Is Europe a Laggard in Pharmaceuticals?
R&D Joint Ventures, Patent Quality and R&D Productivity

Working Paper No. 30

George Messinis

Pharmaceutical Industry Project
Working Paper Series

September 2005

Centre for Strategic Economic Studies
Victoria University of Technology
PO Box 14428 Melbourne VIC 8001 AUSTRALIA
Telephone +613 9919 1340
Fax +613 9919 1350

Email: csesinfo@vu.edu.au
Website: http://www.cfses.com

Is Europe a Laggard in Pharmaceuticals?
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27 September 2005

Abstract

Has the USA overtaken Europe as the powerhouse of new medicines? If so, is this attributable to a flight of business expenditure in R&D to the USA? This paper answers these questions using a methodology that focuses on R&D productivity and patent quality as key indicators of innovation, accounts for R&D price inflation, and examines the role of both 'performed' R&D and 'extra-mural' R&D. The study provides three new insights: (a) the USA has outperformed Europe in R&D productivity but this is due to Europe's superior performance in sales and patent quality; (b) government expenditure on R&D and extra-mural R&D stimulate international patent collaboration, and (c) the latter is a crucial determinant of patent quality.

Keywords: Real BERD; Patent Quality; R&D Joint Ventures; R&D Productivity; Panel Data; Spatial GMM; Cointegration.

J.E.L. Classification: O31; O32; L65; I11; C33.

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* Thanks go to Steven Parker and Alison Welsh for research support as well as to seminar participants at Victoria University for valuable comments. The author alone is responsible for any remaining errors. Correspondence: George Messinis, Centre for Strategic Economic Studies, Victoria University, PO Box 14428, Vic 8001 Australia. E-mail: george.messinis@vu.edu.au. Tel: +613 99191339, Fax: +613 99191350.

1 Introduction

The pharmaceutical literature suggests that the USA has replaced Europe as the powerhouse of new medicines and that this is attributed to a flight of business expenditure in R&D (BERD) to the USA (EFPIA 2003; Gambardella *et al.* 2001; Pammolli and Riccaboni 2004). Comparisons based on national indicators of R&D intensity and per capita patents reinforce the view of a laggard Europe (European Commission 2003b). Thus, Europe is portrayed as a 'free rider' that relies on the USA for innovation while imposing price controls (Gilbert and Rosenberg 2004) and as the place where the pharmaceutical industry faces an uncertain future.

The current literature, however, has neglected three important issues. First, it has relied on GDP price deflators as proxies for R&D price indices[1] but it is now established that these are inappropriate (Dougherty et al. 2003; Jankowski 1993). Second, empirical work has suffered from a dual approach to the measurement of business R&D expenditure whereby a clear dichotomy exists between 'intra-mural' BERD and 'total' BERD. The former highlights the commitment of the industry as the performer of R&D in accord with the *Frascati Manual* (OECD 1994), the latter, also known as the 'expenditure' measure, captures total R&D spending by the industry and includes 'extra-mural' R&D (i.e., R&D sourcing and research joint ventures). Although the two are not equivalent, the exclusive focus on one of the two measures is pervasive in the empirical literature. Rarely the two indicators are seen as complementary.

A third issue involves a preoccupation with R&D expenditure at the expense of innovation output indicators such as patents or R&D productivity. Implicit here is the assumption that the link between R&D and innovation output remains stable over time and across the OECD. The expenditure approach to innovation also permeates public policy. The R&D tax concessions

[1] Cockburn (2004) is an exception. See Schreyer and Koechlin (2002) for more details on GDP PPPs.

offered by many OECD countries is one example.[2] Another is the pursuit of explicit official targets for R&D in Europe and Japan[3] (Sheehan and Wyckoff 2003; Dougherty et al. 2003). These incentives and targets rest on the idea that it is the *level* of R&D expenditure that matters in the discovery of new medicines. Yet, these traditional policies would be ineffective to the extent that R&D efficiency is the key driver of innovation outcomes (Wieser 2005).

Most recently, several studies draw attention to R&D productivity. Cockburn (2004) finds that there has been a steady decline in the number of new drugs approved in the USA for the period 1996-2002. He alludes to three main factors: long lags between R&D and new drug approvals, the rising quality of medicines and more expensive R&D processes.

Yet, the pharmaceutical literature has been slow to embrace new thinking on the economics of R&D productivity. For instance, little attention has been given to the Lanjouw and Schankerman (2004, 1998) hypothesis that an inverse relation exists between patent quality or market share and R&D productivity. Perhaps, this is due to the fact that, in contrast to other industries, the evidence in Lanjouw and Schankerman (2004) did not show patent quality to be a significant predictor of R&D productivity in pharmaceuticals. Yet, the hypothesis offers a new insight: a higher R&D productivity in the USA does not necessarily corroborate the view of Europe as an innovation laggard. Rather, it alludes to spatial shifts in patent quality and market performance.

This paper revisits the hypothesis of a growing spatial imbalance in pharmaceuticals. It extends the literature in three areas. First, it develops industry-specific R&D price deflators to adjust for inflation and examines both 'performed' R&D and 'total' R&D. Second, the paper

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[2] For details, see OECD (2003), European Commission (2003a) and HM Treasury (2005).

[3] The European Community plans to increase R&D spending to 3% of GDP by 2010 (European Commission 2003b).

draws on Lanjouw and Schankerman (2004) to model R&D productivity and outlines the case for international patent collaboration to be considered as an indicator of patent quality. Third, it seeks to model 'extra-mural' R&D and evaluate its impacts on R&D productivity and patent quality. Hence, the paper unfolds as follows. Section two develops the new R&D price deflators and examines trends in the geography of real BERD. Section three models R&D productivity and evaluates the role of 'extra-mural' R&D. Section four summarises and concludes.

2 R&D Price Inflation and Real BERD

This section develops new R&D price deflators for pharmaceuticals in the OECD. These deflators are based on estimates of industry-specific labour costs and non-labour R&D costs. The deflators are then used to examine OECD trends in R&D price inflation and *real* BERD.

3.1 Background

International comparative studies routinely adjust current-price R&D expenditures for price inflation to obtain estimates of real BERD. Ideally, the procedure requires industry-specific data on price and expenditure weights for each R&D input category. Currently, such deflators are not available but their development is an objective of official statistical agencies[4]. In the absence of R&D input-specific data, research has relied on GDP price deflators and GDP PPPs.

The GDP PPP approach, however, has two major limitations. First, industry output prices diverge considerably from aggregate GDP price levels and, thus, GDP PPP's can be misleading (Van Ark 1996). The validity of this criticism has been confirmed for pharmaceuticals in the USA

[4] See, for example, Breitschopf and Grupp (2004).

(Adams and Griliches 1996) and the OECD in general (O'Mahony and Van Ark 2003). Second, output deflators exclude intermediate inputs that form part of R&D and, thus, can lead to misleading comparisons given that these inputs are non-tradable (OECD 1994).

Jaffe (1973) and Griliches (1984) are early attempts towards an alternative to the GDP deflator for the USA. They propose a weighted R&D price index that combines the labour compensation index with a broader output deflator. Due to lack of industry-specific data on value added, they employ the GDP deflator as a proxy for the non-labour cost index. Dougherty *et al.* (2003) have challenged the GDP PPP convention. They compare the Griliches-Jaffe approach with an R&D deflator that includes industry specific information on non-labour costs and are able to show that the Griliches-Jaffe R&D deflators are comparable to the comprehensive deflators. This suggests that highly detailed information on non-labour inputs is not critical for an R&D price deflator.

In pharmaceuticals, the discontent with the GDP PPP approach is most conspicuous in the USA where alternative industry-specific data are available. Developed by the Bureau of Economic Analysis, the Biomedical R&D Price Deflator (BRDPI) is a weighted-average input price index that maintains the purchasing power of funds by the National Institutes of Health.[5] The NIH budget, however, mainly comprises of academic and Federal employee salaries and a pattern of NIH expenditure in favour of basic R&D. Hence, it is unclear how closely BRDPI tracks R&D price inflation in the private sector when we consider that 'research conducted in the public sector is managed and rewarded quite differently from work conducted in the private sector' (Cockburn and Henderson 1997, p. 13). Moreover, BRDPI is only available for the USA.

[5] The BRDPI is utilised in Cockburn (2004) and Adams and Griliches (1996). The latter demonstrates that the BRDPI has persistently grown faster than the implicit GDP deflator.

3.2 New R&D Price Deflators and Real BERD

We construct the new R&D price deflators as Tornqvist (T) indices. We define the R&D price deflator in country *m* as $RDP_{m,t} = \exp\left[\frac{1}{2}\sum_{i=1}^{k}(w_{m,i0}+w_{m,it})\ln\left(\frac{P_{m,it}}{P_{m,i0}}\right)\right]$ where P_{it} is the price level of R&D input *i* in the current period t, P_{i0} is the price level in the base year (1995 here), w_{it} and w_{i0} are the expenditure weights of input *i* in the current and base year respectively and k is the number of R&D inputs considered.

Following Dougherty *et al.* (2003), we depart from the convention of using the GDP deflator as a proxy for RDP_t and expand the range of R&D inputs to consider the case of k=4 for thirteen OECD countries[6] for the period 1990-2000. We draw on SIRF (2001) to identify four main R&D inputs in pharmaceuticals: (1) labour costs; (2) laboratory consumables; (3) laboratory and office equipment, and (4) occupancy & office expenses.

Towards an index of R&D unit labour costs, we adapt Frantzen (2000) to utilise OECD STAN estimates of labour compensation in the industry. STAN estimates of value added price deflators in related industries are used to construct price indices for non-labour R&D costs. In particular, laboratory consumables are linked to the 'chemicals and chemical products' industry (code 2400), laboratory and office equipment to 'electrical & optical equipment' (code 30-33), and occupancy & office expenses to 'business sector services' (code 50-74).

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[6] These are Canada, Belgium, Denmark, Finland, France, Germany, Italy, Netherlands, Norway, Spain, Sweden, the UK and the USA. This selection is purely based on data availability for *total* BERD. Estimates of Europe and Nordic states are weighted averages of all European and Nordic countries on the basis of industry employment. A detailed description of data sources and definitions appears in the Appendix.

Also, we calibrate expenditure weights for non-labour R&D costs using SIRF (2001) estimates in 2000.[7] We assume that the structure of non-labour R&D costs exhibits cross-sectional variation but remains constant over time. On the other hand, OECD data permit time-varying expenditure weights for labour and *total* non-labour costs.

We note briefly that the new R&D price deflator shows that the UK, Nordic countries and the USA have recorded the highest R&D price inflation in the OECD. On the other hand, big European players such as France and Germany have witnessed lower R&D price inflation than the USA.

We proceed to employ the new R&D price deflators to form a comprehensive view of real BERD in pharmaceuticals with a focus on cross-country differences within the OECD. First, we highlight the fact that there exist two alternative measures of *nominal* business R&D expenditure. One derives from the *Frascati Manual* and comprises of funds that directly relate to R&D performed by the industry. 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 that is defined as total business spending on R&D by the industry, also known as the expenditure measure.[8] These data derive from industry association surveys and company accounts of total R&D related expenditures. Here BERD is defined in terms of the financial commitment the industry makes to R&D where both 'intra-mural' and 'extra-mural' R&D expenditures are included.

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[7] We are indebted to Kim Sweeny at Victoria University for making these data available. Note also that the SIRF (2001) survey is limited to seven OECD nations. To overcome this, we invoke neighbourhood effects and assume that the share of labour costs in Belgium is the mean of France, Germany and the UK, the mean of Germany and Sweden for Denmark, Sweden's share for Finland and Norway, and the mean of France and Germany for Italy, Netherlands and Spain.

[8] See for example Gambardella *et al.* (2001) and Cockburn (2004).

Both of these measures have been subjected to criticism. The performance-based measure has difficulty dealing with R&D sourcing and joint ventures given that the *Frascati Manual* lacks clarity in its reference to these activities; it allows for external technical services to the industry but excludes sourcing of clinical trials (Young 2001a). On the other hand, the company-based estimates of BERD are difficult to interpret and compare as a result of diverse accounting practices and regulations across companies and countries (Young 2001a). For example, the Pharmaceutical Research and Manufacturers of America (PhRMA) measure of BERD includes some depreciation and 'R&D funds contracted or granted to commercial laboratories, private practitioners, consultants, educational nonprofit research institutions, manufacturing and other companies, or other research-performing organizations' (PhRMA 2003, p. 82). Thus, the main difference between performed BERD and total BERD is extra-mural expenditure that appears in the latter but not in the former.

The two measures can diverge substantially in reality. The *Frascati Manual* provides a standardised accounting of BERD that is comparable across countries. Yet, 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 importance assigned to alliances and clusters in the literature of innovation (Sheehan and Messinis 2003). It is, thus, perplexing that the above measurement issues are rarely discussed in the empirical literature, the methodological studies of Young (2001a; 2001b) are the exception.

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. We demonstrate below that the two measures are better seen as complementary each providing different insights on the practice of innovation. Nonetheless, caution should be exercised to avoid the eclectic use of BERD estimates when conceptual and measurement differences between the two measures

are not made transparent. For example, consider the case of OECD *Health Data* as a data source of BERD estimates for pharmaceuticals. In order to correct for the ANBERD bias towards 'intra-mural' expenditure, OECD *Health Data* 2003 switched to industry-based BERD data for Canada, Denmark and the USA but maintained ANBERD as the source for the rest of the OECD. The *Health Data* can be useful if the focus of analysis is BERD performance in a single country. Yet, the database can lead to misleading cross-country comparisons if the *Health Data* user is unaware of its varying definitions and sources of BERD.[9]

This study utilises both data sources: the OECD *ANBERD* measure of 'performed' BERD and the industry measure of total R&D expenditure. Data for the latter are from PhRMA (2003) for the USA (1980-2000), PARAXEL (2003) for Europe (1990-2000) collected by the European Pharmaceutical Association (EFPIA), and PMPRB (2001) for Canada (1988-2000). There is, however, one difference between these data sets: the USA data decomposes into domestic expenditure and expenditure abroad but only domestic expenditure estimates are available for Europe and Canada. Given the high growth rate correlation between total and domestic *industry* expenditure of 0.84 for the USA, we adjust the EFPIA and Canadian estimates by the total to domestic expenditure ratio in the USA. This is in order to derive comparable measures of *total* and *extra-mural* R&D expenditure.

Figure 1 depicts real performed BERD using both the GDP deflator and the new R&D price deflator. It shows that real intra-mural R&D expenditure has grown slower when the R&D price deflator is used to adjust for inflation than when the GDP deflator is used in the USA and the UK. For countries other than the USA, figure 2 also divides the two alternative deflators by the corresponding US series to make comparisons with the USA more transparent. Clearly, Europe

[9] OECD *Health Data* 2004 switched back to OECD ANBERD as the exclusive source of BERD data.

has not lagged behind the USA since the late 1980s. Moreover, Europe is not a homogeneous group. Germany has witnessed its share of global intra-mural R&D decline while that of Nordic countries has surged. The latter is surprising given the above average R&D price inflation recorded in Nordic states. What we observe is a trend towards a re-distribution of performed R&D within Europe rather than a growing imbalance between the USA and Europe.

- Figure 1 about here –

When we turn to real *total* R&D expenditure, a major shift in favour of the USA and away from Europe is discernible in the 1990 (figure 2). It is this evidence that has alarmed the industry and policy makers in Europe. Yet again, the Nordic states have gone against this trend but they do little to alter the fact that extra-mural R&D has deserted Europe in the 1990s. Recall, however, that this assessment rests on the critical assumption that the share of extra-mural R&D in the USA contributed by European companies is equal to the share of extra-mural R&D in Europe by US firms. Unfortunately, existing data do not permit an evaluation of this assumption but it seems plausible that Europe is over-represented in extra-mural R&D in the USA if we consider that the growth rates of intra-mural BERD in Europe and total expenditure spent by PhRMA members going abroad exhibit a correlation coefficient of 0.64. Overall, the evidence of a growing spatial imbalance between Europe and the USA is not strong as far as real R&D business expenditure is concerned.

- Figure 2 about here –

3 Patent Quality, Market Performance and R&D Productivity

In this section, we employ the new R&D price deflator to more formally test the view that Europe is an innovation laggard. We focus on R&D productivity as the principal indicator of innovation performance. This is motivated by literature concerns about the optimality of R&D investment in the presence of technological shocks and corporate governance issues.[10] In modelling productivity, we are guided by economic intuition, confront serious measurement problems, and employ dynamic panel data econometrics over the period 1990-2000.

3.1 R&D Productivity in the Literature

The empirical literature has documented a persistent decline in the patents to BERD ratio (i.e., the standard measure of R&D productivity) for pharmaceuticals in both the USA (Lanjouw and Schankerman 2004) and other OECD countries (Lanjouw *et al.* 1998). New molecular entities per R&D expenditure, an alternative measure of R&D productivity, also brings Cockburn (2004) to conclude that R&D productivity has shrunk in the USA over the period 1996-2002.

- Figure 3 about here –

We begin to investigate R&D productivity with figure 3 that summarises the granted patents to BERD ratio using the new R&D price deflator. The decline in productivity reported by Lanjouw and Schankerman (2004) is evident for the period 1980-1995. Yet, we also observe a sharp reversal of this trend since 1995. Even more pronounced is a secular decline in productivity

[10] For details, see Lanjouw and Schankerman (2004) and Jones and Williams (2000).

for the big European players and a strong performance by Nordic countries that have matched USA's surge in R&D productivity in the late 1990s. A bigger concern is that the UK has failed to regain some of the lost productivity, in contrast with France and Germany.

For further intuition, we turn to economic theory. Lanjouw and Schankerman (2004) have proposed a formal model that accounts for change in the quality of patents, q, and market power as key determinants of R&D productivity. It also allows for technological shocks. Resting on firm micro-foundations, the model predicts the following empirical relation:

$$pr_{m,t} = \alpha e(t) + \beta q_{m,t} + \gamma s_{m,t} + v_{m,t} \quad (1)$$

where pr_t is the log of R&D productivity, $e(t)$ is the log of R&D elasticity, q_t is the log of expected quality of inventions, s_t is the log of sales as an approximation of market power and v_t is normal, independently and identically distributed error. The theory predicts that $\beta, \gamma < 0$ in the sense that higher patent quality or sales motivate firms to devote less energy towards new patents. Technological exhaustion (i.e., a falling inventive output) is captured by the $\alpha e(t)$ term when $\alpha < 0$. Thus, the case of greater R&D emphasis on blockbuster drugs (Grabowski 2002) would indicate an increase in patent quality and a subsequent fall in R&D productivity.

3.2 Measurement and Data Issues

Towards estimation of (1), we arrive at two measurement hurdles. One relates to the choice between patent applications and patents granted for the numerator of the patents to BERD ratio. In theory, the second seems a better measure of innovation output but is often treated as inferior in practice since patent grants data become available with a lag of several years – the 'truncation'

problem. Still, this study settles on patents granted for two reasons. First, we propose that the disparity between patents granted and patent applications contains information regarding patent quality. Second, compared to patent applications, patent grants are less sensitive to changes in fees and in applicant *perceptions* of USPTO assessment standards (Jaffe and Lerner 2001).[11]

The second obstacle involves the measurement of patent quality. A number of variables have been proposed including patent citations, claims and renewals. Yet, these individual measures have limitations. For instance, citations and claims may signal increased competition and litigation and, thus, reduced market value (Bosworth *et al.* 2003) or they may simply relate to growth in the practice of patent citation (Hall *et al.* 2001). In an attempt to avoid some of these criticisms, Lanjouw and Schankerman (2004) utilise multiple indicators to develop a single patent quality index. However, the index still stands as a single all-encompassing measure. In contrast, we utilise USPTO data on applications and patents granted to arrive at two distinct but complementary measures of patent quality.

The first, q^1, emphasises patent grant intensity and is defined as the ratio of patent grants in the current year to patent applications in the last four years. Given the Hall *et al.* (2001) finding that the patent grant lag is on average about 2 years, q^1 is unlikely to suffer from 'truncation'. Of course, q^1 can only be seen as a baseline indicator of patent standards set by the US Patents Office. However, Sanyal (2002) and Jaffe and Lerner (2004) have questioned the stability of the USPTO standard. They maintain that the US Patent Office has compromised its assessment standards in the 1990s due to a lack of resources. We take this criticism seriously and adapt the approach proposed by Hall *et al.* (2001). Namely, we scale grant intensity and express it as a ratio

[11] Also, visual inspection of the q^1 series supports this view since there is no apparent downward trend in the grant intensity ratio in the most recent sample period.

to the mean grant intensity of all OECD patents in the same year. Provided the assessment of patent applications by the USPTO is free of a country bias, our first measure of patent quality overcomes the above criticism.

The second measure of patent quality, q^2, is the share of patents granted to country *m* for which at least one co-inventor resides in another OECD country. Below we outline the rationale and evidence in favour of this proposition. First, we note that Lanjouw and Schankerman (2004) define patent quality as the set of attributes of a product that make it superior to existing products on technical grounds and add market value to the firm. However, given that these characteristics are not directly observable, Lanjouw and Schankerman (2004) emphasise the value dimension of patent quality in their empirical work.

Second, we take note of the literature of innovation suggesting that knowledge networks and business alliances promote innovation (Sheehan and Messinis 2003). Adams and Marcu (2004) more precisely focus on research collaboration and find that Research Joint Ventures (RJVs) significantly add value to firms in the USA. Also, a decade since the pioneering paper of Coe and Helpman (1995) research continues to highlight complementarities in skills and capital as the main sources of high productivity returns to R&D international spillovers (Wieser 2005; Bentzen and Smith 2001).

Since q^2 directly relates to innovation output and international R&D spillovers, we maintain that international patent collaboration can be a useful indicator of patent quality. Before we rest our case, however, we seek to substantiate the claim that both q^1 and q^2 associate with market value at the national level. We expect that these two indicators would add to profitability were they to be considered as indicators of patent quality. Namely, we conjecture the short-run relation

$$\Delta\pi_{m,t} = b_1\Delta r_{m,t} + b_2\Delta q^1_{m,t-1} + b_3\Delta q^2_{m,t-1} + u_{m,t} \qquad (2)$$

where π is the log of per capita gross operating surplus as a measure of profitability, r is the log of per capita real intra-mural BERD, q^1 and q^2 are the two patent quality indicators in logs and u is an error term.

Table 1 presents the results of feasible generalized least squares (FGLS) estimation that corrects for AR(1) autocorrelation within panels, contemporaneous cross-sectional correlation and heteroscedasticity across panels. We observe that both coefficient estimates are positive and significant and interpret this as support for the proposition that q^1 and q^2 act as indicators of patent quality.

We pause, however, to reflect on the implications of economic geography for our study. In particular, we suspect that the assumption of cross-sectional independence may be unsustainable in the presence of innovation clusters and R&D spillovers.[12] Thus, we test the empirical validity of the cross-sectional independence assumption, given that standard errors are inconsistent when this assumption is violated (Driscoll and Kraay 1998). We employ the Breusch-Pagan test statistic of cross-sectional independence, BP (Greene 2000) and that proves to be significant in table 1.

Since the FGLS results are still contaminated by spatial correlation, we proceed with alternative estimation techniques that can handle cross-sectional dependence. In addition, it is plausible that Δr_t is endogenous in (2) since Achilladelis and Antonakis (2001) find profit to be a predictor of R&D expenditure. Hence, we employ two spatial GMM estimators: Conley (1999)

[12] Cross-sectional independence may also be violated due to common shocks countries share (Moon and Perron 2004). On the geography of R&D, see Kyle (2004) for pharmaceuticals, and Simmie *et al.* (2002) and Conley and Ligon (2002) for other industries.

and Driscoll and Kraay (1998).[13] The former relies on prior knowledge of the structure of temporal dependence but applies a nonparametric correction that accounts for economic distance. We exploit the CEPII measure of distance between major cities[14] to obtain projected coordinates as in Conley (1999). The results are summarised in table 1 and indicate that Δq^1 and Δq^2 are indeed key determinants of profitability. Note also that the coefficient estimates of Δq^1 and Δq^2 are now larger than those produced by FGLS. Next we apply the Driscoll and Kraay (1998) GMM estimator that is robust to general forms of cross-sectional dependence. Again we obtain similar results in table 1.

– Table 1 about here –

Last, we investigate whether the relation in (2) holds in the long-run. It is well established in the literature that for π_t r_t, q^1_t and q^2_t to enter a long-run or cointegrating relation they must be of the same order of integration as well as being non-stationary or trend-stationary. Panel unit root test suggest that π_t r_t, and q^2_t are all I(1) but q^1_t is I(0). Thus, the long-run relation reduces to

$$\pi_{m,t} = \alpha_m + \delta_m t + \beta_1 r_{m,t} + \beta_2 q^2_{m,t} + e_{m,t} \qquad (2A)$$

where t is a time trend and e_t is a disturbance term. We adopt the Pedroni (1999) residual-based estimation approach to test for cointegration. The advantage of this approach is that it

[13] We are grateful to Professor Conley who made available STATA code for spatial OLS and spatial GMM estimation. We also thank Steve Green for RATS code used to compute Driscoll and Kraay (1998) GMM estimates and RATS code for panel cointegration tests made available by Professor Peter Pedroni.

[14] This is variable 'distwces' available at http://www.cepii.fr/anglaisgraph/bdd/distances.htm

allows for heterogeneity across individual countries in the mean and time effects. Pedroni (1999) provides critical values for seven different statistics. He distinguishes between 'within-dimension' or 'panel' statistics and 'between-dimension' or 'group' statistics. The former are estimators that pool the autoregressive coefficient in the unit-root tests across different countries separately while the latter set of estimators average the individually estimated coefficients for each country. One difference is that the 'group' estimators allow for additional heterogeneity. This feature makes them more robust than the 'panel' estimators in small samples in the sense that they are less susceptible to size distortions. The panel set comprises of *v* (a type of non-parametric variance ratio), ρ (the panel equivalent to the Phillips-Perron ρ-statistic), *pp* (equivalent to the Phillips-Perron *t*-statistic), and *adf* which is analogous to the augmented Dickey-Fuller *t*-statistic. The three 'group' statistics set includes ρ, *pp*, and *adf*.

The cointegration results appear in table 1. Most of the test statistics and especially the group statistics reject the null hypothesis of no-cointegration. For comparison, we also consider a restricted model of (2A) where q^2_t is excluded. The results show that a larger set of statistics reject the null hypothesis when (2A) is unrestricted. Thus, we conclude that π_t r_t, and q^2_t all cointegrate. Overall, the results in table 1 provide strong support for the view that q^1_t and q^2_t are valid indicators of patent quality.

3.3 Lanjouw and Schankerman (2004): New Evidence

Here, we intend to utilise the new R&D price deflator and the two indicators of patent quality to re-visit the Lanjouw and Schankerman (2004) hypothesis. We begin with the estimation of (1) in the short-run. We work in first differences and derive robust feasible GLS estimates as previously. The results are presented in table 2.

– Table 2 about here –

The results are consistent with the predictions of the model in question. All coefficients have a negative sign and are statistically significant. We again take note of the significant BP test statistic.[15] Following Lanjouw and Schankerman (2004), we next treat Δq^1_t as an endogenous variable and proceed with spatial GMM estimation. The coefficient estimates remain consistent with the maintained hypothesis but now exhibit much smaller standard errors.[16]

In the lower panel of table 2, we examine the Lanjouw and Schankerman (2004) hypothesis in the long-run. We consider an unrestricted model where the dependent variable is per capita patents granted, p_t, and per capita real intra-mural R&D expenditure, r_t, appears on the right hand side. Again, we exclude q^1_t for reasons outlined above. The results suggest a cointegrating relation exists between patents, BERD, sales and international patent collaboration. Thus, the evidence in this section seems highly consistent with the Lanjouw and Schankerman (2004) hypothesis.

On the question of a spatial imbalance between the USA and Europe, the hypothesis and the new evidence here suggest that the relative decline of Europe's performance in R&D productivity (figure 3) during 1985-1995 and a partial recovery in 1996-2000 can be explained by its relative performance in patent quality and sales. The Europe-USA differential in patent quality, q^2_t, has risen sharply in the first period and has declined in the latter period (i.e., from 0.11 in 1985 to 0.25 in 1997 and 0.21 in 2000). Also, the ratio between real per capita national sales in Europe and the USA was 1.05 in 1980, 0.67 in 1985, 1.39 in 1995 and 0.87 in 2000. For reasons that will

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[15] We also consider the possibility that spatial correlation is an artefact of missing time effects. However, even when time dummies are included, the BP statistic remains significant in all tests performed here.

[16] See Conley (1999) for a discussion on the asymptotic distribution of standards errors in spatial GMM.

become clearer in the following sub-section, we also note that R&D productivity in Europe (relative to the USA) has improved since 1996 and this is also the period when Europe lost some of the advantage it had over the USA in relation to sales and international patent collaboration, q^2_t. Below, we show that this recent trend can be explained by a link between extra-mural R&D, R&D international spillovers and patent quality.

3.4 Extra-Mural R&D, Research Joint Ventures and Patent Quality

Analysis in the previous sub-section was limited to *performed* BERD. However, the growing disparity between performed BERD and total BERD requires further investigation.[17] We first consider the possibility that extra-mural R&D impacts on R&D productivity. The literature points to a positive association between alliances and innovation but it would be speculative to suggest that the former is equivalent to extra-mural R&D since the latter includes outsourcing and research joint ventures (RJVs). This is based on Adams and Marcu (2004) who find that RJVs in the USA contribute to innovation while outsourcing is limited to cost saving.

Next, we test whether real per capita extra-mural BERD is a predictor of R&D productivity. We repeat the estimation procedures used in table 2 by extending (1) to incorporate extra-mural BERD. Not reported here, the results show that extra-mural BERD has a positive and significant effect on R&D productivity when the FGLS and Conley's Spatial GMM estimator are employed. Cointegration tests suggest that extra-mural BERD also enters a long-run relation with patents, BERD, sales and international patent collaboration. Yet, when the Driscoll and Kraay (1998) GMM estimator is employed, the coefficient estimates of Δs_t and Δq^2_t become insignificant.

[17] Extra-mural BERD in the USA and Europe has grown from 25% (31%) and 16% (13%) of the total (domestic) R&D expenditure in 1990 to 50% (61%) and 61% (50%) in 2000 respectively.

The last finding alludes to collinearity between extra-mural BERD and sales or international patent collaboration. Intuitively, one would expect extra-mural R&D and international patent collaboration to correlate if the former is channelled into research joint ventures (RJVs). It is also plausible that extra-mural R&D forms part of a strategic business response to shifts in the global pharmaceutical market.

We examine these two possibilities next. More precisely, we consider the model

$$\Delta rx_{m,t} = \alpha_1 \Delta s_{m,t} + \alpha_2 \Delta gro_{m,t} + \varepsilon_{m,t} \qquad (3)$$

where rx_t is the log per capita real extra-mural R&D expenditure, s_t is the log of sales and gro_t is the log of per capita *total* government R&D expenditure on health and environment programmes in *other* countries,[18] and ε_t is another error term. The estimation results of FGLS, Spatial OLS (Conley 1999) and cointegration tests appear in table 3. They provide clear evidence that extra-mural R&D reacts positively to government R&D expenditure on health and inversely relates to national pharmaceutical sales. The former is consistent with existing evidence of public sector R&D spillovers on business R&D expenditure (Toole 2002; Cockburn and Henderson 1997).

– Table 3 about here –

[18] That is, $gro_{m,t} = \ln\left(\sum_{j=1}^{14} gr_{j,t}\right)$ where j≠m and $gr_{m,t}$ is per capita government R&D spending on health and the environment. Note, the growth rate of $gr_{m,t}$ did not prove to be a significant predictor of $\Delta rx_{m,t}$.

Finally, we seek to explore further the link between extra-mural BERD and patent quality gains via international collaboration. We hypothesise that extra-mural BERD, q^2_t, contributes to patent quality as a result of international research joint ventures. We examine the relation

$$q^2_{m,t} = \gamma_1 rx_{m,t} + \gamma_2 gro_{m,t} + u_{m,t} \quad (4)$$

In view of results in table 3, we treat extra-mural BERD as endogeneous. In order to estimate (4), we adopt the dynamic panel data estimation (DPD) approach pioneered by Arellano and Bond (1991) and fully developed by Arellano and Bover (1995). The procedure, known as the *System GMM* panel estimator, exploits information on all series to obtain separate instruments for each lag and each time period, and then uses GMM to weight them. We know, however, that the two-step GMM estimator produces standard error estimates that are severely downward biased in small samples (Arellano and Bond 1991). In response, we apply a finite-sample correction as proposed by Windmeijer (2005) who demonstrates that the correction makes the twostep robust GMM estimator more efficient than the onestep estimator. Table 4 reports robust two-step system GMM estimates of (4). It also reports the Hansen J test of over-identifying restrictions[19] and the Arellano-Bond tests (AB) for AR(1) and AR(2).

- Table 4 about here -

[19] System GMM was performed using Roodman's (2005) 'xtabond2' procedure in STATA. We use the 'collapse' sub-option in 'xtabond2' that creates one instrument per variable and lag distance and excludes instruments for each time period. This is to avoid a bias that arises when the number of instruments approaches the number of observations (Bond 2002).

The results in table 4 indicate that extra-mural BERD has a major impact on international patent collaboration and its effect on patent quality is almost double that of government R&D expenditure. Panel cointegration tests confirm the existence of a long-run relation between extra-mural R&D in pharmaceuticals, government R&D in health and patent quality.

Jointly, the results in tables 3 and 4 are very significant since they shed new light on the mechanism via which extra-mural R&D impacts on R&D productivity and facilitates R&D international spillovers in pharmaceuticals. First, extra-mural R&D investment reacts inversely to a downturn in market performance and responds positively to a rise in public R&D expenditure. Consequently, extra-mural R&D mixes with public research at the international level to produce high quality innovation. Finally, the evidence in tables 4 and 1 suggests that, with some lag, high quality patents boost pharmaceutical sales and profitability in the industry. This is illustrated in figure 4 where changes in real per capita 'extra-mural' R&D expenditure (lagged two years for most countries and three years for the USA) predict changes in real per capita national sales. Thus, extra-mural R&D has been a major catalyst in that it has enabled the USA to catch up with Europe with respect to patent quality.

- Figure 4 about here –

4 Summary and Conclusions

The literature has expressed growing concerns that Europe has increasingly lagged behind the USA in the development of new medicines. The emerging view attributes this to a persistent spatial re-distribution of R&D resources in favour of the USA. However, the evidence in support of this view derives from a methodology that (a) uses GDP price deflators to adjust for R&D

price inflation; (b) over-emphasises expenditure at the expense of R&D productivity indicators, and (c) fails to draw on economic theory regarding the modelling of R&D productivity.

This paper addresses all of these three issues. It utilises data on thirteen OECD countries to re-examine the view that Europe is an innovation laggard in pharmaceuticals. The study develops industry-specific R&D price deflators to estimate real BERD, considers the role of both 'intra-mural' and 'extra-mural' R&D expenditure, and focuses on R&D productivity as the principal indicator of innovation. The paper utilises US patents data to measure patent quality. It advances the idea that international inventor collaboration is an important dimension of patent quality. The study also extends to the nexus between 'extra-mural' R&D and R&D productivity.

The empirical evidence here provides several new insights. First, there is no clear evidence of a widening gap between the USA and Europe in regards to real business R&D expenditure; rather, real BERD has been re-distributed within Europe away from traditional players towards the Nordic states. Second, international inventor collaboration proves to be a key element of patent quality. Third, the USA has indeed outperformed Europe but this is mainly due to a better performance by Europe in pharmaceutical sales and patent quality due to international R&D joint ventures. Finally, 'extra-mural' R&D responds to public R&D expenditure in health and both are major drivers of international collaboration and patent quality.

Appendix: Data Description

Labour Compensation and Employment

For Spain, data are not available during 1980-1985 and we extrapolate on the basis of growth in labour costs in France. All series for United Germany are the result of splicing in 1991 that extends the STAN data on the basis of the West Germany data. Total employment data are not available for the UK, we use

total number of employees as a proxy. For Belgium they are only available for the period 1994-2000. We extrapolate the Belgian data back to 1980 on the basis of yearly growth in France.

R&D Expenditure

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 and are only available bi-annually up to 1985; we linearly interpolate to complete the 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 on government R&D expenditure on health and environment programmes are from OECD *Main Science and Technology Indicators* 2004-1 (US$ PPP). Missing values in 1980 and Japan (1980-1987) are filled by extrapolation. Note, all expenditure and output data are in *per capita* values throughout this study.

R&D Cost Structure

The SIRF, Hay Group, Ernst &Young (2001) study covers six of the thirteen countries covered here. They find costs on laboratory consumables, lab and office equipment and occupancy and office expenses respectively to be 21.1%, 27.6% and 51.3% of non-labour costs in Canada; 18.7%, 22% and 59.3% in France; 19%, 24.3% and 56.7% in Germany; 18.5%, 22.2% and 59.2% in Sweden; 14.6%, 17.5% and 67.9% in the UK, and 17.4%, 24% and 58.7% in the USA. 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.

In order to allow the R&D input cost shares to vary across nations and over time, we also estimate R&D business enterprise personnel. The OECD *Main Science and Technology Indicators* database is the primary source for the period 1987-2000. We supplement this source with data from PhRMA (2003) and DiMasi *et al.* (2003) to obtain estimates for the USA. Missing observations have been filled on the basis of the mean annual growth rate in France and Germany for Belgium, Italy and Netherlands; the mean growth rate of France and USA for Canada and the UK, and the growth rate in Sweden for Denmark and Finland. For the period 1980-1986, we exploit information on the R&D personnel share of total employment in the industry and changes in the ratio of BERD to Value Added to expand the R&D personnel series.

National Sales and Sales Price Index

This is the sum of 'total expenditures on pharmaceuticals & other non-durables' (OECD *Health Data* 2004) and net exports (OECD *STAN*). When available, the annual growth rate of 'pharmaceutical sales' (*Health Data* 2004) is used to fill gaps in the former (Italy in 1980-1987, and Norway and Spain in 1998-2000). Missing observations for Belgium, France and the UK are filled by interpolation/ extrapolation on the basis of annual growth rates in adjacent data points. Regrettably, we cannot control for re-exports; i.e., imported goods exported without further transformation. The 'total expenditures on pharmaceuticals & other non-durables' price index (OECD *Health Data* 2004) was used. Missing data are filled on the basis of the mean of growth rates of France and Germany for Belgium, the mean of Germany and Switzerland for Italy, the mean of Denmark and Sweden for Norway and the mean of France and Italy for Spain. Missing observations in France (1981-1984 and 1986-1989) and Japan (1998-2000) are filled by interpolation and extrapolation respectively.

Value Added Implicit Price Deflators

Implicit value added deflators are derived from value-added estimates and value-added volume indices $VAP_{i,t} = 100*VALU_{i,t} / (VALK_{i,t}*VALU_{i,95})$ where $VALU_i$ is the STAN code for value added in industry *i* at national currency units, $VALK_{it}$ is the value added volume index at time *t* and the $VALU_{95}$ is value added in 1995, the base year. VALK data are only available for Canada, Denmark, France, Norway and the UK. VALK data for chemicals industries are used for other countries. These data were not available for Norway and we used the pharmaceutical industry deflator instead. We also extrapolated to fill data gaps for France (1980-1991), Spain (1980-1994) and Sweden (1980-1992) on the basis of annual growth rates in Belgium, Italy and Finland respectively.

USPTO Patents

Patents data were collected in early 2005 at the USPTO web site. The pharmaceutical industry was defined to comprise of technology classes 424 and 514. Patent data for the USA is the sum of patent counts in individual US states. The inventor collaboration series was defined as the number of granted patents for which at least on of the inventors lived in one of the other OECD countries in the sample plus Switzerland, given the status of the latter as a leading player Due to limitations in the USPTO search engine, only the twenty eight leading US states were considered as international locations of patent collaboration for non-US countries. These US states are as follows: AL, AZ, CA, CO, CT, DE, FL, GA, IL, IN, LA, MD, MA, MI, MN, MO, NH, NJ, NY, NC, OH, PA, TN, TX, UT, VA, WA, WI.

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Table 1. Inventor Collaboration, Profitability and Patent Quality:
Feasible GLS, Spatial GMM and Cointegration Tests

Short-Run: $$\Delta\pi_{m,t} = b_1\Delta r_{m,t} + b_2\Delta q^1_{m,t-1} + b_3\Delta q^2_{m,t-1} + u_{m,t} \qquad (2)$$

	Feasible GLS	**Spatial GMM**	
		(Conley 1999)	(Driscoll and Kraay 1998)
b_1	0.687 (0.050)*	0.537 (0.122)*	0.601 (0.154)*
b_2	0.182 (0.023)*	0.196 (0.032)*	0.199 (0.066)*
b_3	0.020 (0.015)*	0.077 (0.014)*	0.071 (0.022)*
BP Statistic	106.5*		
J (5) Statistic		1.03	0.63

Long-Run: $$\pi_{m,t} = \alpha_m + \delta_m t + \beta_1 r_{m,t} + \beta_2 q^2_{m,t} + e_{m,t} \qquad (2A)$$

Panel Cointegration (Pedroni 1999)

	Complete Model		Assuming $\beta_2=0$	
Test Statistic	Panel	Group	Panel	Group
v	-0.28		-0.02	
ρ	1.29*	2.51*	0.62	1.04
pp	-4.80*	-6.99*	-7.36*	-7.26*
adf	-4.43*	-5.74*	-6.90*	-6.53*

π is the log of real per capita gross operating surplus (i.e., value added minus labour compensation). * denotes significance at 5% level. BP is the Breusch-Pagan test of cross-sectional independence, $\chi^2(78)$. J is the test statistic for over-identifying restrictions distributed as $\chi^2(k)$. Here, k =5 since eight instruments were used: two lags of Δr_t and growth in value added, Δy_t, and sales, Δs_t, as well as the two exogenous variables Δq^1_t and Δq^2_t. Cointegration tests include heterogeneous time effects and the maximum number of autoregressive lags is set to two, in the ADF-based tests. A variety of panel unit root tests suggest that π_t, r_t and q^2_t are I(1) processes but q^1_t is I(0).

Table 2. Patent Quality, Sales and R&D Productivity

Short-Run: $$\Delta pr_{m,t} = \alpha \Delta q^{1}_{m,t} + \beta \Delta q^{2}_{m,t} + \gamma \Delta s_{m,t} + v_{m,t} \quad (1)$$

	Feasible GLS	**Spatial GMM**	
		(Conley 1999)	(Driscoll and Kraay 1998)
α	**-0.534** (0.038)*	**-0.370** (0.009)*	-0.376 (0.02)*
β	**-0.207** (0.019)*	**-0.062** (0.004)*	**-0.074** (0.023)*
γ	**-0.565** (0.046)*	**-0.511** (0.025)*	**-0.356** (0.050)*
BP Statistic	140.9*		
J (5) Statistic		1.19	7.05

Long-Run: $$p_{m,t} = \alpha_m + \delta_m t + \beta_1 r_{m,t} + \beta_2 q^{2}_{m,t} + \beta_3 s_{m,t} + e_{m,t} \quad (1A)$$

	Panel Cointegration (Pedroni 1999)	
Test Statistic	Panel	Group
v	-0.64	
ρ	2.16*	3.98*
pp	-4.43*	-3.99*
adf	-2.82*	-2.57*

* denotes significance at 5% level. BP, the Breusch-Pagan test of cross-sectional independence is $\chi^2(78)$. J is the test statistic for over-identifying restrictions, $\chi^2(5)$. Eight instruments were used: two lags of Δq^1_t, growth in value added and growth in patents granted, as well as the two exogenous variables Δq^2_t and Δs_t. Cointegration tests include heterogeneous time effects and the maximum number of autoregressive lags was two in the ADF-based tests. Panel unit root tests suggest that p_t, s_t, r_t and q^2_t are I(1) but q^1_t is I(0).

Table 3. Extra-mural R&D, Sales and Government R&D Expenditure Abroad: Feasible GLS, Spatial OLS and Cointegration Results

$$\Delta rx_{m,t} = \alpha_1 \Delta s_{m,t} + \alpha_2 \Delta gro_{m,t} + \varepsilon_{m,t} \quad (3) \qquad rx_{m,t} = \alpha_1 s_{m,t} + \alpha_2 gro_{m,t} + u_{m,t} \quad (3A)$$

	Feasible GLS	**Spatial OLS**	**Cointegration Tests**		
		(Conley 1999)	Test Statistic	Panel	Group
α_1	**-0.895** (0.017)*	**-1.023** (0.176)*	v	-1.25	
α_2	**1.026** (0.026)*	**1.006** (0.091)*	ρ	0.76	2.23*
			pp	-7.41*	-7.19*
BP Statistic	103.1*		adf	-6.68*	-6.69*

rx_t is the log of real per capita extra-mural BERD and gro_t is the log of real per capita *total* government R&D outlays on health and environment in countries other than m. * denotes significance at 5% level. BP is the Breusch-Pagan test of cross-sectional independence, $\chi^2(78)$. Cointegration tests include heterogeneous time effects and the maximum number of autoregressive lags set to two. Panel unit root tests suggest that rx_t, s_t and gro_t are I(1) processes.

Table 4. International Patent Collaboration, Extra-mural R&D and Government R&D Expenditure Abroad: System GMM and Cointegration Results

$$q^2_{m,t} = \gamma_1 rx_{m,t} + \gamma_2 gro_{m,t} + u_{m,t} \quad (4)$$

	System GMM	**Cointegration Tests**		
	Arellano and Bover (1995)	Test Statistic	Panel	Group
γ_1	**0.709** (0.219)*	v	-2.29*	
γ_2	**0.407** (0.094)*	ρ	0.99	2.45*
J (9)	11.24	pp	-7.32*	-7.12*
AB AR(1)	-1.56	adf	-6.34*	-6.37*
AB AR(2)	-0.85			

rx_t is the log of real per capita extra-mural BERD and gro_t is the log of real per capita *total* government R&D outlays on health and environment in countries other than m. * denotes significance at 5% level. J is the Hansen test statistic for over-identifying restrictions distributed as $\chi^2(9)$. In system GMM, 11 instruments were used: lags 1-9 of rx_t and Δgro_t in the first difference equation, and Δrx_t in the levels equation. Cointegration tests include heterogeneous time effects and the maximum number of autoregressive lags set to two. Panel unit root tests suggest that q^2_t, rx_t, and gro_t are I(1) processes.

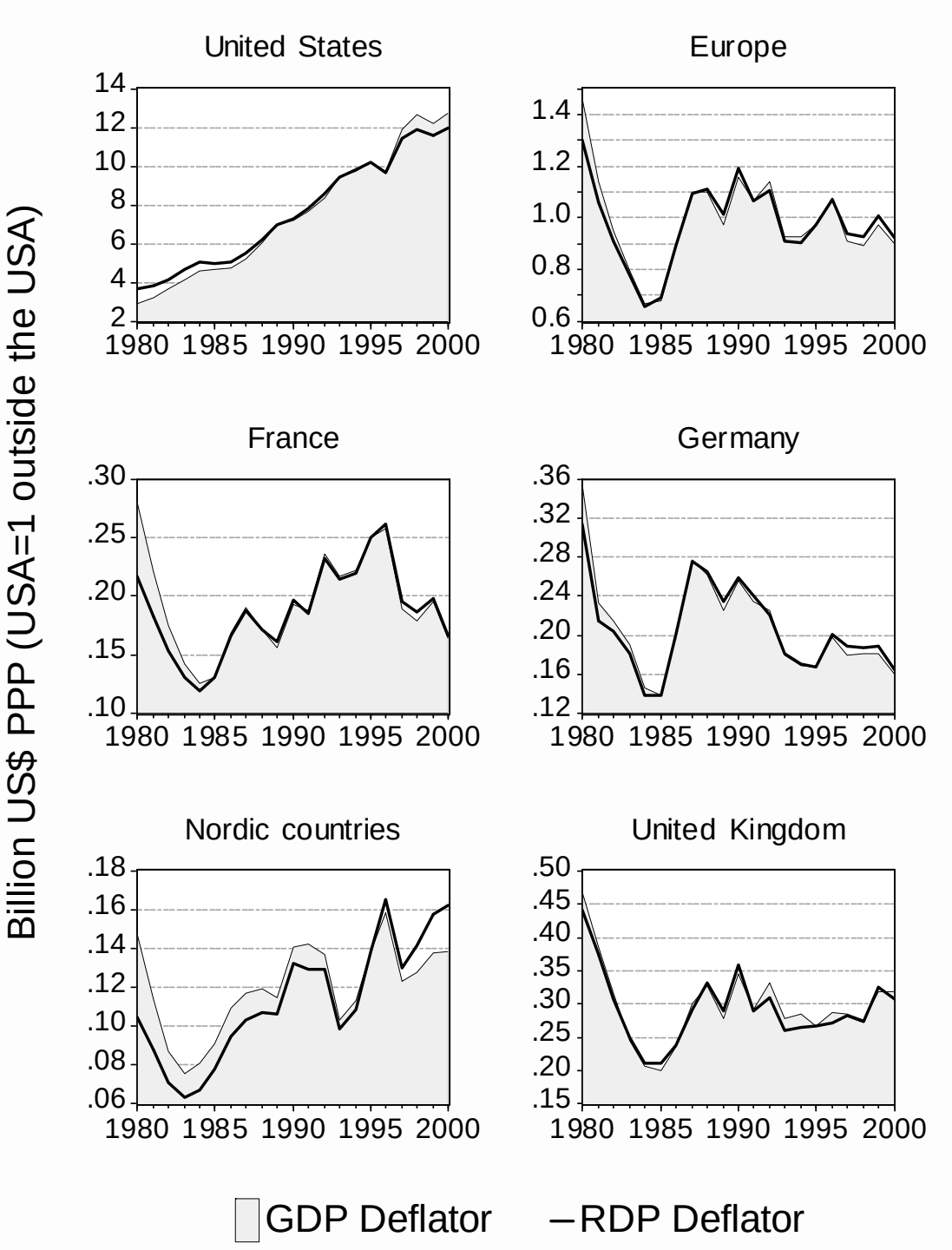

Figure 1. Real Performed BERD, Pharmaceuticals

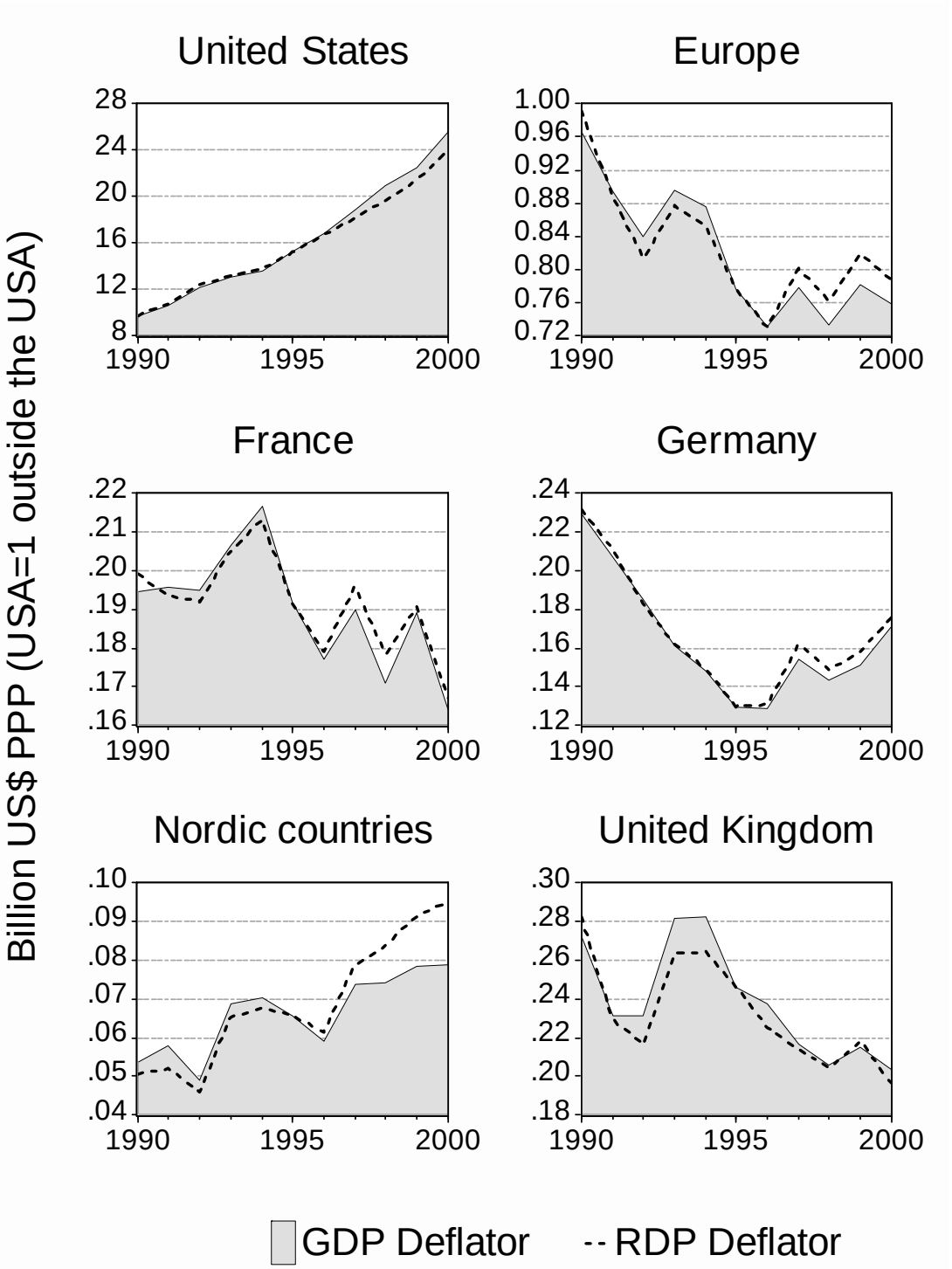

Figure 2. Real Total BERD, Pharmaceuticals

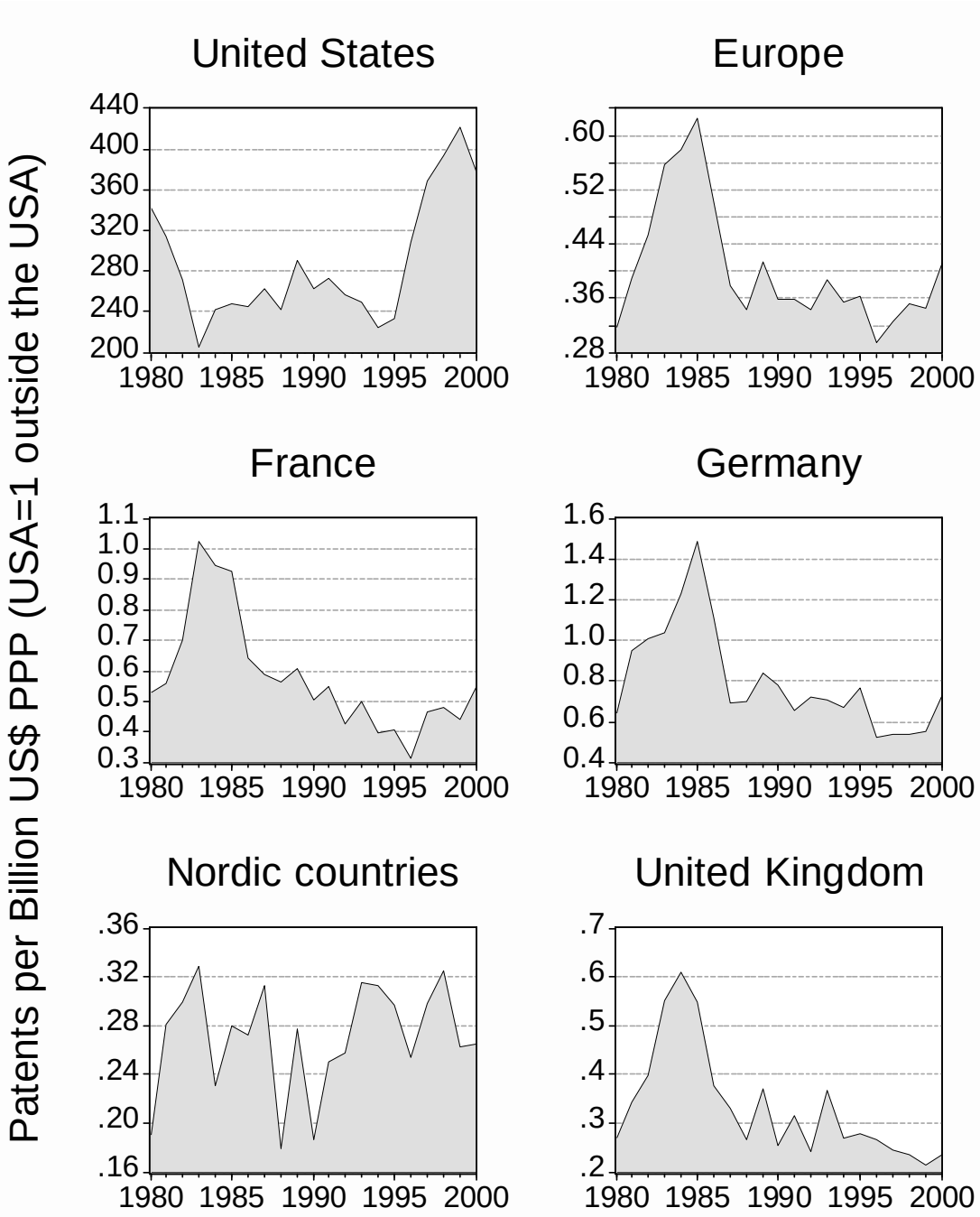

Figure 3. Relative R&D Productivity, Pharmaceuticals

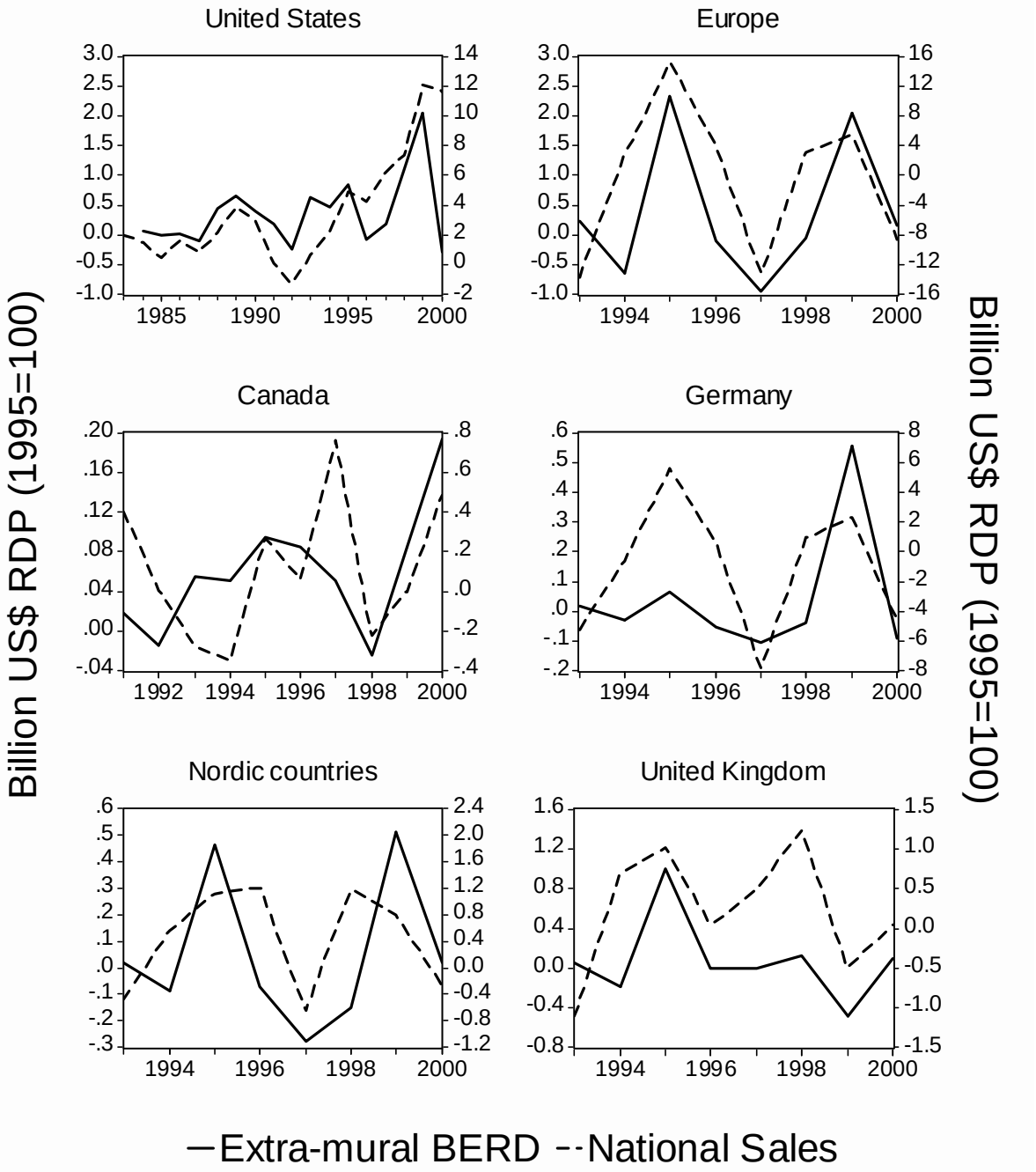

Figure 4. Extra-mural BERD and Sales: Annual Changes