R&D Price Inflation, Real BERD and Innovation: Pharmaceuticals, OECD 1980-2000

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Abstract

Research in pharmaceuticals suggests there is a growing imbalance in the spatial distribution of business expenditure in R&D (BERD) and R&D productivity has declined. This evidence derives from data using GDP price deflators to adjust for price inflation but Dougherty et al. (2003) show them to be inappropriate.

This paper draws on economic theory and panel estimation techniques to develop Griliches-Jaffe-type R&D price deflators for the pharmaceutical industry in the OECD. The paper also re-examines the hypotheses that Europe is an innovation laggard and that R&D productivity has declined. The evidence shows Europe is not a laggard in real BERD, R&D productivity has improved throughout the OECD except Japan, and the USA has consolidated its leadership in patents and R&D productivity.

JEL classification: L65; I11; O3.

Keywords: R&D Expenditures; Drugs; Inflation; Innovation; Patents.

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1. Introduction

Major scientific advances in health care and the 'astonishing surge of medicines' (Landau *et al.* 1999) have established the pharmaceutical industry as a world leader in the knowledge economy. The industry places enormous emphasis on R&D, recording the second highest R&D intensity in the OECD in the 1990s (OECD 2003).

Recently, however, major concerns have emerged in the literature. One relates to the spatial distribution of world R&D activity. Several empirical studies have reported a persistent shift in R&D resources in favour of the USA. Business expenditure in R&D (BERD) in the USA seems to have exploded and Europe is increasingly seen as a laggard (Gambardella *et al.* 2001; Pammolli and Riccaboni 2004). Further, there are claims that Europe acts as a 'free rider' by relying on the USA for the discovery of new drugs while imposing price controls on new drugs (Gilbert and Rosenberg 2004).

A more serious issue concerns the industry's recent innovation track record. Cockburn (2004) presents evidence of a steady decline in the number of new medicines approved by the U.S. Food and Drug Administration over the period 1996-2002. In view of surging BERD, this trend can be interpreted as a decline in R&D productivity but Cockburn (2004) emphasises long lags, the rising quality of medicines and more expensive R&D processes as the most plausible causal factors.

These empirical assessments have important policy implications. An example is the policy drive towards explicit targets for BERD in the European Community and other OECD countries (Sheehan and Wyckoff 2003; Dougherty et al. 2003). Also, a decline in R&D productivity and rising R&D costs would raise serious questions regarding profitability, drug price controls and access to new medicines by low-income consumers (Grabowski 2002; DiMasi *et al.* 2003).

The literature has paid little attention to the fact that the above evidence on BERD is overwhelmingly based on data that is not properly adjusted for R&D price inflation. Due to data limitations, empirical research has relied on GDP price deflators to arrive at real R&D expenditures. When combined with information on exchange rates, these series yield the familiar GDP PPPs indexes¹ widely adopted in the OECD ANBERD database. This convention has prevailed for practical purposes, mainly due to the absence of alternative R&D price deflators. Yet, it is now established that the use of

¹ For more detail on the definition and measurement of PPPs, see Schreyer and Koechlin (2002).

GDP PPPs in structural analysis is highly problematic since they tend to miss sectoral variation in input prices and they ignore intermediate goods and services (Dougherty et al. 2003; Jankowski 1993).

This paper develops new estimates of R&D price deflators for pharmaceuticals for fifteen OECD countries (OECD-15)². For consistency and parsimony, the estimates derive from a methodology that relies on existing data, economic theory and modern panel data econometric techniques. The paper utilises these new estimates to revisit the debate on the spatial imbalance between the USA and Europe and the decline in R&D productivity in the USA. The paper unfolds as follows. Section two outlines the methodology adopted in this study and presents the results. Section three examines trends in the geography of real BERD within the OECD and in R&D productivity. Section four concludes.

2. New R&D Price Deflators: Pharmaceuticals

Background

Empirical analysis of the contribution of the pharmaceutical industry to the knowledge economy necessitates the adjustment of nominal R&D expenditures using industry-specific R&D PPPs to account for differences in local currencies and price inflation. Conversion to a common currency is routine but the adjustment to constant price values is not trivial. Ideally, the latter would require data on both price and weights for each R&D input category. Such a comprehensive database is not currently available but its development is a long-term objective of the OECD, Eurostat and the National Science Foundation in the USA. Obviously, this database would facilitate the construction of comparable indicators but it would also impose a heavy burden on taxpayers, given the need for national industry-specific surveys.

In the absence of R&D input-specific data, empirical research has overwhelmingly relied on economy-wide price indexes and GDP PPPs, and has given little attention to international differences in R&D input prices.³ There are three major difficulties with the GDP PPP approach. First, the industry output prices diverge considerably from aggregate GDP price levels and, thus, GDP PPPs lead to misleading

² OECD-15 includes Australia, Canada, Belgium, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Spain, Sweden, the UK and the USA. Europe is defined as OECD-15 without Australia, Canada, Japan and the USA.

³ Freeman and Young (1965) is an early but rare inquiry.

comparisons (van Ark 1996). US evidence confirms this view for pharmaceuticals: the Biomedical R&D price index (BRDPI) indicates much stronger price growth than the implicit GDP deflator (Adams and Griliches 1996). Second, output deflators exclude prices of intermediate goods and services that form a major part of R&D. Since these inputs are not traded internationally, standard GDP PPPs can be grossly misleading if substantial structural differences exist between OECD countries (OECD 1994). Last but not least is the fact that unit labour costs vary considerably within the OECD (O'Mahony and van Ark. 2003). Therefore, the GDP PPP convention has the potential to contaminate comparative analysis with a significant bias given the dominant role of labour compensation in BERD.

The above measurement issues call for an alternative approach to GDP PPP that facilitates international comparisons, continuity and parsimony in the construction of R&D price deflators for the pharmaceutical industry. This seems even more essential in view of the rise of the industry as one of the most innovative in the OECD and the increasing focus of public policy on the industry. The latter concerns the policy dilemma of 'accommodating' the demand for sustainable drug innovation by the industry while providing access to new medicines in the context of surging health expenditures (Dickson *et al.* 2003).

Early attempts towards an alternative to the GDP deflator for the USA are Jaffe (1973) and Griliches (1984). They draw on the fact that the price of labour constitutes the largest component of R&D expenditure to propose a weighted R&D price index that combines a labour costs index with a broader output deflator. The assumption here is that price changes of the output produced by the industry should reflect price movements of non-labour R&D inputs. Given the lack of industry-specific value added deflators, they employ the GDP deflator as a proxy for the non-labour cost index. Dougherty et al. (2003) go the extra mile to compare the Griliches-Jaffe approach with a fully developed R&D deflator that incorporates industry specific information on non-labour costs. They are able to show that the Griliches-Jaffe R&D deflators of combining the price of labour with output prices (Jaffe 1973; Griliches 1984) perform as well as the fully developed R&D PPPs. The Dougherty et al. (2003) result suggests that detailed data on non-labour input prices are not essential.

In contrast, recent US studies have employed the National Institutes of Health (NIH) Biomedical R&D Price Deflator (BRDPI) as an alternative measure of R&D price index. Cockburn (2004) uses the BRDPI to correct for R&D price inflation but his adjusted series does not alter the fact of strong BERD growth in the USA. Compared to the GDP price deflator, the use of the BRDPI series is certainly an improvement since it more directly relates to medical R&D. Unfortunately, however, there is no information on the suitability of BRDPI as a proxy of R&D price inflation in the *private* sector. The series, developed by the Bureau of Economic Analysis, is an input price index for the NIH budget that is dominated by labour compensation of academic and Federal employees. It is weighted according to the pattern of expenditures supported by NIH awards (mainly basic R&D) and, thus, it would not necessarily track R&D input price inflation in the private sector, especially if wages and salaries inflation in the private sector varies from the pattern for academics and for Federal employees.⁴ More importantly, an equivalent to BRDPI does not exist for other OECD countries.

Methodology

This section builds on Dougherty et al. (2003) to develop a Griliches-Jaffe type of R&D price deflator for the pharmaceuticals industry in the OECD. It extends the current literature by adjusting for improvements in the quality of R&D personnel and by utilising value added price deflators as a proxy for non-labour R&D costs. The approach allows a global view of R&D price inflation in pharmaceuticals and facilitates the parsimonious construction of comparable R&D and innovation indicators for the OECD. Further, value added price deflators can be useful in comparative analyses of manufacturing productivity (Rao and Trimmer 2003).

Overall, the new R&D price deflator for country j is defined as:

$$RDP_j = (1 - \alpha_j) * OP_j + \alpha_j * LCP_j, \quad j = 1, 2, ..., 15$$
 (1)

where OP_j is the non-labour price deflator for R&D inputs in country j, LCP_j is the labour compensation price index and α is the share of labour costs in R&D expenditure.⁵ Estimates for α_j are based on SIRF, Hay Group, Ernst &Young (2001).⁶

We begin with the construction of a labour price index (LCP) that includes earnings by self-employed. The OECD STAN database provides data on total labour compensation and the number persons employed in the industry (N). It is common

⁴ We are indebted to James A. Schuttinga at the NIH for detailed information on the BRDPI series.

⁵ The Data Appendix provides a detailed account of data sources and variable definitions.

⁶ Greatly appreciated were unpublished data made available by the author of the report Kim Sawyer.

practice to use these data to derive a unit labour compensation index. This, however, ignores qualitative changes in the labour force and we know that the price index will contain an upwards bias if it is not adjusted for product quality changes (Griliches 1992). In order to correct for labour force quality, we make two adjustments. First, we acknowledge labour heterogeneity by distinguishing between scientific/professional R&D personnel (S), and other supporting staff (O) on the basis of DiMasi *et al.* (2003). Second, we employ Eurostat bibliometrics data to adjust for changes in the quality of R&D scientific and professional personnel. More precisely, this is defined as the product of S and the exponential of change in per capita scientific publications (LS)⁷ in Life Sciences since 1980. Hence, we re-define labour employment as:

$$L_{j,t} = \theta_t * N_t * \exp(LS_{j,t} - LS_{j,80}) + (1 - \theta_t) * N_t$$
(2)

where θ_t is the R&D employment share of S.⁸

Next, we present our results for labour cost inflation. Figures 1 and 2 plot the growth rate of two versions of LCP for the USA and Europe respectively. For brevity, LCP1⁹ stands for the growth rate of LCP1, the standard unit labour compensation without any adjustments, and LCP2 is the adjusted index according to (2). As a point of reference, figure 1 also includes the inflation rate implied by BRDPI and the implicit GDP deflator. The results can be summarised as follows. First, they confirm the view that price aggregation yields a GDP deflator that fails to reflect movements in the price of R&D in the pharmaceutical industry. Second, BRDPI has grown faster than the GDP deflator in the USA, as in Adams and Griliches (1996). Note, however, BRDPI exhibits much less cyclical variation than the GDP deflator. This finding seems consistent with our suspicion that BRDPI is not a good proxy of R&D price inflation in the private sector. Our estimates seem more consistent with recent evidence of strong growth in labour costs in the range of 7.4% - 9.3% (DiMasi et al. 2003). Third, the USA and Europe have experienced huge differences in R&D price inflation. The USA shows much higher inflation rates than Europe in the late 1990s while the opposite was true in the late 1980s and early 1990s. The high late 1990s inflation in the USA and the great wage moderation in Europe in the late 1990s confirm evidence in DiMasi et al. (2003) and O'Mahony and van Ark (2003, p.33).

⁷ LC_t is defined as the number of articles published in the fields of clinical medicine, biomedical and biology per 1000 population. It varies between 0.04 (Spain, 1980) to 1.06 (Sweden, 2000).

⁸ DiMasi *et al.* (2003) provide estimates of θ for 1980 and 2000. These are representative of all major US and other international firms. The complete series is derived by linear interpolation.

⁹ Note that all inflation rate series are named as their corresponding index series in all illustrations.



Moreover, R&D inflation in the USA tends to move in the opposite direction to that observed in Europe, figure 3. Finally, the new LCP1 and LCP2 series exhibit greater variation in inflation than BRDPI, and there is little difference between the two due to the slow change in the quality of R&D personnel.



We proceed to account for price inflation in non-labour R&D inputs. For an OP proxy, we seek an alternative to the implicit GDP deflator. Again, STAN data are employed to construct two alternative deflators for the pharmaceutical industry. The first is:

$$OP1_{i,t} = VAP_{i,t} = VALU_{i,t} * 100 / (VALK_{i,t} * VALU_{i,95})$$
(3)

where VAP_j is the Value Added Price Deflator, VALU is the STAN code for value added at national currency units, VALK is the value added volume index and the VALU₉₅ is value added in 1995, the base year. Note, however, that VALK data is only available for five countries: Canada, Denmark, France, Norway and the UK. For the rest of the countries, data on the next level of sectoral aggregation is used: chemicals industries. Thus, this deflator should be used with caution. The second alternative, OP2, is the average of VAP and the GDP deflator in order to correct for double counting since VAP encompasses the labour compensation index, LCP1.

Based on (1), OP1 and OP2 are then combined with LCP2 to arrive at two sets of R&D price indexes, RDP1 and RDP2 respectively. The results maintain the pattens observed in figures 1-2 and confirm the view that R&D price inflation is largely driven by labour costs. Note also that R&D price inflation has increased substantially in the



Figure 4: R&D Price Inflation, USA

USA in the late 1990s, figure 4. This is consistent with micro-data evidence in DiMasi *et al.* (2003). Further, the new R&D price deflators exhibit some cyclical volatility in the early 1990s and around 1997. The former period coincides with the recession while the latter correlates with the surge of patent activity in the USA.

The stark differences in the labour markets between Europe and the USA warrant further investigation. We seek to expand our intuition on the sources of such diversity by comparing the pharmaceutical industry with total manufacturing. We replicate the current approach to arrive at a unit labour compensation index for manufacturing in Europe and the USA. We find that in Europe wage inflation in pharmaceuticals closely resembles that experienced in manufacturing but the pharmaceutical industry in the USA recorded much higher inflation than the manufacturing sector.

Manufacturing as a whole, however, may be a weak comparison to pharmaceuticals. Towards a better benchmark, we also examine labour cost inflation in the machinery and equipment industry (STAN code 29-33) that is renown for its high R&D intensity (OECD 2001). The time-series plots in figures 5a and 5b compare the performance of the pharmaceutical industry to that of machinery and equipment for Europe and the USA respectively. Again, the experience of the latter sector is similar to that of manufacturing, except that inflation rates in machinery and equipment in the USA are now more comparable to those in pharmaceuticals in the late 1990s. Overall, although labour market behaviour in pharmaceuticals deviates from the trend in other manufacturing industries in the USA, the fact remains that both pharmaceuticals and manufacturing in the USA contrast sharply to the European experience. This finding indicates that previous evidence of strong growth in labour costs in the USA (DiMasi *et al.* (2003) and of a great wage moderation in Europe in the late 1990s (O'Mahony and van Ark 2003, p.33) apply not only to pharmaceuticals but also to manufacturing.



Finally, we subject the new R&D price deflators and LCP2 to econometric scrutiny. In order to qualify as price indexes, we expect these series to pass two tests. First, it is

expected that growth in *nominal* BERD, RD,¹⁰ and R&D price inflation, RDI, correlate positively. Second, economic theory suggests that the demand for R&D should inversely relate to the price of R&D. Thus, we expect changes in *real* BERD, RRD, to inversely relate to, RDI. In growth rate terms, we express these two tests by means of two stochastic relations:

$$\mathsf{RD}_{j, t} = \alpha + \beta * \mathsf{RDI}_{j, t} + \mathsf{u}_{t}$$
(4)

and

$$\mathsf{RRD}_{j, t} = \gamma + \delta^* \mathsf{RDI}_{j, t} + \mathbf{e}_t \tag{5}$$

Panel data econometric techniques are employed to test for two null hypotheses: H_{0}^{1} : $\beta > 0$ and H_{0}^{2} : $\delta < 0$. In the first test, the underlying series are R&D expenditures in US\$ and four price indexes: GDP PPP, LCP2, RDP1 and RDP2. In the second, BERD in US\$ is adjusted using the corresponding deflator before it is transformed to growth rates. The added complication in the first test is the possibility that β may also capture the effect of reverse causation from nominal expenditure to prices. In order to overcome this problem, we estimate (4) using Instrumental Variables (IV) and Generalised Methods of Moments (GMM) with the first two lags of RDI as the instruments. Table 1 summarises the estimation results with GDP PPP as a proxy for R&D inflation in column (A), LCP2 in column (B), RDP1 in (C) and RDP2 in (D). As expected, β is positive in all four regressions but the GDP PPP deflator series is not statistically significant.

In the second test, we obtain random and fixed effects panel estimates where the two differ in their assumption regarding the disturbance term in (5). Table 2 presents the results. Here, only the LCP2 and RDP1 coefficients are negative in statistical terms. This seems intuitive as RDP2 is greatly determined by the implicit GDP deflator. The absence of a negative coefficient for the GDP PPP series once again confirms its inadequacy as an R&D price deflator. Also, a Hausman specification test in panel (c) cannot reject the null that the random effect model is the correct model.

¹⁰ RD and RRD stand for the first difference of the natural log of BERD and real BERD respectively. This is based on panel unit root tests showing the levels series are non-stationary. Results are available upon request.

(a) IV Estimation							
()	(A)	(B)	(C)	(D)			
constant	0.08	0.06	0.07	0.06			
	(0.000)	(0.000)	(0.000)	(0.004)			
β	0.90	1.24	1.04	1.54			
	(0.038)	(0.000)	(0.000)	(0.000)			
p-values in parentheses							

Table 1: IV and GMM Panel Estimation, OECD 1980-2000

Equation (4): $RD_{j, t} = \alpha + \beta * RDI_{j, t} + u_t$

p-values in parentneses

(b) GMM Estimation						
	(A)	(B)	(C)	(D)		
constant	0.08	0.06	0.07	0.06		
	(0.016)	(0.000)	(0.000)	(0.000)		
β	0.90	1.24	1.04	1.54		
	(0.23)	(0.000)	(0.000)	(0.000)		

p-values in parentheses

(A) uses GDP PPPs, (B) LCP2, (C) RDP1 and (D) RDP2

Table 2: Panel Estimation, OECD 1980-2000							
Equation (5): RRD _j , $_{t} = \gamma + \delta * RDI_{j, t} + e_{t}$							
(a) Random Effects							
	(A)	(B)	(C)	(D)			
constant	0.09	0.07	0.08	0.07			
	(0.000)	(0.000)	(0.000)	(0.000)			
δ	0.58	-0.13	-0.17	0.17			
	(0.001)	(0.011)	(0.001)	(0.016)			
p-values in parentheses							
(b) Fixed Effects							
	(A)	(B)	(C)	(D)			
β	0.64	-0.13	-0.16	0.18			
	(0.002)	(0.019)	(0.003)	(0.012)			
(c) Hausman Specification Test							
	(A)	(B)	(C)	(D)			
χ2(1)	0.48	1.74	2.02	1.52			
	(0.48)	(0.19)	(0.15)	(0.22)			
p-values in parentheses							

(A) uses GDP PPPs, (B) LCP2, (C) RDP1 and (D) RDP2

We, thus, retain both LCP2 and RDP1 as complementary estimates for the R&D price index, given the above limitations in the construction of VAP.

3. Real BERD and Innovation: Is Europe a Laggard?

The demand for more active industry policy on innovation has greatly increased in recent times upon evidence of a major spatial re-distribution of BERD in favour of the USA and a decline in R&D output in terms of new drug approvals. According to Gambardella et al. (2001), the birth of the pharmaceutical industry is almost synonymous with Europe but more recently there is a 'diffused perception' that Europe has become an innovation laggard when compared with the USA. This view is restated in Gilbert and Rosenberg (2004).

The above empirical assessments have important policy implications. An example is the policy towards explicit targets for R&D spending by the European Community and other OECD countries (Sheehan and Wyckoff 2003; Dougherty et al. 2003). Also, the view that R&D costs have grown considerably while productivity has declined poses serious questions about the sustainability of drug innovation and access to more expensive medicines by low-income groups (Grabowski 2002; DiMasi *et al.* 2003).

It is, however, puzzling that BERD has increased rapidly at a time when productivity has been 'shrinking' (Cockburn 2004) and R&D costs have grown rapidly (DiMasi *et al.* 2003). Given the surge in R&D costs and a declining productivity, one would expect a downward adjustment in R&D expenditure in the pharmaceutical industry.

The literature has attributed this phenomenon to technological change in the conduct of R&D (Cockburn 2004). As a result, the current debate on medicinal innovation emphasises returns to R&D and R&D productivity with little attention given to the adequacy of *real* R&D expenditure. A similar debate was also taking place in the early 1980s with the attention then being on patent life. At the time, Hutt (1982) was able to demonstrate that the rapid growth in BERD was mainly due to R&D price inflation and real BERD had actually declined.

Towards a better understanding of the above puzzles, it is essential we gain greater clarity on two important measurement issues. The first relates to the fact that there exists no single and unambiguous measure of business R&D expenditure (BERD). In fact, there are two clearly distinguishable measures of BERD. One derives from the *Frascati Manual* (OECD 1994) that concentrates on funds that directly relate to R&D performed by the industry and may include outsourced technical services to the

industry (Young 2001a). The measure was designed to facilitate international comparisons and the OECD ANBERD database has been the standard data source.

The literature has increasingly relied on an alternative measure of BERD. Thus is defined as total business spending on R&D by the industry, also known as 'source-based' expenditure.¹¹ The measure relies on industry surveys conducted by industry associations and is based on company accounts of total R&D related expenditures. Here BERD is defined in terms of the source of R&D funds made available by the industry and includes 'intra-mural' (performed) as well as 'extra-mural' (outsourced) R&D expenditures. For example, the USA data are derived from the *Annual Membership Survey* of Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA (2002) defines R&D expenditures as the 'total cost incurred for all pharmaceutical R&D activity" which includes depreciation and "total outlays for all research and development work contracted to others (manufacturers, independent research laboratories, academic institutions, etc.)' (p. 94). Thus, a major difference in the treatment of BERD between ANBERD and PhRMA is extramural expenditure that is excluded in the former but included in the latter.

The two measures can diverge substantially in practice. The *Frascati Manual* provides a standardised accounting of BERD that is comparable across countries while company-based estimates of BERD are difficult to interpret and compare as a result of differing accounting practices and national regulations between companies and countries (Young 2001a). On the other hand, the OECD ANBERD database neglects the industry's contribution to R&D via outsourcing and research alliances. The latter seems as a serious omission when considering the literature of innovation that has increasingly emphasised the importance of alliances and clusters (Sheehan and Messinis 2003). Thus, it is a paradox that, beyond OECD studies such as Young (2001a; 2001b), these measurement issues are rarely discussed in the literature.

Given the limitations in the above measures of BERD, empirical analysis of the industry's BERD performance could consider the utilisation of both of these measures. The two measures are better seen as complementary since they provide different insights on the practice of R&D. Nonetheless, caution should be exercised to avoid the eclectic use of BERD estimates when conceptual and measurement differences between the above two measures are not transparent. An example is the

¹¹ See for example Gambardella *et al.* (2001) and Cockburn (2004).

increasing use of OECD *Health Data* as the data source for BERD in pharmaceuticals. In order to correct for the ANBERD bias towards 'intra-mural' expenditure, OECD *Health Data* has recently switched to 'source-based' BERD data for Canada, Denmark and the USA but has maintained ANBERD as the source for the rest of the OECD. The *Health Data* can be useful if the focus of analysis is on the industry's aggregate BERD performance of a single country. Yet, the database can also lead to misleading cross-country comparisons if the *Health Data* user is unaware of its varying definitions and sources of BERD.¹²

The second measurement issue relates to the choice of R&D price deflators. While Cockburn (2004) is an exception, it is worth noting that most of the evidence on BERD to date is based on expenditure data that are adjusted by GDP PPPs. Figure 6 depicts real (performed) BERD in the USA and Europe based on GDP PPPs. Europe seemed to lag behind in the 1990s but the two series converged in 2000.



Yet, much of the innovation debate has focused on total R&D expenditure that includes extra-mural BERD. For a more balanced view, we also utilise industry data on total R&D expenditure. Data for the USA are from PhRMA (2002). European data are available for the period 1990-2000 by the European Pharmaceutical Association (EFPIA) in PARAXEL (2003). In figure 7, a major shift of R&D spending in favour of the USA and away from Europe is discernible in the 1990. It is this evidence that has alarmed the industry and policy makers in Europe.

¹² NSF (2002, p. 4-57) comments on the gap between 'performer-based' and 'source-based' and advices that ANBERD is the 'most reliable source' of international comparisons. Note also that in its 2004 edition, OECD *Health Data* has reverted back to OECD ANBERD as the exclusive source of BERD data.

This section utilises the new R&D price deflators, LCP2 and RDP1, to re-examine the view that Europe is an innovation laggard. We first take notice of a strong positive correlation between nominal BERD growth and R&D price inflation in Europe, Japan and the US¹³. This is consistent with the results in table 1 and a two-way causation between R&D price inflation and changes in nominal BERD that, in turn, impact on the spatial distribution of R&D activity.



Figure 7: Total BERD, Pharmaceuticals (US\$ PPP)

The sensitivity of nominal BERD to price changes also suggests that the USA and Europe would not diverge in terms of real BERD performance if purchasing-power theory is to hold in the long-run. The evidence here confirms the view that analyses of BERD can be misleading when nominal or US\$ PPP expenditures are used. Figure 8 illustrates real performed BERD for Europe, Japan and the USA when





¹³ The Pearson correlation coefficient for Europe, Japan and the USA are 0.94, 0.89 and 0.65 with LCP2 as the deflator and 0.95, 0.86 and 0.38 with RDP1. The last excluded, all coefficients are significant at the 0.01 level.

RDP1 is used as the R&D price deflator. This utilises the OECD ANBERD database that excludes extra-mural expenditure by the industry. The plot clearly shows that Europe is anything but a laggard. Moreover, even when total source-based BERD data are adjusted on the basis of the new R&D price deflators, LCP2 and RDP1, we again are unable to support the view of Europe as an innovation laggard (figures 9). In fact, we observe that the pattern in *real* total business expenditure on R&D is very similar in Europe and the USA and there is no evidence of divergence.



Figure 9: Real Total BERD, Pharmaceuticals (RDP1)

Although the claim that Europe is a laggard is not supported by the evidence presented here, the disparity between figures 6 and 7 and between figures 8 and 9 requires further investigation in future research. Certainly, the disparity confirms the view that the two measures of BERD seem to yield conflicting results when the geography of R&D activity is the focus of analysis.

More importantly, the joint utilisation of the two measures may offer useful insights on the practice of innovation in pharmaceuticals. For instance, figures 7-8 combined indicate a major shift in R&D activities towards outsourcing and research alliances with other industries and public research centres in the USA but not in Europe. It, thus, seems important to examine further the link between extra-mural R&D expenditure and R&D productivity in the race for new medicines. Although the innovation literature points to a positive association between alliances and innovation (Sheehan and Messinis 2003), this cannot be inferred from the surge in extra-mural expenditure for pharmaceuticals since the latter includes outsourcing and research joint ventures (RJVs). This is on the basis of Adams and Marcu (2004) who find that in the USA only RJVs contribute to innovation while the effect of R&D outsourcing has been limited to cost saving.

Finally, we consider the view that R&D productivity has declined in pharmaceuticals in the late 1990s. We are interested to know whether the new R&D price deflators developed here can confirm this view. First, we examine the link between BERD and the number of new molecular entities (NMEs) approved by the FDA in the USA over the period 1980-2000. Figure 10 depicts the 3-year average of NMEs per Billion of US\$ when using GDP PPPs and our R&D price deflator (RDP1). The first series gives credibility to the idea that major drug innovations have become harder to obtain. In terms of the number of NMEs, the solid line suggests that R&D productivity in the industry has persistently declined. Of course, this measure fails to account for the degree of innovation and its importance for consumers. Nonetheless, when the new R&D price deflator, RDP1, is used to arrive at real BERD, a very different picture emerges. This new estimate indicates a more stable pattern in R&D productivity. Rather than a secular decline in R&D productivity, the late 1990s look more like a cyclical downturn or a correction from the peak of 1997 and there is no evidence of a long-run trend in R&D productivity.



Patents data provide further insights on the innovation record of the pharmaceutical industry. Figures 11 and 12 summarise the performance of the industry in terms of patent applications per million US\$ of BERD. When conventional GDP PPPs are used as a proxy for R&D price inflation we see a secular decline in R&D productivity with a brief rebound in patents in 1993-95 (solid lines). Paradoxically, the decline is

more pronounced for the USA. The use of industry-specific R&D price deflators, however, leads to totally different conclusions. The new deflators indicate that the industry has, in fact, lifted its R&D productivity in the 1990s. However, the USA remains far more effective in converting R&D into patents than Europe.



Source: USPTO, unpublished (http://patft.uspto.gov)



Source: USPTO, unpublished (http://patft.uspto.gov)

Finally, it seems that the USA has consolidated its position as a leader and the R&D productivity gap between the USA and Europe or Japan has widened. Figure 13 makes this point crystal clear and highlights the fact that real R&D productivity (i.e., patents per real *performed* BERD) has improved in both Europe and the USA but this is not the case for Japan. Here, a secular downward trend is obvious.

The evidence in this study has several policy implications. First, it suggests that the recent shift towards business incentives and targets for pharmaceutical BERD in Europe and Japan may be ineffective if the main objective is to stimulate further innovation in the industry. This is on the basis of two important findings: Europe has had no difficulty in attracting real BERD which, in turn, has matched that of the USA, and a spatial re-distribution of business expenditure is likely to be offset by subsequent adjustments in the price of R&D.



Figure 13: Patents and Performed BERD, USA, Europe & Japan (2-year Average)

Source: USPTO, unpublished (http://patft.uspto.gov)

Second, the global pharmaceutical industry has achieved sustainable higher levels of R&D productivity during the 1990s. Amongst the fifteen OECD countries examined here, Japan stands out as the single case where R&D productivity has persistently declined. Given that real BERD in Japan has kept pace with the rest of the OECD (figure 8), the evidence here calls for a shift in policy focus away from BERD and towards policies that boost R&D productivity and returns to R&D.

4. Conclusion

The recent health literature has paid much attention to evidence of a growing spatial imbalance with respect to business expenditure on R&D. As a result, research and public policy have adopted the view that the USA has become a supreme leader and Europe has increasingly lagged behind. This view has major policy implications but greatly relies on data that is not appropriately adjusted for R&D price inflation.

This paper refrains from using GDP price deflators to adjust for inflation and develops new R&D price deflators for pharmaceuticals. The methodology builds on Jaffe (1973) and Griliches (1984) and is consistent with recent evidence in Dougherty et al. (2003). The construction of new price deflators is guided by economic theory and modern panel data estimation techniques. The paper also explores several avenues to test the robustness of the new R&D price deflators.

The evidence presented here indicates that the 'perception' of Europe as a laggard is not consistent with the data on *real* BERD. This paper has shown that previous evidence on BERD in the pharmaceutical industry may be a mirage due to R&D price inflation and to major differences in R&D price inflation between the USA and Europe. The evidence here also contrasts with previous claims of a declining rate of innovation in new drugs and shows that the pharmaceutical industry has achieved higher levels of R&D productivity.

The evidence here calls for a major re-assessment of the debate on patterns in real BERD and the sustainability of innovation in pharmaceuticals. More precisely, the results suggest that future research pays greater attention to thee key questions:

- Is the decline in real performed BERD in the USA responsible for the decline in the number of NMEs and new drugs?
- Has extra-mural R&D expenditure played an important role in drug innovation and R&D productivity?
- Why have Europe and Japan lagged behind the USA in patents and R&D productivity?

Data Appendix

Throughout the paper, the OECD-15 consists of the following countries: Australia, Canada, Belgium, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Spain, Sweden, the UK and the USA. Accordingly, Europe is defined as the OECD-15 without Australia, Canada, Japan and the USA.

Labour Compensation

OECD Health Data is the source of Australian data for the period 1980-1995. Unpublished Australian Bureau of Statistics (ABS) data on 'wages and salaries' are used to extend the sample to 2000. The ABS data, however, combines the 'Medicinal and Pharmaceutical Product Manufacturing' industry (code 2543) with 'Pesticides' (2544) and only since 2000-01 the two are separated. Based on the 2000-01 estimates, we adjust the wages and salaries figures by a factor of 0.902.

STAN data for Spain are not available for the period 1980-1985. We extrapolate on the basis of labour cost movements in France. All series for Germany are the result of splicing in 1991 that extends the STAN series for United Germany on the basis of the West Germany data.

Employment

The OECD Health Data provide Australian data for the period 1980-1992 and ABS covers the period 1996-2000. We resort to linear interpolation for missing values. STAN is used for total employment data. These are not available for the UK while for Belgium they are only available for the period 1994-2000. For the UK, the total number of employees is used as a proxy and we extrapolate the Belgian data back to 1980 on the basis of yearly growth in France.

R&D Business Expenditure

Industry data on total BERD are as recorded by the pharmaceutical associations in Europe, Canada and the USA. The European expenditures data (PAREXEL 2003), denominated in Euros, were converted to US\$ on the basis of current exchange rates in the FRED Database, Federal Reserve Bank of St. Louis, <u>http://research.stlouisfed.org/fred2/</u>. Canadian data are for the period 1988-2000 and come from PMPRB (2001, table 7, p.27) while the USA data are from PhRMA (2002).

The OECD ANBERD database is the source for most OECD-15 countries. A change of classification from *ISIC Rev. 2* (code 3522) to *ISIC Rev 3* (code 2423) in ANBERD 2001 apparently maintains compatibility for pharmaceuticals. *Rev 2* of ANBERD 2001 is the primary source for the period 1973-1986 and *Rev 3* for the period since. Due to data limitations, there are some exceptions. We draw more extensively from ANBERD 2001 *Rev 2* for Germany and Italy for the period 1980-94. Belgium data for 1980-1986 come from OECD Health Data 2003. Since only bi-annual data are available up to 1985, we use linear interpolation to obtain an annual series. For Germany, there is a break in the series due to the unification of Germany. We used 1991-99 data for "UDEU" (ANBERD code) in order to arrive at a (multiplicative) spliced series with 1991 as the base year. Thus, "Germany" stands for Unified Germany. Data for Norway are from Health Data 2002.

R&D Employment Share of Scientists and Professional

The SIRF, Hay Group, Ernst &Young (2001) study covered nine countries. Here, we use the mean of the France and Germany estimates as a proxy for Italy, Netherlands and Spain, the mean of France, Germany and the UK as a proxy for Belgium, the mean of Germany and Sweden for Denmark and the Sweden estimate for Finland and Norway.

Scientific Articles

Unpublished data were provided by Viola Peter at the *Competitiveness, Economic Analysis, and Indicators* unit, European Commission. These are available for the period 1980-1998 for all EU countries, Japan and the USA, and for the period 1980-1995 for the other four non-EU countries. We extend coverage to 2000 by linear extrapolation based on average growth in the last two years.

References

Adams, J.D. and Griliches, Z. (1996) 'Measuring Science: An Exploration', National Bureau of Economic Research (NBER) Working paper No. 5478.

Adams, J.D. and Marcu, M. (2004) 'R&D Sourcing, Joint Ventures and Innovation: A Multiple Indicators Approach', NBER Working paper No. 10474.

Cockbrurn, I.M. (2004) "The Changing Structure of the Pharmaceutical Industry' *Health Affairs* 23(1), 10-22.

Dickson, M., Hurst, J., and Jacobzone, S. (2003) 'Survey of Pharmacoeconomic Assessment Activity in Eleven Countries', OECD Health Working Papers No. 4, Paris: OECD.

DiMasi, J.A., Hansen, R.W. and Grabowski, H.G. (2003) 'The Price of Innovation: New Estimates of Drug Development Costs', *Journal of Health Economics*, 22(2), 151-85.

- Dougherty, S.M., Inklaar, R., McGuckin, R.H. and van Ark, B. (2003) 'International Comparisons of R&D Expenditure: Does an R&D PPP Make a Difference?' The Conference Board and Growth and Development Center, University of Groningen, Working Paper 03-03.
- Freeman, C. and Young, A. (1965) The Research and Development Effort in Western Europe, North America and the Soviet Union: An Experimental International Comparison of Research Expenditures and Manpower in 1962, Paris: OECD.
- Gambardella, A., Orsenigo, L. and Pammelli, F. (2001) 'Global Competitiveness in Pharmaceuticals: A European Perspective', European Commission, DG Enterprise, Working Paper No.1, Brussels (<u>http://pharmacos.eudra.org</u>).

Gilbert, J. and Rosenberg, P. (2004) 'Addressing the Innovation Divide: Imbalanced Innovation', World Economic Forum, Annual Meeting, Bain & Company: Davos.

- Grabowski, H. (2002) Patents, Innovation and Access to New Pharmaceuticals Patents, Innovation and Access to New Pharmaceuticals', *Journal of International Economic Law*, 5(4), 849-860
- Griliches, Z. (1992) ' The Search for R&D Spillovers', *Scandinavian Journal of Economics*, 94(0), S29-47.
- Griliches, Z. (1984) *R&D, Patents, and Productivity*, National Bureau of Economic Research, Cambridge, MA: University of Chicago Press.
- Gruber, J. and Koszegi, B. (2000) 'Is Addiction "Rational"? Theory and Evidence', NBER Working paper 7507.
- Hutt, P.B. (1982) 'The Importance of Patent Term Restoration to Pharmaceutical Innovation', *Health Affairs*, Spring 1(2), 6-24.
- Jaffe, S. (1973) A Price Index for Deflation of Academic R&D Expenditure, National Science Foundation, NSF 72-310.
- Jankowski, J.E. (1993) 'Do we need a price index for industrial R&D?', *Research Policy* 22(3), June, 195-205.
- Kaitin, K.I., Mattison, N., Northington, F.K., and Lasagna, L. (1989) 'The Drug Lag: An Update of New Drug Introductions in the United States and in the United Kingdom, 1977 through 1987', *Clinical Pharmacology & Therapeutics* 46(2), August, 121-38.
- Landau, R., Achilladelis, B. and Scriabine, A. (1999) *Pharmaceutical Innovation*, Chemical Heritage Press: Phladelphia PA.
- National Science Foundation (NSF) (2002) Science and Engineering Indicators 2002, Vo.1, U.S. Government Printing Office: Washington DC.
- OECD (2003) OECD Science, Technology and Industry Scoreboard, OECD: Paris.

OECD (2001) Science, Technology and Industry Scoreboard 2001, OECD: Paris.

- OECD (1994) Main Definitions and Conventions for the Measurement of R&D: A Summary of the Frascati Manual, OECD: Paris. (<u>http://www.oecd.org</u>).
- O'Mahony, M and van Ark, B. (2003), *EU Productivity and Competitiveness: An Industry Perspective. Can Europe Resume the Catching-up Process?*, Office for Official Publications of the European Communities, Luxembourg, November
- Pammolli, F. and Riccaboni, M. (2004) 'Market Structure and Drug Innovation', *Health Affairs* 23(1), 48-50.

PAREXEL 2003, PAREXEL's Pharmaceutical R&D Statistical Sourcebook 2002/2003, Boston.

- PhRMA (2002) *Industry Profile 2002: New Medicines, New Hope*, Pharmaceutical Research and Manufacturers of America, downloaded from <u>http://www.phrma.com</u>.
- Patented Medicine Prices Review Board (PMPRB) (2001) Annual Report 2001 Patented Medicine Prices Review Board. (<u>http://www.pmprb-cepmb.gc.ca</u>)
- Rao, DS.P and Trimmer, M.P. (2003) 'Purchasing Power Parities for Industry Comparisons Using Weighted Elteto-Koves-Szulc (EKS) Methods', *Review of Income and Wealth*, Dec, 49 (4), 491-512.
- Schreyer, P. and Koechlin, F. (2002) 'Purchasing Power Parities: Measurement and Uses', OECD Statistics Briefs No. 3, March.

- Sheehan, J. and Wyckoff, A. (2003) 'Targeting R&D: Economic and Policy Implications of Increasing R&D Spending', OECD STI working paper 2003/8, Paris: OECD
- Sheehan, P. and Messinis, G. (2003) 'Innovation in Australia', in I. McAllister, S. Dowrick and R. Hassan (eds.), *Cambridge Handbook of Social Sciences in Australia*, Cambridge: Cambridge University Press.
- SIRF, Hay Group, Ernst &Young (2001), 'Benchmarking Study of R&D Costs in Selected Segments of Australian Biotechnology', Canberra: Invest Australia.
- van Ark, B. (1996) 'Issues in Measurement and International Comparison Issues of Productivity: An Overview', in OECD Industry Productivity, International Comparison and Measurement Issues, Paris: OECD (http://www1.oecd.org/dsti/sti/stat-ana/prod/).
- Young, A. (2001a) 'Improving National Surveys and their International Comparability: Clinical Trials and R&D in Hospitals', in OECD, *Measuring Expenditure on Health-related R&D*, OECD: Paris.
- Young, A. (2001b) 'Other Views and Classifications of Health-Related R&D', in OECD, *Measuring Expenditure on Health-related R&D*, OECD: Paris.