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Regulatory policy and the location of bio-pharmaceutical foreign direct investment in Europe☆

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ABSTRACT

This paper examines the relationship between cross-country differences in drug price regulation and the location of biopharmaceutical Foreign Direct Investment (FDI) in Europe. Simple theory predicts that price regulation in one country might affect total investment, but not the location of that investment, if sales are global. Nevertheless, some manufacturers threaten that the introduction of price regulation in a country will motivate them to move their investments to other countries. Are such threats cheap talk, or is there evidence that firms avoid price-controlling countries when making FDI location choices? We use data on 527 investments initiated in 27 European countries between 2002 and 2009 and find that investors are less likely to choose countries with price controls, after controlling for other determinants of investment. We also observe a relative decline in investment in countries that increased the stringency of regulatory regimes during our sample period. The effect is restricted to non-manufacturing investments and is most robust for those related to administrative functions.

1. Introduction

Pharmaceutical firms' decisions to invest abroad are at the center of public attention in Europe, as part of the broader debate over international outward investment. Can rich countries remain an attractive location for manufacturing firms when confronted with fierce competition from low-wage countries? A frequent response by economists to concerns about such off-shoring is that rich countries have a comparative advantage in high-tech skill-intensive industries, and that outflows of traditional manufacturing will be compensated for by inflows or creation of innovation-based manufacturing plants. The pharmaceutical industry is one example of this type of industry.

The European pharmaceutical industry is among the most regulated in the world. Regulation takes the form of strong safety norms with certification processes for drugs, intellectual property rights, and price control mechanisms. Governments justify price regulation as a means to promote equity in access to drugs and reduce costs to national health care systems. Simple theory predicts that price regulation in any particular country might affect the total investment of the pharmaceutical industry, if regulation reduces total expected profits from investment. However, to the extent that the market for pharmaceuticals is a global one, we might not expect to observe any correlation between regulatory regimes and the *location* of investment. And yet it has been suggested that pharmaceutical firms respond to controversial policy choices by "voting with their feet" and avoiding locations with stricter price regulation. A report of the U.S. Trade Representative observes that, "R&D in the United States quadrupled between 1990 and 2003, while R&D in Europe grew by only 2.6 times. One of the factors that may be contributing to this relative decline is the regulatory and competitive environment for pharmaceuticals in Europe" (see U.S. Dept. of Commerce, 2004, p. 34). Most recently, in response to price cuts of up to 23% on patented drugs in Spain, the president of the Spanish pharmaceutical industry association Farmaindustria predicted job losses and said that the cuts "will mean the destruction of the current model of pharmaceutical industry that operates in Spain." (*The Pharmaletter*, May 17 2010, "Spain announces big drug-price cuts, aiming for 1.6 billion savings"). Merck was said to be "re-evaluating" its investment in Brazil after that country

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imposed compulsory licensing on efavirenz, Merck's anti-retroviral AIDS drug. (*The Economist*, May 10 2007, "Brazil's AIDS Program: A conflict of goals"). In response to reform proposals in Germany 2002, the Pharma Marketletter reported that the pharmaceutical company Merck KGaA "warned that the reforms could ... influence where it locates a new 300-million euro biopharmaceuticals product plant, its largest-ever investment." Die Welt reported on August 25, 2003 that "the American pharmaceutical firm Pfizer plans to reduce certain activities in Germany following upcoming reforms to the health system. Pfizer has decided to transfer an R&D group from Freiburg, Germany to the United Kingdom. 150 jobs will be affected by this decision." There is also evidence that drug launches are delayed in countries with more stringent price regulations (Danzon et al., 2004; Kyle, 2006, 2007a).

In this paper, we investigate the determinants of the locations of foreign investments in the biopharmaceutical sector in 27 European countries between 2002 and 2009. We investigate whether variation in policy regimes across countries helps explain variation in the locations of foreign investments in the pharmaceutical sector. We present the first evidence of the impact of regulatory constraints on the location choice of affiliates by multinational pharmaceutical firms. Our empirical results suggest that manufacturing investments are not associated with regulatory policy. Non-manufacturing investments in Western Europe are negatively associated with the strength of price regulation in a given country. However, these findings appear to be driven in large part by a decline in investments related to administrative functions.

The rest of the paper is structured as follows. Section 2 describes the regulatory policy schemes in the pharmaceutical industry in Europe and sketches the theoretical framework. Section 3 presents the empirical strategy to estimate the effect of regulatory policy on the location choices of pharmaceutical firms. In Section 4 we present the investment data, Section 5 explains the results and Section 6 concludes.

2. Regulatory policy and investment in the pharmaceutical industry

We first describe the different policies used by European countries to control the pricing of drugs and reimbursement of expenditures. Then we discuss the theoretical effect of price regulations on the location of pharmaceutical investment.

2.1. Price regulation policies in Europe

The pharmaceutical industry is perhaps the industry most affected by regulatory choices. Policies concerning the duration and strength of exclusivity awarded by patents are particularly important. The latter policies are essentially consistent across European countries (although the pharmaceutical industry has expressed concern over the enforcement of these rights in some countries), as are policies relating to advertising, wholesale distribution, packaging and labeling of drugs. These homogenized policies are by definition not expected to influence the profitability of the different countries. This is however not the case in the medical sector. As discussed at length by Permanand and Mossialos (2005), "Despite the harmonizing imperative of the SEM, there is still no single European market in medicines." European countries retain control over the pricing of drugs and reimbursement of expenditures. Countries vary in the use of reference pricing, fixed pharmacy profit margins, profit controls for manufacturers, as well as along other dimensions (see Table 2 of Kyle (2007a) as well as Jacobzone (2000)). Countries also vary in their attitudes to parallel trade, or the re-importation of drugs from countries in which prices are lower. All EU countries exert some degree of influence over expenditures on drugs marketed within their boundaries, but individual governments employ different policies. Governments may use formularies (lists of drugs for which patients will be reimbursed), controls on doctors' prescribing behavior, pharmacists, reimbursements of prescription costs, and/or price controls. A common mechanism for controlling prices is to set a price not higher than that of a currently available generic substitute, or to set the price with reference to prices of the same drug in neighboring countries. Some countries (like Spain and the UK) place controls on the profits of pharmaceutical companies. Others, like Denmark, do not control the price charged by the manufacturer, but prohibit price increases after a drug is introduced. Many EU countries also regulate the profit margins of pharmacists. Some countries (like Belgium, France, Spain and the UK) also regulate expenditures on drug marketing (Kyle, 2007a).

Our empirical investigation concentrates on the following price regulation policies, which we now define: price controls, reference pricing, and therapeutic reference pricing, in each of which price freezes and price cuts can be introduced. Detailed information on the use of these polices in different countries is available in Tables 1–3.

Price controls refer to policies that directly control the manufacturer's, wholesale, or retail price of pharmaceuticals. The determinants of the price vary from country to country. Countries like Belgium, Spain, France, Hungary, Poland, Latvia, and Lithuania set prices after negotiation with drug companies (Kyle, 2007a; Kanavos, 2002; Mossiolos et al., 2004). Other countries (Bulgaria, Czech Republic, Estonia, Finland, Greece, Hungary, Ireland, Latvia, Lithuania, Norway, Poland, Romania, Slovenia, Sweden) use a weighted average of prices charged for the same drug in selected other countries (Norway substituted reference pricing for a price cap starting in 2003 for a limited number of off-patent drugs (Brekke et al., 2008)). Reference pricing is a practice in which governments set a maximum reimbursement amount for drug purchases with reference to prices of substitute drugs. It is used in Belgium, Bulgaria, Czech Republic, Denmark, Estonia, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Netherlands, Norway,[1] Poland, Portugal, Romania, Slovakia, and Spain (Kyle, 2007a; Mossiolos et al., 2004; Podnar et al., 2007). Danzon and Ketcham (2003) notes that it has typically been used in countries without price controls, and is seen as a less stringent alternative to explicit price controls. However, Danzon notes, "In practice, certain forms of reference pricing can be de facto at least as stringent...particularly for new products." The stringency of reference pricing largely depends on which drugs' prices are used for reference. In some cases, only generic equivalents with the same active ingredient fall into the reference group. In other cases, the reference group consists of any therapeutic substitute on the market, and the drug's prices in other countries are taken into consideration. Most, but not all, countries exempt patented drugs from reference pricing schemes. As Danzon notes, "The decision whether to include on-patent products and to cluster on-patent products with off-patent products raises a critical trade-off between cost control and incentives for R&D, in addition to the issues of therapeutic substitutability." These two forms of price setting for reimbursement will be respectively denoted RP (reference pricing) and TRP (therapeutic reference pricing) in the empirical section of this paper. We define a country as having a reference pricing regime when it sets reimbursement levels for drugs with reference to prices of

[1] Norway uses a step-price system known as "trinnpreiser" for off-patent drugs that clusters at the ATC5 level and resembles a reference price system (PPRI Country Profile, Norway). We follow Kyle (2007a,b), in which this is classified as a RP system for the purposes of data analysis.