

This article was published in a slightly different form in the February 9, 2009 issue of *Global Competition Policy*.

The Undetected Elephant in the Room: An Analysis of DG Competition's Preliminary Report on the Pharmaceutical Sector Inquiry

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I. INTRODUCTION

On November 28, 2008, DG Competition's ("DG COMP") published its Preliminary Report ("the Report") on the pharmaceutical sector inquiry.¹ The Report claims that Research & Development ("R&D")-based pharmaceutical companies ("originator companies"²) have recourse to a *toolbox* ("toolbox")³ of practices in order to delay the entry of generic medicines onto the market and that these practices, where successful, result in significant additional costs for public health budgets and reduce incentives to innovate. The Report also states that originator companies applied defensive patenting strategies, primarily aimed at blocking other originator companies in the development of new medicines.

However, when one looks behind these headlines, it becomes clear that the Report is almost entirely silent on the key issue of causality, i.e. whether there can be said to be a causal link between the potentially anticompetitive practices which the Report identifies and the alleged resulting delays. This

article analyzes this issue of causality in an attempt to understand why the Report does not address this fundamental issue.

First, we explore whether the Report reveals any causal link between the practices it has identified between originator and generic companies (the so-called toolbox) and the delay in generic entry that the report hypothesizes.⁴ The Report does not itself analyze causation. Moreover, the data in the Report appears inconsistent with the idea that the toolbox was the major cause of the delay. On the contrary, the data suggests the primary source of the delay in generic entry may be regulatory in nature.

Second, we assess whether the Report reveals any causal link between the practices it has identified among originator companies and the decline in innovation (to which DG COMP attributes a decline in the number of new chemical entities ("NCEs") gaining marketing authorization). Again, there is no analysis of causation. Nor does the data in the Report obviously suggest a causal link. Instead, there are a number of regulatory



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factors which appear to be a plausible cause, none of which have been examined in the Report.

We therefore conclude that the absence of meaningful analysis as to causation is a significant gap in the Report, as is DG COMP's failure fully to examine the regulatory framework in this uniquely regulated sector. While we appreciate that DG COMP's approach may be driven by the fact that its powers to conduct sector inquiries under Regulation 1/2003 are limited; we believe that DG COMP cannot draw sound conclusions about the European pharmaceuticals sector without looking at the topic of regulation, the missing element in the Report's analysis—the elephant in the room.

II. WHY DID DG COMP OPEN A SECTOR INQUIRY INTO THE PHARMACEUTICALS SECTOR?

On January 15, 2008, DG COMP opened⁵ a sector inquiry into the pharmaceuticals industry by way of unannounced inspections. At that time, it said it had started the inquiry to examine (a) the reasons behind fewer new pharmaceutical products being brought to market and (b) delays to generic entry, as the Competition Commissioner's words make clear:

Individuals and governments want a strong pharmaceuticals sector that delivers better products and value for money. But if innovative products are not being produced, and cheaper generic alternatives to existing products are being delayed, then we need to find out why and, if necessary, take action.

The Competition Commissioner was therefore interested in investigating causation when the inquiry was opened ("we need to find out why"). Our submission explores this issue of causation. In particular, we examine whether regulation might be the major factor behind both the issues that DG COMP wished to examine in the sector inquiry.

III. CAUSATION WHEN IT COMES TO DELAYS IN GENERIC ENTRY

A. The Report's findings

The Report states that savings of EUR 14 billion already occurred due to generic entry in the EU in 2000-2007. It found that the average time for generics to enter after loss of exclusivity was 7 months, while it was only 4 months for the most highest-selling medicines.

The Report states that a further EUR 3 billion could have been saved assuming (p. 74) that generic entry had happened immediately, i.e. on day one after patent expiry in 2000-2007 in the EU Member States for essentially all⁶ the medicines that went off patent in that period. Thus, the notion of a well-functioning market in DG COMP's eyes is immediate generic entry upon loss of exclusivity—a laudable objective, but one that ignores other barriers to entry that currently prevent perfect competition at the time of loss of exclusivity.

We note at the outset that this it is simply not realistic to expect generic entry on day one for all drugs given the regulatory hurdles and commercial and technical issues associated with bringing a generic version of a drug to market. In addition to the regulatory elements explored below, (for example) a drug with low sales that is complex to produce may never stimulate generic entry—or only very slow entry.

The Report finds that originator companies have recourse to a toolbox to delay generic entry. According to the Report (¶¶ 890-899), the toolbox is made up of the following elements: secondary patenting; disputes and contacts; patent litigation; patent settlements; interventions before regulatory bodies; other interventions; and life cycle strategies. The Report found that the toolbox is most used for the best-selling products (¶902).

B. What the Report Does Not Say

The Report does not contain any concrete findings on causation, i.e. a finding that the toolbox caused the delay. The wording of the Report is clearly chosen carefully, because at no stage does the Report find that the toolbox *did* cause delayed generic entry. The Report always says that the toolbox *may* cause delay—in other words, the Report only finds that there is a *possibility* that the toolbox causes delay.

For example, the Executive Summary reads as follows:

The report also finds that originator companies have designed and implemented strategies (a “toolbox” of instruments) aimed at ensuring continued revenue streams for their medicines. **Although there may be other reasons for delays to generic entry, the successful implementation of these strategies may have the effect of delaying or blocking such entry.** The strategies observed include filing for up to 1,300 patents EU wide in relation to a single medicine (so-called “patent clusters”), engaging in disputes with generic companies leading to nearly 700 cases of reported patent litigation, concluding settlement agreements with generic companies which may delay generic entry and intervening in national procedures for the approval of generic medicines. The additional costs caused by delays to generic entry can be very significant for the public health budgets and ultimately the consumer. [emphasis added]

If we deconstruct this paragraph we see that the first sentence includes a concrete finding—originator companies have designed these strategies. The second sentence acknowledges the existence of other possible causes and then says that “the successful implementation” of the toolbox “may have the effect of delaying or blocking such entry”—i.e. no concrete finding of causation plus an implicit question about the effectiveness of the toolbox. The final sentence says nothing about causation and is partially circular.

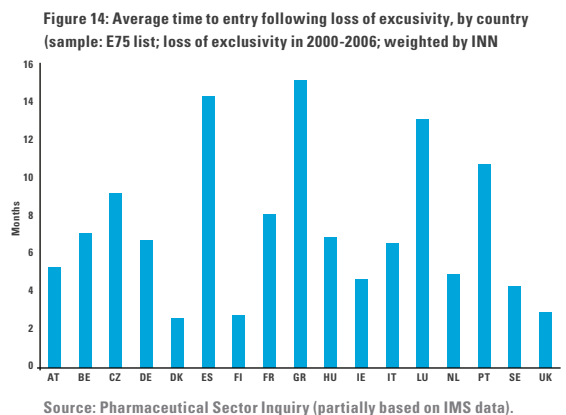
Similarly, if we look at the body of the Report, there is no finding of causation. For example, at page

322, the Report says that originator companies make use of the toolbox and that this “may increase the likelihood of delays to generic entry” and “may significantly increase legal uncertainty to the detriment of generic entry and can cost public health budgets ... significant amounts of money.” Again we see the use of “may” rather than “will.”

The absence of any concrete findings as to causation is understandable to the extent that the Report does not at any point analyze causation. But we submit that the data in the Report does allow one to examine causation and suggests that, viewed globally, the toolbox is not the major cause of the delay found by DG COMP.

C. Factors Suggesting That the Toolbox Was Not the Major Cause of Delays in Generic Market Access

The key fact that makes us believe that the toolbox was, and still is, not the major cause of the delays is the very significant variations among different EU countries. The following chart from the Report (p. 68) shows the very significant disparities between countries when it comes to the average time for generic entry.



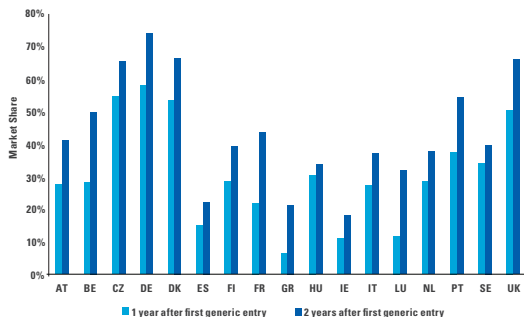
Looking at the chart, we are struck by the very large disparities that exist between countries of a similar size (e.g. Belgium versus Denmark; United Kingdom versus France; Germany versus Spain), countries

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which should have similar demand for particular drugs. If the toolbox were the sole cause or even the major/most significant cause of delayed generic entry, then we would expect the delays to be the same—unless originator companies engaged in a heavily selective use of the toolbox, e.g. it is not used at all in Spain but heavily used in the United Kingdom. However, the Report contains no such finding of selective application of the toolbox—and we think that a selective application of the toolbox would be difficult given that many of the patenting strategies would have to be carried out at a pan-EU level. The national disparities thus in effect disprove that the toolbox was the major cause of the delay.

There are also similar disparities when it comes to the speed at which generics acquire market share in different European countries. This

Figure 27: Generic penetration by volume, by MS (sample: E75 list, all INNs with entry; weighted by INN; measured one and two years after entry)



Source: Pharmaceutical Sector Inquiry (partially based on IMS data).

suggests that there are other factors at play. We note some of the other reasons why the toolbox may not be the major cause of the delays:

- First, if the toolbox were the major cause of delayed generic entry, logic would dictate that the average time for generics to enter after loss of exclusivity would be higher for the highest-selling products, as these are the products where originators make most use of the toolbox (see ¶902). However, as noted above, the Report concludes that average generic entry-time is actually faster for the most valuable products (4 months) than for all products. If we examine the toolbox alone (and

take no account of other factors—which is to an extent what the Report does), we would reach the conclusion that increased use of the toolbox is associated with faster, not slower, generic entry.

- Second, while the delays ascribed to the toolbox elements individually generally exceed a year, the Report concludes that the average delay in generic entry following loss of exclusivity is actually a lot shorter. For example, the average duration of patent litigation was 2.8 years (¶ 515) and of interim injunctions 18 months (¶ 525), i.e. at least twice as long as the seven-month average delay for generic entry after loss of exclusivity. When one also factors in the Report’s conclusion that originator companies “resorted to the cumulative use of all these instruments for certain medicines,” there is an inconsistency between the cumulative delays to generic entry that DG COMP says occur due to the toolbox (i.e. it should be well over a year) and the much faster speed of generic entry in practice (average 7 months). This again suggests that DG COMP may have overstated its case.
- Finally, as the Report recognizes, the speed of generic entry has increased over the period 2000-2007, notably in France and Italy (see figure 12, ¶163). This can only be explained if use of the toolbox has been declining significantly, a finding the Report does not make. Indeed, the Report suggests the opposite, e.g. it finds that patent litigation increased fourfold over the period (p. 199). We therefore suggest that the increase in speed of generic entry may instead be due to changes in the regulatory approach adopted by Member States, as explained below.

D. If Not the Toolbox, What Could Be the Major Cause of Delays in Generic Market Access?

We believe that regulatory factors may be the major factor behind delayed generic entry. We believe that the following two elements merit particular consideration.

The first element is the way that Member States incentivize generic entry. For example, price controls

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set at a low level (for originator products) may create insufficient margins to encourage generic entry. These ideas are supported by a 2006 report by Simeons and De Coster,⁷ commissioned by the European Generics Association, which confirms that generic entry depends to a large extent on the approach adopted by the Member States:

Penetration of generic medicines is more successful in countries that permit (relatively) free pricing of medicines (e.g. Germany, Netherlands, United Kingdom) than in countries that have pricing regulation (e.g. Austria, Belgium, France, Italy, Portugal, Spain). This is because countries that adhere to free market pricing generally have higher medicine prices, thereby facilitating market entry of generic medicines and a higher price difference between originator and generic medicines.

In Italy and Spain, the limited volume of generic medicines consumption in combination with low medicine prices due to certain supply-side measures has undermined the economic viability of the generic medicines market.

Higher medicine prices stimulate generic medicines companies to enter the market. This contrasts with regulated markets, where pricing regulation drives down the originator price over the life cycle of the medicine. This lowers the potential profit margin for a generic medicine company and discourages market entry.

Countries that have promoted generic medicines for 10-15 years naturally have a more mature generic market than countries that have only recently implemented measures to stimulate generic medicines use.

This report also explains why countries like France and Spain have seen an increase in generic penetration recently, i.e. because more regulatory measures are being taken to promote generic entry.

The second element is delays that generic producers face when getting through the regulatory process:

- First, marketing authorization bottlenecks. The Report explains (¶ 1125) that bottlenecks were due to delays in procedures and accessibility of slots, with some agencies already “fully booked” for 2008 and 2009—which has potential for a much greater delay than 4 or 7 months.
- Second, pricing and reimbursement delays—which only affect certain countries. In markets such as the United Kingdom or Germany where there is no need for generic companies to obtain pricing and reimbursement approval prior to launch, generic entry is almost immediate. By contrast, in Member States such as France, Spain, or Italy, where it can take over 6 months for a generic to be granted a reimbursement price, generic entry is necessarily slower. Indeed, at the public presentation of the Report's findings on November 28, 2008, one speaker said pricing and reimbursement approval can take up to 13 months in Belgium.⁸ This is a significant factor when compared to the 4 month average delay for generic entry in relation to most valuable products.

We believe that these two elements, among other possible regulatory measures, explain the significant national disparities as to the average time for generic entry better than the toolbox. This suggests that national regulation may be the major element at work here—rather than the toolbox.

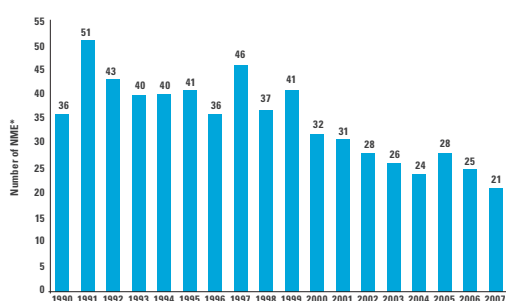
We respectfully submit that the Report is incomplete without an investigation of the prevailing regulatory environment, especially as it seems to play such an important role. No meaningful conclusion on causation is possible without it.

IV. CAUSATION AND THE LACK OF NEW INNOVATIVE PRODUCTS REACHING THE MARKET IN RECENT YEARS

A. The Report's Findings

The other main reason put forward by DG COMP for starting its sector inquiry in the pharmaceuticals sector was its perception of a lack of new, innovative products reaching the market in recent years. While between 1995 and 1999, an average of 40 new NCEs were launched, between 2000 and 2007, that number had dropped to an average of 27 NCEs (¶ 63).

Figure 5: Number of new molecular entities (NME) first launched worldwide (1990-2007)



Source: EFPIA and CMR International (Thomson Reuter)

The Report first considers defensive patents, which it concludes are “problematic” (though at this stage no competition law analysis is undertaken to explain why) where they are used for the sole purpose of excluding competitors:

From society’s viewpoint, however, restriction of another company’s freedom to operate may be problematic where the originator company maintains and uses patents to block the development of a new, competing product rather than for protecting an invention of its own. This is sometimes referred to as ‘defensive patenting’ (¶ 986).

The Report also looks at patent-related exchanges between originator companies and finds 1100 cases where there were overlaps between originators’ R&D poles (¶ 986); however, requests for licenses were only refused in 20 percent of these cases (¶ 996).

Finally, the Report states that 38 percent of originator companies in the inquiry were involved in patent litigation during the 8 year period of investigation (¶ 1005). This does not seem particularly high in light of the importance of patents to the pharmaceuticals sector.

B. What the Report Does Not Say

As in relation to generic entry, the Report does not contain any concrete findings on causation, i.e. a finding that specific conduct of originator companies caused the drop in the number of NCEs.

While the Report identifies a number of practices by originator companies which it claims may explain the drop in the number of NCEs, such analysis remains speculative as the Report does not conclude that such practices do, in fact, produce such an effect. For example, in relation to the overlap between the patents of one company and patent/R&D program of another, the Report concludes that this “creates significant potential for originator companies to find their research activities blocked, with detrimental effects on the innovation process” (p. 350), without quantifying or assessing such detrimental effects or concretely finding that they exist.

C. Other Possible Causes for the Drop in the Number of NCEs

We believe there are other, more plausible reasons why there has been a drop in the number of NCEs. Again, some of these are regulatory in nature.

First, the Report does not consider in any detail⁹ the impact of national pricing and reimbursement and cost-containment strategies on the launch of new NCEs. Member States are increasingly unwilling to

fund the cost of developing new medicines when they feel that the benefits of these new medicines, when compared to existing medicines in the same class, are insufficient or when their budgetary constraints dictate otherwise. National pricing and reimbursement policies also have a knock-on impact on the research priorities of originator companies and the numbers of new NCEs:

- Originator companies increasingly try to differentiate their new products from existing products and to focus on unmet medical needs in order to guarantee reimbursement. This implies more risky research projects with a higher likelihood of failure. In essence, many of the “easy” cures have already been discovered.
- Originator companies also increasingly terminate research projects in Phase II and III before incurring the heavy costs of trials when they feel that Member State buyers will be unwilling to pay for such incremental innovation.

Second, it is often said that the regulatory requirements for approval of NCEs are higher now than they were a decade ago. If there is a higher regulatory failure rate, this in itself could explain part of the trend of lower number of NCEs reaching the market.

Finally, the Report fails to evaluate the impact of increased costs of clinical trials. While originator R&D budgets continue to grow,¹⁰ costs are also growing. Trials have become more complex, due to increased difficulties in enrolling patients—patients already have treatments for many diseases—and diseases are more complex. The increased cost of trials may also make certain research projects uneconomic (in combination with the impact of pricing and reimbursement and cost containment strategies).

These regulatory factors could plausibly explain the decline in the number of NCEs reaching the market. DG COMP has not investigated them in any depth, nor has it investigated causation. In the absence of such an analysis, DG COMP cannot

conclude that conduct of originator companies has had any impact on the number of NCEs reaching the market.

V. CONCLUSION: THE IMPORTANCE OF REGULATION

Regulation appears to us to be one of the most relevant and important elements in the sector inquiry—a factor that goes to the heart of the question of causation. Yet the Report does not address this issue in any meaningful way.

The Report presumably adopts this approach because the legal focus of DG COMP's sector inquiries is on company practices, not regulation:

A sector inquiry looks ... into the question of whether and to what extent the behaviour of undertakings is amongst the causes for the perceived malfunctioning of the market. However the Commission services are fully aware that the pharmaceutical sector is highly regulated. ... In particular, the regulations relating to patents, marketing authorisations and pricing and reimbursement decisions appear to affect the competitive process. The Commission services therefore welcomed comments submitted by companies on the regulatory framework in which they operate. **This did not, however, change the focus of the inquiry, namely, on the extent to which company practices affect market entry.** (p.7—emphasis added)

While we appreciate that DG COMP's powers under Regulation 1/2003 are narrower than, for example, the UK Competition Commission and focus almost solely on the conduct of undertakings,¹¹ this approach misses an important part of the picture. Carrying out a sector inquiry without carrying out an in-depth review of the regulatory framework makes little sense in heavily regulated sectors such as pharmaceuticals.

Indeed, the Community Courts have consistently held that competition law analysis has to take account of how competition occurs in a particular market.¹²

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The scope of the Report does not, therefore, allow DG COMP to draw sound conclusions about the industry, as it has failed to consider regulation of the industry, the missing element in the analysis—the elephant in the room.¹³ Without considering regulation, DG COMP cannot draw any robust conclusions as to causation—and address the question posed by the Competition Commissioner at the outset: Why are there fewer NCEs and delays in generic entry?

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1 Available at http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/preliminary_report.pdf. DG COMP's final report is expected in summer 2009.

2 Which the Commission defines as companies that sell novel drugs that benefited from patent protection when launched onto the market.

3 Comprised of five cumulative elements: (i) Patent clusters; (ii) Weak secondary patents, litigation and opposition procedure; (iii) Patent settlement agreements; (iv) Interventions before national marketing authorisation authorities; and (v) Follow-on or second-generation products.

4 DG COMP's analysis (most notably its headline EUR 3 billion figure) is based on the hypothesis that essentially all generics would enter the day after patent expiry across the EU, absent anticompetitive conduct. We do not think that this is a realistic hypothesis on which to base the analysis, as we do not think it is currently realistic to expect generic entry for all products in all European markets on day 1 after patent expiry, given regulatory hurdles plus commercial and technical issues.

5 Commission Decision of 15 January 2008 initiating an inquiry into the pharmaceutical sector pursuant to Article 17 of Council Regulation No 1/2003 [2008] OJ C59/06.

6 We recall that the EUR 3 billion number is based on an analysis of the E75 sample, which represents essentially all the compounds that went off patent during the period under investigation (see ¶¶ 153, 187 and nn. 64, 77). The Report states that "the list of E75 molecules represents over 90% of the value of all expiries in France, Germany, and the UK in the period 2000 – 2007... It is likely to comprise the vast majority of expiries in other Member States as well." (n. 77)

7 *Sustaining Generic Medicines Markets in Europe*, Leuven, April 2006, available at http://www.egagenerics.com/doc/simoens-report_2006-04.pdf

8 Rory O'Riordan, Vice-President, European Generics Association, presentation available at <http://webstream.ec.europa.eu/scic/comp/081128/day1en-3.wmv>

9 It only contains a limited discussion about pricing and cost control policies (therapeutic reference pricing, restrictions in use, and payback systems) at ¶¶ 1149-1155.

10 For example, in its 2008 Communication entitled *Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector*, the Commission states that the European pharmaceutical sector accounts for more than 17 percent of the EU's annual R&D expenditure.

11 See Powell & Innes-Stubb, *A Tale of Two Sector Inquiries: Comparing and Contrasting Experiences in the U.K. and EU*, GCP MAGAZINE, November 2008, <http://www.globalcompetitionpolicy.org/index.php?id=1798&action=600>

12 Joined Cases T-374/94, T-375/94, T-384/94 and T-388/94, *European Night Services Ltd. and others v. Commission*, [1998] ECR II-3141, ¶ 136. "Before any examination of the parties' arguments as to whether the Commission's analysis as regards restrictions of competition was correct, it must be borne in mind that in assessing an agreement under Article 85(1) of the Treaty [now 81(1)], account should be taken of the actual conditions in which it functions, in particular the economic context in which the undertakings operate, the products or services covered by the agreement and the actual structure of the market concerned, unless it is an agreement containing obvious restrictions of competition such as price-fixing, market-sharing or the control of outlets. In the latter case, such restrictions may be weighed against their claimed pro-competitive effects only in the context of Article 85(3) of the Treaty [now 81(3)], with a view to granting an exemption from the prohibition in Article 85(1) [now 81(1)]."

13 See Killick, *Regulatory issues and the pharma sector inquiry: is regulation the elephant in the room?* <http://professorgeradin.blogs.com/files/killick--pharma-sector-inquiry-conference-.pdf>