to try to assure that our final sample of 37 laboratories represents the large pharmaceutical sector.

The first is to know if the economic activity of our sample of 37 large laboratories represents a large proportion of the total activity of the pharmaceutical laboratory sector. The second is related to the absence of a time dimension in our DEA model because a time dimension is only included in our DEA analysis when discounting the number of days that a new drug has been authorized.

To address both issues, we compared the market capitalization, net sales, and net income of the Datastream list of 241 laboratories versus those of the final 37 laboratories year by year. Our 37 laboratories were seen to represent 80 % of the market value of the 241 laboratories, and similar figures were obtained for net sales and net income. Thus, this analysis suggests that our 37 laboratories represent a large proportion of the large pharmaceutical companies' economic activity. However, the time effect over the period 2008–2013 shows that laboratories excluded from the 37 gained increasing importance in terms of creating value, increasing sales and increasing net profit. The details are shown in Table 8 of "Appendix 1".

Given that the number of new drugs authorized by the EMA [22] or the FDA [23] per year is very small, we accounted for the aggregate number of drugs authorized to each laboratory over the whole period 2008–2013. It must be stressed that we only consider innovative drugs, i.e., generic drugs are NOT taken into consideration and are totally excluded from our analysis. If we had considered new drugs authorized per year, we would have had to rule out additional laboratories every time they had no authorized new drugs in a given year and we would not have been able to compute the DEA efficiencies at the year level for such laboratories.

Description of variables: inputs and outputs

In this non-parametric DEA approach aimed at measuring the relative efficiency of pharmaceutical laboratories, we used different combinations of inputs and outputs in order to measure the performance of the laboratories and applied sensitivity techniques to verify the consistency of the

[1] Large pharmaceutical companies operate globally, so they market their innovative drugs in more markets than Europe and the USA. Thus, our measure for innovative drugs that have been authorized by the EMA and the FDA for a given laboratory is a proxy for the expected authorization of the same innovative drug for other markets. Europe and USA are two key markets, and an innovative drug can be expected to be innovative in all the relevant markets. Given that laboratories operate globally, we consider our proxy to be a good one.

results. This selection of the inputs and outputs of the model is a key part of a DEA study. The larger the number of inputs and outputs, the less discriminatory the model becomes. Boussofiane et al. [8] stated that, as a rule of thumb, in most situations satisfactory discrimination is obtained if the number of units in the assessment set (DMUs) is three times the number of inputs times the number of outputs. Cooper et al. [17] uphold that the number of DMUs should be at least three times higher than the number of inputs and outputs. The more inputs and ouputs included in a DEA model, the higher the relative efficiency and the higher the number of laboratories that are likely to be at the efficient frontier. There should be a balance between including all relevant inputs and outputs and being able to differentiate between efficient and inefficient labs.

Seven variables were used in the final models to measure the business efficiency of large pharmaceutical firms in the period 2008–2013. Three of them were considered inputs, and another three outputs. The remaining one was considered both an input and an output in different models as it may be understood either way.

The inputs (I1, I2, I3) represent proxies of the investment in innovation by the pharmaceutical firms:

- *Size of the workforce (I1–SW)* This refers to the average number of employees in the company (including all the business functions) in the above-mentioned period.
- *Total assets (I2–TA)* This is expressed as the average assets (land cost, building cost, inventory, machine and equipment, and so forth) of the company in the above-mentioned period, which represent a measure of the total size of the company.
- *Investment in R&D (I3–IRD)* This is the average expenditure by the company on R&D from 2008 to 2013.

The outputs (O1, O2, O3) are common indicators, related to the firms' main goals:

- *Net profit (O1–NP)* This variable considers the average net results (i.e., after depreciation, amortization, interest, and tax) in the period 2008–2013.
- *Market capitalization (O2–MC)* This refers to the average market value of the company from 2008 to 2013. Unlike the previous variable, this one takes into account not only the company's current results, but also its expectations for the future.[2]
- *Total sales (O3–TS)* This is expressed as the average sales of the company within the above-mentioned time period and contains information on one of the key indicators in companies, market share.

Many of our 37 laboratories have zero drugs authorized in a given year and DEA requires a balanced data set in order to compute the frontier and estimate relative efficiencies. Given that we take averages for financial data, we also had to add up all the new drugs during the period. One simple alternative would have been to directly consider the number of new chemical entities authorized by EMA and/or FDA during the study period from 2008 to 2013. However, it is not the same to have a new drug authorized at the beginning of the study period (generating cash flow during the whole period) than at the end of the study period. We show in Table 9 of "Appendix 1" the evolution over time of new drugs authorized by EMA and/or FDA. We also show the accumulated number of days until 31st December 2013 and the number of days discounted. To account for this time effect, we computed a new variable that we define below.

In any case, it is striking from our authorized drug sample summarized in Table 9 that the number of new drugs authorized by the EMA, in any of the years between 2008 and 2013, is higher than the number of new drugs authorized by the FDA. We carefully double-checked our database and, to the best of our knowledge, we believe that the authorized drug information has been extracted correctly. Thus, our interpretation of the available data is related to the fact that there is not a clear-cut difference between a really new chemical entity and a generic drug. There is a grey zone in between for drugs that are not a radical innovation but an incremental innovation. This may explain why in Table 9 of the Appendix, the EMA has more authorized new drugs than the FDA. The EMA database includes generic and non-generic drugs and provides a field named "generic", while the FDA separates new chemical entities from the rest.

As mentioned above, one variable is considered both an input and an output:

- *Number of days of authorized innovative medicines considering the time effect (I4/O4-NDAIMCTE)* A simple approach for considering new authorized drugs in the analysis would have been just to count the number of authorized drugs per laboratory during our study period. However, we wished to take into account the time effect. Thus, *NDAIMCTE* refers to the number of days that each innovative medicine has been authorized in the US and in the EU until the end of the period (or until the date of removal, if the medicine is no longer sold), taking into account the time effect – in order to consider the decline in innovation in medicines as time passes.

[2] Market capitalization is the result of a consensus in the market about current cash flows and expected future cash flows. In the case of pharmaceutical labs, it takes into account innovative drugs that are in the pipeline but have not yet been authorized because they are in the different phases of clinical research (Phase I, Phase II, Phase III), as well as some innovative drugs that have been authorized but are still in postmarketing surveillance (Phase IV).

Note that, although both the EMA and the FDA also provide information for new generic drugs, which are a very important part of the pharmaceutical drugs picture [25], there were substantial differences between EMA generic authorizations and FDA generic authorizations. This is because the FDA considered many minor changes as new authorizations so these were not directly comparable to EMA generic authorizations.

This final variable was devised from the initial variable 'number of authorized innovative medicines', with the aim of checking consistency in the results. After exploring several alternatives, the time effect—required for modeling the passing of time on the effect of an innovative medicine on company profits—was introduced by means of a mathematical function expressed in (2). Equation (3) represents the value of this variable for each medicine. Afterwards, the local results were added to obtain the global value of each laboratory. Note that t_F refers to the end of the period (December 31, 2013) or date of removal and t_0 represents the date of authorization. After testing several alternatives, the parameters were set at the values $k_1 = 0.000632208$ and $k_2 = 0.01$.

$$f(t) = 1 - k_2(e^{k_1(t-t_0)} - 1) \tag{2}$$

$$\begin{aligned} \text{NDAIMCTE} &= \int_{t_0}^{t_f} \left[1 - k_2\left(e^{k_1(t-t_0)} - 1\right)\right] \mathrm{d}t \\ &= \int_{0}^{t_f - t_0} \left[1 - k_2\left(e^{k_1 \Delta t} - 1\right)\right] \mathrm{d}\Delta t \\ &= \left[(1+k_2)\Delta t - \frac{k_2}{k_1} e^{k_1 \Delta t}\right]_0^{t_f - t_0} \\ &= (1+k_2)(t_f - t_0) - \frac{k_2}{k_1} e^{k_1(t_f - t_0)} + \frac{k_2}{k_1}. \end{aligned} \tag{3}$$

Table 1 presents the descriptive statistics of the seven variables considered for the database comprising 37 pharmaceutical laboratories.

The dataset for the 37 pharmaceutical laboratories and the seven relevant variables (inputs and outputs) for the different DEA models are given in Tables 11 and 12 of "Appendix 2".

Models

The iterative process followed led to the consideration of three models that are summarized in Fig. 3.

Model I only considers the six macroeconomic variables (three inputs and three outputs) explained above. Models II and III take into account the NDAIMCTE variable: model II as an input, and model III as an output. A double approach is adopted for this variable according to the following interesting interpretations:

- NDAIMCTE can be understood as an input, because the more approvals of medicines the laboratory has, the more its outputs can be expected to improve (more sales, more net income, and more market value). That is to say, this approach considers that the authorization of a medicine makes sense only if reflected in these indicators.
- NDAIMCTE can be considered an output, because the higher the inputs (the more employees the laboratory has, the bigger the investment, and the more investment in R&D), the more authorizations of medicines it can expect. In other words, if this variable is set as an output, the model measures how efficient the laboratory is in developing new products. This approach, which considers innovative medicines as an output indicator, highlights the importance of innovation in this sector.

For the three models, we consider an output-oriented DEA model where there are as many objectives as output variables in each case- net profit, market capitalization, and total sales—and the issue of new drugs in model II.

It is also important to consider the relationship between the number of DMUs and the number of inputs and outputs in the model. Since the number of DMUs (37) is more than three times higher than the numbers of inputs and outputs (six in model I, and seven in models II and III), the Cooper et al. [17] criterion is verified, hence the models are appropriate. Regarding the Boussofiane et al. [8] criterion, satisfactory discrimination is obtained as the number of inputs is at least three times the number of inputs times the number of outputs (nine in model I, 12 in models II and III).

Table 1 Summary statistics for the database

Variable	Unit	Average	Min	Max	St. Dev.
I1-SW	Employees	34,788.61	272.5	120,300.00	39,910.4
I2-TA	Million USD	33,521.3	106.7	176,414.2	41,399.7
I3-IRD	Million USD	2601.5	0.6	9092.6	2743.6
O1-NP	Million USD	2829.2	1.6	12,150.8	3326.9
O2-MC	Million USD	44,847.0	136.7	190,890.1	49,688.5
O3-TS	Million USD	17,506.9	32.7	65,151.2	19,208.5
I4/O4-NDAIMCTE	Days	7368.3	111.7	43,543.9	9077.1

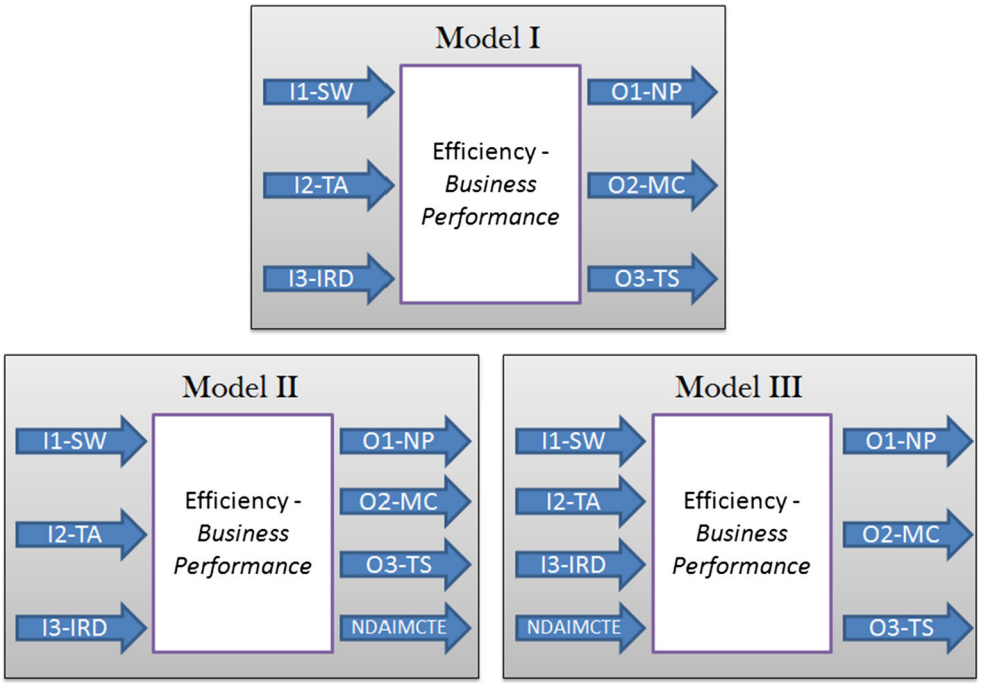

Fig. 3 Overview of the three final models

Note that our iterative process led us to study different alternatives. Our first approaches were based on considering the NDAIMCTE as a core output in the study. However, when considering new authorized drugs, not all of them are equally innovative or equally successful. Innovation is difficult to measure, while success is difficult to predict. Researchers approach this problem in different ways. Kesselheim et al. [39] perform a systematic search for papers measuring drug innovation characteristics and compare different approaches. Light [42] evaluates drug innovation from 1982 to 2003 in three geographic areas (the US, Europe, and Japan) by calculating the "research productivity", which is defined as the ratio of the number of new molecular entities (NMEs) to the amount of investment in R&D.

One way to capture this future uncertainty about the success of a new drug is based on including market capitalization as an output. Analysts following large pharmaceutical firms will recommend buying or selling shares according to the pipeline and future prospects of existing and yet to be drugs. On the other hand, current success of chemical entities is captured by total sales and net income. In summary, these three outputs (market capitalization, total sales, and net profit) are good proxies to capture the innovation and success of authorized new drugs.

The use of these variables is a common approach. In their variable returns to scale DEA model, Shimura et al. [52] utilize three variables to evaluate R&D productivity (cumulative R&D expenses in the period 2002–2007, number of new molecular entities and aggregate net present value). In our analysis, we had to decide whether to include only new chemical entities or to include both new drugs and generic drugs. After analyzing both databases (EMA and FDA), we decided to exclude generic drugs because, at the FDA, minor changes (i.e., in the prospect or leaflet) were included for generic drugs while this was not the case at the EMA.

DEA efficiency: results and discussion

The main efficiency results of this research are reported in this section. It should be clarified that, as previously explained, we evaluated the efficiency of the 37 pharmaceutical firms only under the VRS assumption because the CRS model is not valid given the importance of scale effects in the pharmaceutical industry.[3]

Table 2 re ports the main results of models I, II, and III under the VRS assumption, in which the overall ranking is not influenced by the size of the company. The relative efficiencies of the 37 pharmaceutical laboratories are displayed. Note that, firstly, this table points out the companies that are relatively efficient in model I, and, secondly, their significant change rates (greater than 5 % in model II) are highlighted in bold in models III and IV. Table 3 summarizes the main results.

[3] We thank one reviewer for this insight and suggestion.

Table 2 Efficiency of the pharmaceutical laboratories using DEA (models I, II, and III): VRS assumption

Company	Model I	Model II		Model III	
	Efficiency (%)	Efficiency (%)	Change rate (%)	Efficiency (%)	Change rate (%)
ABBOTT	100.00	100.00	0.00	100.00	0.00
ALLERGAN	86.30	86.30	0.00	96.30	**10.00**
AMGEN	100.00	100.00	0.00	100.00	0.00
ASTELLAS	100.00	100.00	0.00	100.00	0.00
ASTRAZENECA	95.20	97.00	1.80	95.20	0.00
BAYER	100.00	100.00	0.00	100.00	0.00
BIOGEN	88.20	88.20	0.00	100.00	**11.80**
BRISTOL	91.90	95.20	3.30	91.90	0.00
CELGENE	100.00	100.00	0.00	100.00	0.00
CELLTRION	100.00	100.00	0.00	100.00	0.00
CSL	100.00	100.00	0.00	100.00	0.00
EISAI	100.00	100.00	0.00	100.00	0.00
ELI LILLY	97.60	100.00	2.40	97.60	0.00
GILEAD	100.00	100.00	0.00	100.00	0.00
GLAXOSMITHKLINE	100.00	100.00	0.00	100.00	0.00
H. LUNDBECK	91.10	91.10	0.00	91.20	0.10
HOSPIRA	100.00	100.00	0.00	100.00	0.00
IPSEN	81.60	81.60	0.00	83.30	1.70
JOHNSON & JOHNS.	100.00	100.00	0.00	100.00	0.00
MEDA AB	100.00	100.00	0.00	100.00	0.00
MEDICINES COMP.	100.00	100.00	0.00	100.00	0.00
MERCK (KGAA)	100.00	100.00	0.00	100.00	0.00
MERCK & CO	82.80	91.50	**8.70**	82.80	0.00
MITSUBISHI	72.10	72.10	0.00	93.60	**21.50**
NOVARTIS	86.80	100.00	**13.20**	86.80	0.00
NOVO NORDISK	100.00	100.00	0.00	100.00	0.00
ORION	100.00	100.00	0.00	100.00	0.00
OTSUKA	95.10	95.10	0.00	96.30	1.20
PFIZER	100.00	100.00	0.00	100.00	0.00
REGENERON	100.00	100.00	0.00	100.00	0.00
RICHTER	70.20	70.20	0.00	82.60	**12.40**
ROCHE	100.00	100.00	0.00	100.00	0.00
SANOFI	75.00	81.60	**6.60**	75.00	0.00
SHIRE	97.60	100.00	2.40	97.60	0.00
TAKEDA	93.90	100.00	**6.10**	93.90	0.00
TEVA	100.00	100.00	0.00	100.00	0.00
UCB	52.10	75.40	**23.30**	52.10	0.00

The 'change rate' columns show in bold those companies whose improvement in efficiency is significant (greater than 5 %)

Table 3 shows that average efficiency rises to 93.45 % in model II, while the number of efficient companies amounts to 21. These are ABBOTT, AMGEN, ASTELLAS, BAYER, CELGENE, CELLTRION, CSL, EISAI, GILEAS GLAXOSMITHKLINE, HOSPIRA, JOHNSON & JOHNSON, MEDA AB, MEDICINES COMP., MERCK (KGAA), NOVO NORDISK, ORION, PFIZER, REGENERON, ROCHE and TEVA.

From Table 2, it is possible to see that—as expected—more companies are judged to be part of the efficient frontier in models II and III since the number of variables is greater, so efficiency is measured over more dimensions.

When the NDAIMCTE variable is added to the model, average efficiency tends to increase, because the model is less discriminatory. Nonetheless, the increase is slight: 1.83 % when it is considered an output, and 1.59 % when it is considered an input. The number of efficient firms increases to 25 in the first case, as ELI LILLLY, NOVARTIS, SHIRE, and TAKEDA become efficient. In the second case, the number of efficient laboratories increases to 22 as BIOGEN becomes a new member of the frontier.

It must be highlighted that, given the slight change when the NDAIMCTE variable is considered either as an output (only five firms increase their efficiency more than 5 %) or as an input (four firms in this case improve their efficiency more than 5 %), the robustness of model I under the VRS assumption is verified. Thus, our study can be interpreted as a realistic approach for measuring efficiency in the pharmaceutical industry.

Broadly speaking, the results provide evidence of the good position of pharmaceutical companies in terms of competitiveness in innovation. In model I, 31 out of the 37 companies analyzed in this study present a level of efficiency greater than 85 %. In models II and III, this number increases to 32.

Finally, Table 4 presents the DEA-based analysis of peers for models II, III, and IV under the VRS assumption. The benchmark peers of each pharmaceutical company refer to the efficient laboratories that are taken as references to calculate their efficiency. Note that benchmark peers are ordered from the most influential to the least influential. Obviously, the most efficient companies do not have benchmark peers.

M&A activity and other financial transactions by pharmaceutical laboratories

In the introduction, we have indicated that large pharmaceutical laboratories have two nonexclusive alternatives for managing their portfolio of new drugs and we have discussed previous contributions. Simultaneously, they may develop new drugs internally but they may also engage in mergers and acquisitions or other transactions to obtain new drugs or to change the composition of their portfolio of promising drugs (selling new drugs and buying other types of new drugs).

In this section, we discuss, first, the direct effect of M&A activity among laboratories with drugs authorized by EMA and FDA during our study period and, second, the effect of large and smaller transactions. We analyze the effect of large merger and acquisition (M&A) activity (with direct effects on the number of new drugs authorized by EMA and FDA) in the pharmaceutical industry during the period 2008–2013 and its potential effect on the estimated DEA relative efficiency of pharmaceutical laboratories. Some pharmaceutical laboratories acquire other innovative laboratories that have new chemical entity authorizations from the EMA and the FDA. If we restrict the mergers considered in [16] to those that occurred during our study period, there were four major mergers (Pfizer + Wyeth 2009, Novartis + Alcon 2009, Roche + Genentech 2009 and Sanofi + Genzyme 2011) with acquirers from our sample of 37 laboratories and targets with new drugs authorized by either FDA or EMA. After considering the four large successful M&As relevant for our research, eleven additional new chemical entities were included in the list of drugs authorized by EMA and FDA.

We then re-estimated our DEA models, and found very small changes (or none at all) in the relative efficiencies of pharmaceutical laboratories. Table 10 in the Appendix describes new drugs authorized by EMA and FDA to laboratories that do not belong to our sample of 37 laboratories but to laboratories that have been acquired by, or have merged with, any of our 37 laboratories.

In order to further address financial transactions by pharmaceutical labs, we also obtained much more detailed data on transactions announced by our 37 pharmaceutical laboratory sample in the period 2008–2013. We provide two summary tables (transactions announced by year and by pharmaceutical lab) including information about all announced transactions from the S&P Capital IQ transactions database performed by our sample of 37 pharmaceutical laboratories during the period 2008–2013. In total, 2071 transactions were announced by our sample of large pharmaceutical labs. Transactions include merger and acquisitions, private placements and buybacks (Table 5).

The total size of announced transactions during the study period for our sample of laboratories was 982,036 million USD. Given that for some of the 2071 transactions the size was not reported, this is a conservative figure (Table 6).

We split our sample in two. One subsample is made up of 21 efficient laboratories that are at the DEA frontier according to our DEA model I and the other is made up of the remaining 16 inefficient labs. Our sample of inefficient laboratories has an average efficiency of 84.8 %.

The size of the announced transaction was not available for all transactions (in smaller transactions some transaction details were not reported). Whenever this information was available, we used it to estimate the total size of these announced transactions for the two subsamples (efficient laboratories and inefficient labs).

We now make a simple comparison of these two subsamples. The total number of announced transactions is very similar in our two subsamples: 1025 announced transactions by 21 efficient laboratories, and 1046

Table 3 Summary of the results for models II, III, and IV under the VRS assumption

Company	Model I	Model II		Model III	
	Efficiency	Efficiency	Change rate	Efficiency	Change rate
Average	93.45 %	95.28 %	1.83 %	95.03 %	1.59 %
St Dev	11.02 %	8.59 %	4.64 %	9.63 %	4.61 %
Efficient firms (*)	21	25	(5)	22	(4)
Efficiency: [85, 100 %)	10	7		10	
Efficiency: [70, 85 %)	5	5		4	
Efficiency: [50, 70 %)	1	0		1	
Efficiency: [0, 50 %)	0	0		0	

The 'Change rate' columns show the number of companies whose improvement in efficiency is significant (greater than 5 %)

announced transactions by 16 inefficient laboratories. On average, each efficient laboratory made 48.8 transaction announcements during our study period while each inefficient laboratory made 65.4.

The average size of the announced transactions is higher for efficient laboratories (575,039 mm USD) than for inefficient laboratories (407,258 mm USD).

As a robustness check, we excluded Mitsubishi (an inefficient laboratory with 365 announced transactions) from the comparison given that this company is a conglomerate and some announced transactions are not directly related to the pharmaceutical sector. Once Mitsubishi is excluded, the total number of announced transactions is: 1025 transactions by all efficient laboratories (as before) and only 681 transactions by all inefficient laboratories in our sample. On average, each efficient laboratory made 48.8 transaction announcements during our study period (as before), while on average each inefficient laboratory (excluding Mitsubishi) made 45.4.

As an additional robustness test, we used yearly data on announced transactions during our study period to run two OLS regression s, see (4) and (5). The results are shown in Table 7, see respectively OLS 1 and OLS 2.

$$\frac{\text{Announced transaction SIZE}_{it}}{\text{Total assets}_i} = \beta_0 + \beta_1 \times \frac{R\&D_i}{\text{Total assets}_i} + \beta_2 \times \text{Efficiency}_i \quad (4)$$

$$\frac{\text{Announced transaction SIZE}_{it}}{\text{Total assets}_i} = \beta_0 + \beta_1 \times \frac{R\&D_i}{\text{Total assets}_i} + \beta_2 \times \text{Efficiency dummy}_i. \quad (5)$$

The dependent variable is the size of the total transactions per year per lab divided by average total assets of the lab during the study period. There are two independent variables: the ratio of R&D to total assets, and a measure of efficiency (either relative efficiency of each pharma lab during the whole study period or, alternatively, a dummy that takes value 1 when the pharma lab is at the frontier and zero otherwise).

In both cases, our two OLS regressions show that both R&D/TA and Efficiency (or efficiency dummy) have a positive and significant impact on the number of announced transactions relative to total assets. That is to say, the labs that invest more in R&D and that have with higher DEA efficiency strike more deals (more announced transactions relative to the size of the lab measured as total assets). Relative Efficiency is significant at the 1.5 % level and the efficiency dummy is significant at the 1 % level. R&D relative to total assets is also significant at the 1 % level in both OLS regressions.

Given our study period and considering only 36 laboratories, in our two OLS regressions, efficient laboratories make on average more transaction announcements, and the relative size of each transaction announcement is higher. Also, labs with more R&D relative to total assets strike more deals than labs with lower R&D relative to total assets.

We ran two additional OLS regressions with an interaction term in each regression, see (6) and (7) corresponding to OLS 3 and OLS 4 in Table 7.

$$\frac{\text{Announced transaction SIZE}_{it}}{\text{Total assets}_i} = \beta_0 + \beta_1 \times \frac{R\&D_i}{\text{Total assets}_i} + \beta_2 \times \text{Efficiency}_i + \beta_3 \times \frac{R\&D_i}{\text{Total assets}_i} \times \text{Efficiency}_i \quad (6)$$

$$\frac{\text{Announced transaction SIZE}_{it}}{\text{Total assets}_i} = \beta_0 + \beta_1 \times \frac{R\&D_i}{\text{Total assets}_i} + \beta_2 \times \text{Efficiency dummy}_i + \beta_3 \times \frac{R\&D_i}{\text{Total assets}_i} \times \text{Efficiency dummy}_i. \quad (7)$$

After including the interaction term, results continued to be significant and positive for the estimates of β_1 and β_2

Table 4 Benchmark peers of each pharmaceutical laboratory (models I, II and III): VRS assumption

Company	Ref.	Model I	Model II	Model III
ABBOTT	[1]	1	1	1
ALLERGAN	[2]	6-26-27-14	26-14-6-27	10-7-1-14-26-32
AMGEN	[3]	3	3	3
ASTELLAS	[4]	4	4	4
ASTRAZENECA	[5]	32-26-19-14	32-16-19-14-26	26-32-14-19
BAYER	[6]	6	6	6
BIOGEN	[7]	26-12-14-21	26-21-12-14	7
BRISTOL	[8]	14-32-3-19	35-14-15-32-19	14-3-19-32
CELGENE	[9]	9	9	9
CELLTRION	[10]	10	10	10
CSL	[11]	11	11	11
EISAI	[12]	12	12	12
ELI LILLY	[13]	26-32-19-14	13	19-32-26-14
GILEAD	[14]	14	14	14
GLAXOSMITHKLINE	[15]	15	15	15
H. LUNDBECK	[16]	4-26-12-21	4-27-26-12-21	14-26-4-21
HOSPIRA	[17]	17	17	17
IPSEN	[18]	26-27-21	21-26-27	21-26-10-14
JOHNSON & JOHNS.	[19]	19	19	19
MEDA AB	[20]	20	20	20
MEDICINES COMP.	[21]	21	21	21
MERCK (KGAA)	[22]	22	22	22
MERCK & CO	[23]	32-3-29-19	29-35-25-19	32-3-19-29
MITSUBISHI	[24]	6-14-26-27	26-14-6-27	1-7-10-32
NOVARTIS	[25]	14-19	25	14-19
NOVO NORDISK	[26]	26	26	26
ORION	[27]	27	27	27
OTSUKA	[28]	14-32-26-6	14-32-6-26	26-14-10-6-32
PFIZER	[29]	29	29	29
REGENERON	[30]	30	30	30
RICHTER	[31]	11-17-20-22	11-20-22-17	1-17-10-36-11
ROCHE	[32]	32	32	32
SANOFI	[33]	6-19-14	15-36-6-19	14-6-19
SHIRE	[34]	14-12-26-21	34	14-12-26-21
TAKEDA	[35]	14-3 -32	35	32-14-3
TEVA	[36]	36	36	36
UCB	[37]	6-14 -26 -27	25-34	26-6-27-14

Table 5 Transactions per year in the sample of 37 pharmaceutical laboratories

Company	Number of announced transactions	Total accumulated size
2008	346	154,762.56
2009	335	211,270.56
2010	338	159,756.12
2011	339	218,567.56
2012	369	106,518.07
2013	344	131,421.59
Overall	2071	982,296.46

and the estimate of the interaction term β_3 is significant but negative. We interpret the results as follows.

When we include the interaction term, the interpretation of this interaction term is that the labs that simultaneously are both more efficient and also invest more internally in R&D relative to total assets, announce smaller transactions relative to total assets of the lab (if you are very efficient and you invest more in R&D then you do not need so much to make more external acquisitions and other transactions).

One concern when interpreting the results of our regression results would be that R&D/TA is a ratio variable

Table 6 Transactions per pharmaceutical laboratory in the period 2008–2013

Company	Number of announced transactions	Total accumulated size
ABBOTT	39	80,697.08
ALLERGAN	20	3032.35
AMGEN	42	38,462.54
ASTELLAS	47	8434.67
ASTRAZENECA	53	31,058.81
BAYER	87	9978.34
BIOGEN	32	7735.07
BRISTOL	26	43,903.35
CELGENE	43	23,724.35
CELLTRION	8	156.41
CSL	0	0
EISAI	12	406.54
ELI LILLY	64	25,353.78
GILEAD	14	28,020.47
GLAXOSMITHKLINE	156	29,984.79
H. LUNDBECK	18	1767.05
HOSPIRA	11	1129.29
IPSEN	24	4743.54
JOHNSON & JOHNS.	168	64,503.65
MEDA AB	28	2341.58
MEDICINES COMP.	10	1909.29
MERCK (KGAA)	58	19,057.58
MERCK & CO	74	79,208.71
MITSUBISHI	365	42,644.27
NOVARTIS	158	83,839.67
NOVO NORDISK	28	11,698.79
ORION	5	459.63
OTSUKA	4	260.19
PFIZER	112	159,115.88
REGENERON	4	75.53
RICHTER	22	1104.19
ROCHE	83	64,088.58
SANOFI	87	43,349.41
SHIRE	35	8547.54
TAKEDA	48	28,933.18
TEVA	70	30,793.83
UCB	16	1776.53
OVERALL	2071	982,296.46

made up of two variables that are also inputs in our DEA efficiency models. Thus, it is important to check if the two regressors (R&D/TA and Efficiency) are independent or not (if they are weakly or strongly correlated). If they were strongly correlated, our OLS results would be biased. We tried to assess whether R&D/TA and DEA efficiency (or DEA efficiency dummy) are independent of each other or not. First, we analyzed the correlation matrix of all the variables used in our four regressions. Also, we made two additional regressions (R&D/TA on DEA efficiency and R&D/TA on DEA efficiency dummy). The R square is 0.0022 in one case and 0.0409 in the other. Given these robustness checks, we conclude that the results obtained in our OLS models are valid and not biased. For reasons of space, we do not report the correlation matrix and the extra regressions although they are available upon request.

Table 7 Summary of the results of the regression models

Explanatory variables	OLS 1	OLS 2	OLS 3	OLS 4
R&D/total assets	5.528*** (1.162)	6.275*** (1.239)	41.541** (16.272)	10.010*** (1.915)
DEA efficiency	1.107*** (0.320)		4.149*** (1.207)	
DEA efficiency dummy		0.255** (0.101)		0.777*** (0.196)
R&D/total assets* DEA efficiency			−37.464** (16.921)	
R&D/total assets* DEA efficiency dummy				−5.141** (2.441)
Constant	−0.690** (0.289)	0.134 (0.125)	−3.620*** (1.169)	−0.263 (0.168)
R-squared	0.159	0.163	0.190	0.183
Number of observations	178	178	178	178

*, **, *** Indicate significance at the 1, 5 and 10 % level. Robust standard errors in parentheses

Conclusions

This paper estimates the relative efficiency in the period 2008–2013 of 37 large pharmaceutical firms that received authorization for innovative medicines in the United States and/or the European Union within this time period. Authorized drugs are concentrated in a small number of large and efficient pharmaceutical laboratories and it make sense for health authorities at the national level in the US (FDA) or at the European level (EMA) to discuss R&D strategies for the future with a small number of large laboratories. In addition, we analyze announced financial transactions by our sample of pharmaceutical laboratories as an alternative way to gain access to new drugs and new R&D.

The novelty of our approach is that we considered 37 large laboratories from different countries in the period 2008–2013 and, simultaneously, we combined information from several different sources: Datastream financial and market information, EMA, and FDA drug approvals and announced financial transactions from Capital IQ.

Although studies considering patents adjust for the quality of patents considering the number of times that a patent has been cited, in our case, only the most successful new drugs in the pharmaceutical pipeline are approved by EMA and FDA, so this measure is a better proxy for successful R&D.

We used DEA non-parametric techniques, considering multiple inputs and outputs, and defined several dimensions in which large laboratories are considered to be efficient. While the inputs refer to different ways of measuring investment in the company, the outputs consider performance indicators. The relevance of R&D in this sector was also taken into special consideration. 21 companies proved to be efficient and 16 inefficient when considering three inputs and three outputs under the VRS assumption. The average level of efficiency in the base model was 93.45 %. In addition, ten companies are not efficient, but present a level of efficiency greater than 85 %. Broadly speaking, this indicates the high competitive level of companies in this sector.

Some previous papers estimate either DEA efficiency or DEA total factor productivity of pharmaceutical firms but most studies focus on a single country. Also, when measuring R&D efficiency, most previous papers consider the number of patents as a proxy for R&D. In this study, as a proxy for R&D we considered not only the number of new chemical entities approved by EMA and FDA for each laboratory but we also adjusted this figure considering the specific date of authorization of each new chemical entity.

Shimura et al. [52] perform statistical analysis to explore links between R&D and industry consolidation in the period 2002–2007 considering a sample of 21 pharmaceutical laboratories. We, however, focus only on DEA estimates but consider more efficiency dimensions and we explore in detail peers at the frontier for the pharmaceutical laboratories that are not fully efficient. We perform an efficiency analysis without a DEA second stage approach given that DEA second stages are subject to some controversy as discussed above.

We extend prior literature related to markets for technology and internal and external R&D strategy by considering in much more detail announced transactions and including not only a few very large M&As or a few hundred acquisitions but also many smaller transactions.

Prior related contributions on acquisitions and innovation [3, 7, 16, 26, 31, 32, 38, 47, 52] focus on different characteristics of the acquirer and/or target and whether and how acquisitions create value. In our case, we estimate first the relative efficiency of each pharma lab and then we introduce financial transactions into the analysis. Thus, we searched for further evidence of the link between lab efficiency and financial transactions in the pharmaceutical industry during our study period. Large M&As have been

studied in previous papers but we contribute by analyzing in detail 2071 announced transactions by our sample of 37 laboratories. Our sample is split in two. One subsample is made up of 21 efficient laboratories that are at the DEA frontier according to model I. The second subsample is made up of 16 inefficient firms. After adjusting for the market cap of each pharmaceutical laboratory (as a proxy for size), the transaction size relative to the size of the pharmaceutical laboratory is slightly larger for efficient laboratories (0.597) than for inefficient laboratories (0.530).

Given our study period and considering only 36 laboratories (excluding Mitsubishi), efficient laboratories make on average more transaction announcements, and the relative size of each transaction announced is higher. Also, labs with more R&D relative to total assets strike more deals than labs with lower R&D relative to total assets. However, when we include the interaction term, this term suggests that labs that simultaneously are more efficient and also invest more internally in R&D announce smaller transactions relative to total assets of the lab.

Although we think that new drugs authorized are a better proxy for successful research than patents, the authorization procedure is not perfect. New drugs submitted for authorization to EMA and FDA are subject to close scrutiny, especially during phase III. However, part of the results of the clinical trials is never published or is published with a considerable delay. Recent legislation tackles this problem. The USA passed legislation in 2007 and, in Europe, new legislation will come into force in 2016. The FDA has the power to fine laboratories that do not comply but it is reported that it has never actually done so [54].

We propose several possible extensions of our paper. We did not consider information from laboratories with zero new drugs authorized during the study period. This was because of our DEA methodology for estimating efficiency as well as the fact that many laboratories had zero new drugs authorized in many of the years of our sample. However, different approaches and a different methodology may be able to exploit the data in order to further contribute to the subject. Censored regression models could be used to incorporate more pharmaceutical laboratories into the analysis and to consider many laboratories with zero drugs authorized.

Alternatively, with an unbalanced data set, the use of panel data would be helpful in order to account for unobserved heterogeneity and to study the dynamics of the population. Pindado et al. [49] show how firm characteristics influence the relationship between R&D and firm value but, when constructing the unbalanced panel, they impose the restriction that there should be six consecutive years of information available from companies in the sample. This is only possible with a very large database comprising more sectors than the pharmaceutical sector. Another possible extension would be to estimate a two-stage DEA using, in the second stage, variables that were not used in the first stage. Explaining DEA inefficiency in a second stage analysis is a common practice for identifying factors whose impact on efficiency is statistically significant. However, the use of ordinary least squares, Tobit or other alternatives is subject to controversy, as well as to limitations and biases according to recent papers. Simar and Wilson [53] compare the pros and cons of the different alternatives, but one alternative which is not subject to controversy is to incorporate all the relevant variables in the first step. This is what we did.

In the case of EMA authorizations, there is authorization information since 1995 and, in the case of the FDA, there is information about new molecular entities since 1999 so this could be used to estimate changes in Total Factor Productivity adopting a DEA/Malmquist methodology in order to study the frontier shift, while also comparing relative efficiency and interpreting the individual evolution of companies. Another alternative would be to explore the differences between generics and new drugs authorized by EMA or FDA.

Another alternative for future research would be to identify the sources and key factors of innovation of the different laboratories in different geographical regions. These factors may be identified at firm level or at country or regional level. In the latter case, factors such as the regulatory environment or approval times are important for pharmaceutical innovations—see e.g., [10, 20, 21]. Recently, Kinch [40] used information on FDA approved NMEs and merged this information with patent information. Grabowski and Wang [28] is another relevant paper on the subject that finds that biotech and orphan products enjoyed tremendous growth, especially for cancer treatment. Naci et al. [46] examined why the drug development pipeline is not delivering better medicines. Finally, it would be possible to explore in much more detail announced financial transactions in order to gain further insights regarding external R&D acquisitions.

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Appendix 1

See Tables 8, 9 and 10.

Table 8 Datastream output measures; 37 laboratories versus 241 laboratories (data in million USD)

Output	Number of pharma labs	2008	2009	2010	2011	2012	Sum 2013
O1-NP	37	87,018	113,048	100,980	109,562	107,580	108,967
O1-NP	241	93,279	121,845	115,168	125,961	124,379	123,492
Percentage (%)	–	93.3	92.8	87.7	87.0	86.5	88.2
O2-MC	37	1,316,178	1,497,453	1,479,184	1,591,657	1,797,990	2,242,927
O2-MC	241	1,465,046	1,693,558	1,742,159	1,856,308	2,181,790	2,823,773
Percentage (%)	–	89.8	88.4	84.9	85.7	82.4	79.4
O3-TS	37	543,044	602,776	673,175	685,712	692,554	676,711
O3-TS	241	628,929	721,607	820,815	856,171	883,483	867,525
Percentage (%)	–	86.3	83.5	82.0	80.1	78.4	78.0

Table 9 New drugs authorized by EMA and FDA in the period 2008 to 2013 without the effect of M&A

Agency	Year	Number of authorized drugs	Number of days	Number of days discounted
EMA	2008	38	72,209	67,676
EMA	2009	44	70,465	66,915
EMA	2010	22	25,205	24,229
EMA	2011	38	32,876	32,005
EMA	2012	22	11,252	11,082
EMA	2013	43	7135	7088
FDA	2008	10	19,759	18,504
FDA	2009	12	19,847	18,819
FDA	2010	7	9116	8753
FDA	2011	14	12,969	12,611
FDA	2012	17	8430	8304
FDA	2013	14	2430	2413
EMA + FDA	2008	48	91,968	86,180
EMA + FDA	2009	56	90,312	85,734
EMA + FDA	2010	29	34,321	32,982
EMA + FDA	2011	52	45,845	44,616
EMA + FDA	2012	39	19,682	19,386
EMA + FDA	2013	57	9565	9502

Table 10 New drugs authorized by EMA and FDA in the period 2008 to 2013 belonging to M&A

Agency	Year	Number of authorized drugs	Number of days	Number of days discounted
EMA	2008	1	1862	1752
EMA	2009	2	3279	3111
EMA	2010	0	0	0
EMA	2011	0	0	0
EMA	2012	0	0	0
EMA	2013	1	110	110
FDA	2008	1	2132	1985
FDA	2009	0	0	0
FDA	2010	1	1453	1388
FDA	2011	0	0	0
FDA	2012	3	1755	1725
FDA	2013	2	401	398
EMA + FDA	2008	2	3994	3736

Table 10 continued

Agency	Year	Number of authorized drugs	Number of days	Number of days discounted
EMA + FDA	2009	2	3279	3111
EMA + FDA	2010	1	1453	1388
EMA + FDA	2011	0	0	0
EMA + FDA	2012	3	1755	1725
EMA + FDA	2013	3	511	508

Appendix 2

See Tables 11 and 12.

Table 11 Outputs for the DEA model

Company	Ref.	O1–NP (*) Net income basic	O2–MC (*) Market capitalization	O3–TS (*) Net sales	O4–NDAIMCTE (*) Number of days discounted until December 13
ABBOTT	[1]	4,728,933	81,795	32,672,025	127
ALLERGAN	[2]	703,150	23,442	5,225,333	1205
AMGEN	[3]	4,422,833	63,146	16,029,000	6921
ASTELLAS	[4]	1,312,290	20,471	11,049,964	6924
ASTRAZENECA	[5]	6,535,839	64,026	29,901,216	9045
BAYER	[6]	2,843,425	69,912	48,787,267	7291
BIOGEN	[7]	1,204,907	28,791	5,121,517	1148
BRISTOL	[8]	3,006,000	55,933	19,023,167	6972
CELGENE	[9]	724,639	35,263	4,233,646	6347
CELLTRION	[10]	1560	137	32,695	112
CSL	[11]	941,535	21,068	4,072,829	3040
EISAI	[12]	472,294	11,645	8,224,303	7081
ELI LILLY	[13]	3,407,917	48,338	22,548,833	7129
GILEAD	[14]	2,669,696	52,759	8,263,849	3113
GLAXOSMITHKLINE	[15]	7,117,737	109,774	42,449,777	28,802
H. LUNDBECK	[16]	310,826	3818	2,607,541	2614
HOSPIRA	[17]	184,750	6478	3,929,667	1362
IPSEN	[18]	121,484	3282	1,543,927	1616
JOHNSON & JOHNS.	[19]	12,150,833	190,890	65,151,167	14,429
MEDA AB	[20]	183,033	2858	1,805,137	2283
MEDICINES COMP.	[21]	35,758	1122	486,871	1853
MERCK (KGAA)	[22]	12,745	185	108,256	936
MERCK & CO	[23]	6,391,050	112,088	39,450,600	24,469
MITSUBISHI	[24]	373,502	8144	4,491,237	341
NOVARTIS	[25]	9,307,241	162,456	53,173,503	43,544
NOVO NORDISK	[26]	2,982,551	54,037	11,684,809	4140
ORION	[27]	247,665	1056	1,184,442	2549
OTSUKA	[28]	924,146	15,321	12,549,824	3174
PFIZER	[29]	9,172,833	159,328	57,351,500	13,270
REGENERON	[30]	116,311	9003	834,308	3810
RICHTER	[31]	237,170	3387	1,392,848	664
ROCHE	[32]	9,703,329	30,595	48,172,073	5838

Table 11 continued

Company	Ref.	O1–NP (*) Net income basic	O2–MC (*) Market capitalization	O3–TS (*) Net sales	O4–NDAIMCTE (*) Number of days discounted until December 13
SANOFI	[33]	6,550,360	105,872	42,740,575	17,114
SHIRE	[34]	586,697	16,201	3,844,582	6694
TAKEDA	[35]	2,669,367	36,543	16,746,817	19,833
TEVA	[36]	2,015,502	41,540	16,822,439	6186
UCB	[37]	310,067	8635	4,046,009	6149

* Datastream data is in thousand USD for Net Income Basic and Net Sales, while market cap is in million USD

** The number of days discounted is computed for each pharmaceutical laboratory until December 2013. M&A activity only affected two pharmaceutical laboratories with authorized drugs in the period 2008 to 2013 (Pfizer and Roche)

Table 12 Inputs for the DEA model

Company	Ref.	I1–SW (*) Employees	I2–TA (*) Total assets	I3–IRD (*) Investment in R&D	I4–NDAIMCTE (**) Number of days discounted until December 13
ABBOTT	[1]	80,500	52,395,697	3,153,094	127
ALLERGAN	[2]	9740	8,365,350	842,350	1205
AMGEN	[3]	17,883	48,142,000	3,234,833	6921
ASTELLAS	[4]	15,651	15,273,737	2,059,089	6924
ASTRAZENECA	[5]	58,200	52,071,173	4,231,109	9045
BAYER	[6]	110,650	68,614,409	3,982,957	7291
BIOGEN	[7]	5350	9,361,089	1,267,042	1148
BRISTOL	[8]	28,833	32,178,833	3,507,500	6972
CELGENE	[9]	3949	9,113,421	1,309,492	6347
CELLTRION	[10]	273	186,354	975	112
CSL	[11]	10,303	5,279,541	306,281	3040
EISAI	[12]	10,977	11,545,267	1,808,208	7081
ELI LILLY	[13]	38,928	31,830,383	4,813,633	7129
GILEAD	[14]	4159	14,730,257	1,291,045	3113
GLAXOSMITHKLINE	[15]	98,679	61,559,984	5,668,148	28,802
H. LUNDBECK	[16]	5582	3,400,398	503,502	2614
HOSPIRA	[17]	15,000	5,582,733	269,217	1362
IPSEN	[18]	4518	1,953,324	306,635	1616
JOHNSON & JOHNS.	[19]	120,300	103,129,833	7,470,000	14,429
MEDA AB	[20]	2769	5,071,538	92,668	2283
MEDICINES COMP.	[21]	478	742,416	111,289	1853
MERCK (KGAA)	[22]	1267	106,656	640	936
MERCK & CO	[23]	82,367	96,384,650	6,901,817	24,469
MITSUBISHI	[24]	9478	9,188,473	794,988	341
NOVARTIS	[25]	117,179	107,311,781	8,699,227	43,544
NOVO NORDISK	[26]	31,633	10,737,626	1,647,363	4140
ORION	[27]	3320	1,075,103	122,836	2549
OTSUKA	[28]	24,526	17,422,894	1,828,382	3174
PFIZER	[29]	96,967	176,414,167	7,828,500	13,270
REGENERON	[30]	1556	1,405,310	143,325	3810
RICHTER	[31]	9315	2,719,582	140,159	664
ROCHE	[32]	81,886	65,889,688	9,092,583	5838

Table 12 continued

Company	Ref.	I1–SW (*) Employees	I2–TA (*) Total assets	I3–IRD (*) Investment in R&D	I4–NDAIMCTE (**) Number of days discounted until December 13
SANOFI	[33]	107,079	115,924,165	6,339,443	17,114
SHIRE	[34]	4631	5,896,458	743,059	6694
TAKEDA	[35]	22,336	35,046,990	3,610,550	19,833
TEVA	[36]	41,617	41,970,743	1,075,776	6186
UCB	[37]	9300	12,265,666	1,057,417	6149

* Datastream data is in thousand USD for Total Assets and Investment in R&D, and for the other input is in number of employees

** Note this variable is used as both an input and an output. Again, the number of days discounted is computed for each pharmaceutical laboratory until December 2013. M&A activity only affected two pharmaceutical laboratories with authorized drugs in the period 2008 to 2013 (Pfizer and Roche)

References

1. Achilladelis, B., Antonakis, N.: The dynamics of technological innovation: the case of the pharmaceutical industry. Res. Policy **30**, 535–588 (2001)
2. Ahn, J.H., Chang, S.G.: Assessing the contribution of knowledge to business performance: the KP^3 methodology. Decis. Support Syst. **36**, 403–416 (2004)
3. Arora, A., Fosfuri, A., Gambardella, A.: Markets for technology and their implications for corporate strategy. Ind. Corp. Change **10**, 419–451 (2001)
4. Banker, R.D., Thrall, R.M.: Estimation of returns to scale using Data envelopment analysis. Eur. J. Oper. Res. **62**, 74–84 (1992)
5. Barr, R.S.: DEA software tools and technology: a state-of-the-art survey. Handb. Data Envel. Anal. Int. Ser. Oper Res. Manag. Sci. **71**, 539–566 (2004)
6. Baršauskas, P., Šarapovas, T., Cvilikas, A.: The evaluation of e-commerce impact on business efficiency. Balt. J. Manag. **3**, 71–91 (2008)
7. Bena, J., Li, K.: Corporate innovations and mergers and acquisitions. J. Finance **69**, 1923–1960 (2014)
8. Boussofiane, A., Dyson, R.G., Thanassoulis, E.: Applied Data envelopment analysis. Eur. J. Oper. Res. **52**, 1–15 (1991)
9. Bowns, S., Bradley, I., Kneec, P., Williams, F., Williams, G.: Measuring the economic benefits from R&D: improvements in the MMI model of the United Kingdom National Measurement System. Res. Policy **32**, 991–1002 (2003)
10. Cabiedes, L.: Authorisation and withdrawal of pharmaceutical innovations in the European. Working paper, University of Oviedo, Spain (2005)
11. Castelli, A., Street, A., Verzulli, R., Ward, P.: Examining variations in hospital productivity in the English NHS. Eur. J. Health Econ. **16**(3), 243–254 (2015)
12. Caves, D., Christensen, L., Diewert, E.: The economic theory of index numbers and the measurement of input, output, and productivity. Econometrica **50**(6), 1393–1414 (1982)
13. Charnes, A., Cooper, W.W., Rhodes, E.: Measuring the efficiency of decision making units. Eur. J. Oper. Res. **2**, 429–444 (1978)
14. Charnes, A., Cooper, W.W., Golany, B., Seiford, L.M., Stutz, J.: Foundations of data envelopment analysis and Pareto–Koopmans empirical production functions. J. Econom. **30**, 91–107 (1985)
15. Coelli, T.J.: A guide to DEAP version 2.1: a data envelopment analysis (Computer) Program. Department of Econometrics, University of New England, Armidale, Australia (1996)
16. Comanor, W.S., Scherer, F.M.: Mergers and innovation in the pharmaceutical industry. J. Health Econ. **32**, 106–113 (2013)
17. Cooper, W.W., Li, S., Seiford, L.M., Thrall, R.M., Zhu, J.: Sensitivity and stability analysis in DEA: some recent developments. J. Prod. Anal. **15**, 217–246 (2001)
18. Cooper, W.W., Seiford, L.M., Zhu, J.: Data envelopment analysis: history, models, and interpretations. Handb. Data Envel. Anal. Int. Ser. Oper Res. Manag. Sci. **164**, 1–39 (2011)
19. Cruz-Cáceres, C., Bayona-Sáez, C., García-Marco, T.: You can't manage right what you can't measure well: technological innovation efficiency. Res. Policy **42**, 1239–1250 (2013)
20. Danzon, P.M., Wang, Y.R., Wang, L.: The impact of price regulation on the launch delay of new drugs—evidence from twenty-five major markets in the 1990s. Health Econ. **14**(3), 269–292 (2005)
21. Dukes, G.: The effects of drug regulations: a survey based on the European studies of drug regulation. MTP Press Limited, Lancaster (1985)
22. European Medicines Agency: European Public Assessment Reports. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&mid=WC0b01ac058001d125 (2015)
23. Food and Drug Administration: Drug Approval Reports. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Reports.ReportsMenu (2015)
24. García-Sánchez, I.M.: Efficiency and effectiveness of Spanish football teams: a three-stage-DEA approach. Cent. Eur. J. Oper. Res. **15**, 21–45 (2007)
25. Gascón, F., De la Fuente, D., Puente, J., Lozano, J.: On macroeconomic characteristics of pharmaceutical generics and the potential for manufacturing and consumption under fuzzy conditions. Artif. Intell. Med. **41**, 223–235 (2007)
26. Girotra, K., Terwiesch, C., Ulrich, K.T.: Valuing R&D projects in a portfolio: evidence from the pharmaceutical industry. Manage. Sci. **53**(9), 1452–1466 (2007)
27. González, E., Gascón, F.: Sources of productivity growth in the Spanish pharmaceutical industry (1994–2000). Res. Policy **33**, 735–745 (2004)
28. Grabowski, H.G., Wang, Y.R.: The quantity and quality of worldwide new drug introductions, 1982–2003. Health Affair. **25**(2), 452–460 (2006)
29. Guan, J., Chen, K.: Modeling the relative efficiency of national innovation systems. Res. Policy **41**, 102–115 (2012)
30. Hashimoto, A., Haneda, S.: Measuring the change in R&D efficiency of the Japanese pharmaceutical industry. Res. Policy **37**, 1829–1836 (2008)
31. Hagedoorn, J., Wang, N.: Is there complementarity or substitutability between internal and external R&D strategies? Res. Policy **41**(6), 1072–1083 (2012)

32. Higgins, M.J., Rodriguez, D.: The outsourcing of R&D through acquisitions in the pharmaceutical industry. J. Financ. Econ. **80**, 351–383 (2006)
33. Honjo, Y., Haneda, S.: R&D evaluation of Japanese pharmaceutical firms using DEA. J. Sci. Policy Res. Manag. **13**, 96–105 (1998)
34. IMS Institute for Healthcare Informatics: The Global Use of Medicines: Outlook Through 2015. http://www.imshealth.com (2011)
35. IMS Institute for Healthcare Informatics: Global Outlook for Medicines Through 2018. http://www.imshealth.com (2014)
36. Jalili, M., Rangriz, H., Shabani, S.: Using data envelopment analysis to rate pharmaceutical companies: a case study of Iran. Life Sci. J. **10**, 336–341 (2013)
37. Jiménez-Sáez, F., Zabala-Iturriagagoitia, J.M., Zofio, J.L., Castro-Martínez, E.: Evaluating research efficiency within National R&D Programmes. Res. Policy **40**, 230–241 (2012)
38. Kang, K.H., Jo, G.S., Kang, J.: External technology acquisition: a double-edged sword. Asian J. Technol. Innov. **23**(1), 35–52 (2015)
39. Kesselheim, A.S., Wang, B., Avorn, J.: Defining "innovativeness" in drug development: a systematic review. Clin. Pharmacol. Ther. **94**(3), 336–348 (2013)
40. Kinch, M.S., Raffo, J.: Sources of innovation: an assessment of intellectual property. Drug Discov. Today **20**(5), 500–504 (2015)
41. Kounetas, K., Papathanassopoulos, F.: How efficient are Greek hospitals? A case study using a double bootstrap DEA approach. Eur. J. Health Econ. **14**(6), 979–994 (2013)
42. Light, D.W.: Global drug discovery: Europe is ahead. Health Affair. **28**(5), w969–w977 (2009)
43. Mao, Y., Li, J., Liu, Y.: Evaluating business performance of China's pharmaceutical companies based on data envelopment analysis. Stud. Ethno Med. **8**, 51–60 (2014)
44. Mazumdar, M., Rajeev M.: A comparative analysis of efficiency and productivity of the Indian pharmaceutical firms: a malmquist-meta-frontier approach. Working Paper, The Institute for Social and Economic Change, Bangalore (2009)
45. Motohashi, K.: The changing autarky pharmaceutical R&D process: causes and consequences of growing R&D collaboration in Japanese firms. Int. J. Technol. Manage. **39**, 33–48 (2007)
46. Naci, H., Carter, A.W., Mossialos, E.: Why the drug development pipeline is not delivering better medicines. BMJ **351**, h5542 (2015). doi:10.1136/bmj.h5542
47. Nishimura, J., Okada, Y.: R&D portfolios and pharmaceutical licensing. Res. Policy **43**(7), 1250–1263 (2014)
48. Parker, D.: The performance of BAA before and after privatisation: a DEA study. J. Transport Econ. Policy **33**, 133–146 (1998)
49. Pindado, J., de Queiroz, V., de la Torre, C.: How do firm characteristics influence the relationship between R&D and firm value? Financ. Manage. **39**, 757–782 (2010)
50. Ramanathan, R.: Evaluating the comparative performance of countries of the Middle East and North Africa: a DEA application. Socio-Econ. Plan. Sci. **40**, 156–167 (2006)
51. Sarrico, C.S., Dyson, R.G.: Using DEA for planning in UK universities—an institutional perspective. J. Oper. Res. Soc. **51**, 789–800 (2000)
52. Shimura, H., Masuda, S., Kimura, H.: Research and development productivity map: visualization of industry status. J. Clin. Pharm. Ther. **39**, 175–180 (2014)
53. Simar, L., Wilson, P.W.: Two-stage DEA: caveat emptor. J. Prod. Anal. **36**, 205–218 (2011)
54. The Economist. Clinical trials. Spilling the beans. Failure to publish the results of all clinical trials is skewing medical science. Published in the print edition on July 25, 2015. http://www.economist.com/news/science-and-technology/21659703-failure-publish-results-all-clinical-trials-skewing-medical (2015)
55. Thomas, R.R., Bar, R.S., Cron, W.L., Slocum Jr., J.W.: A process for evaluating retail store efficiency: a restricted DEA approach. Int. J. Res. Mark. **15**, 487–503 (1998)
56. Wang, E.C., Huang, W.: Relative efficiency of R&D activities: a cross-country study accounting for environmental factors in the DEA approach. Res. Policy **36**, 260–273 (2007)
57. Wang, W.K., Lu, W.M., Liu, P.Y.: A fuzzy multi-objective two-stage DEA model for evaluating the performance of US bank holding companies. Expert Syst. Appl. **41**, 4290–4297 (2014)
58. Wanke, P., Barros, C.: Two-stage DEA: an application to major Brazilian banks. Expert Syst. Appl. **41**, 2337–2344 (2014)
59. You, T., Chen, X., Holder, M.E.: Efficiency and its determinants in pharmaceutical industries: ownership, R&D and scale economy. Appl. Econ. **42**, 2217–2241 (2010)
60. Zhu, J.: Imprecise data envelopment analysis (IDEA): a review and improvement with an application. Eur. J. Oper. Res. **144**, 513–529 (2003)