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Regulatory issues and the pharma sector inquiry: is regulation the elephant in the room?

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The reasons for having a Sector Inquiry

Might regulation might be the major factor behind both these elements?

"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."

Neelie Kroes, European Commissioner for Competition, 15 January 2008

Outline

- Two key regulatory elements in the pharma sector
- The regulatory elements examined in the report (Part D)
  - Patents
  - Marketing authorisations
  - Pricing and reimbursement
- How regulation affects the other two topics examined in the sector inquiry
  - Competition between originator and generic companies, i.e. perceived delays in generic entry (Part C.2)
  - Competition between originator companies, i.e. perceived reduction innovation by originator companies (Part C.3)
- Conclusions

Two key elements of regulation in the pharma sector

- Marketing authorisation
  - A product must be authorised (either by EMEA or national regulator) before it can be placed on the market
    - Originator, needs to show safety and efficacy
    - Generic, shows either safety and efficacy or equivalence (so it can rely on an originator dossier)

- Pricing and reimbursement
  - In most Member States, national regulator must approve pricing and reimbursement before originator product can be put on market
  - Many Member States also regulate generic pricing and reimbursement with a formal approval process prior to launch

The Regulatory aspects covered by Part D of the Report - 1

- Patents
  - Lack of Community patent
    - Originators concerned about high costs of national patents
    - Generic concerns about complexity, need to enforce/challenge in each country
    - Commission calls for creation of Community patent
  - No unified Court system for patent litigation in Europe
    - Broadly shared concerns about problems of conflicting decisions, costs and need for expert judges
    - Commission recommends creating unified EU patent judiciary
  - EPO practices: opposition procedures and granting of patents
    - Broad calls for speeding up of opposition procedure
    - Generic companies suggested EPO granted secondary patents too easily
    - Commission makes no recommendation

The Regulatory aspects covered by Part D of the Report - 2

- Marketing authorisations
  - Shortcomings and bottlenecks for both originators and generics
    - Bottlenecks due to delays in procedures and accessibility of slots – some agencies were already "fully booked" for 2008 and 2009
    - Question whether resources were adequate in certain agencies
    - No Commission comment, save to suggest some participants made "unnecessary" bookings (but no evidence cited on this – p.381)
  - Problems with regulatory framework in EU
    - Allegation that 4 Member States (HU, LV, MT and PL) failed to incorporate "8+2+1" data exclusivity period into national laws
    - Discrepancies between regulatory agencies as regards MA assessment criteria
  - Harmonisation at international level
    - Suggestion that more international harmonisation, especially EU/US, in certain areas (MAs, scientific advice and design of clinical trials) could be positive

The Regulatory aspects covered by Part D of the Report - 3

- Pricing and Reimbursement
  - Delays in obtaining P&R decisions for both originators and generics
    - Shortens exclusivity period for originators
    - Prevents generics getting onto market, often for significant periods
      - Commission only analyses delays for generics caused by originators, not delays caused by the regulatory system (pp. 394-396)
  - Uncertainty in P&R decisions for both originators and generics
    - Unpredictability and lack of clarity in applicable criteria for originators
      - Unrealistic standard of proof applied for some innovative products
      - Discrepancies between approach of different Member States
    - No Commission analysis of uncertainty, just brief discussion on price linkage, raised by generic companies
  - Limited discussion about P&R and cost control policies
    - Report outlines comments on therapeutic reference pricing, restrictions in use and payback systems
    - No Commission analysis of impact of these policies on entry or innovation

The Regulatory aspects – summary

- Part D is shorter than other parts of the report and it tends to repeat what respondents said without analysis by the Commission
  - It presumably adopts this approach because the legal focus of the sector inquiry is 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)
  - But this approach misses an important part of the picture

Delays to generic entry – Commission findings

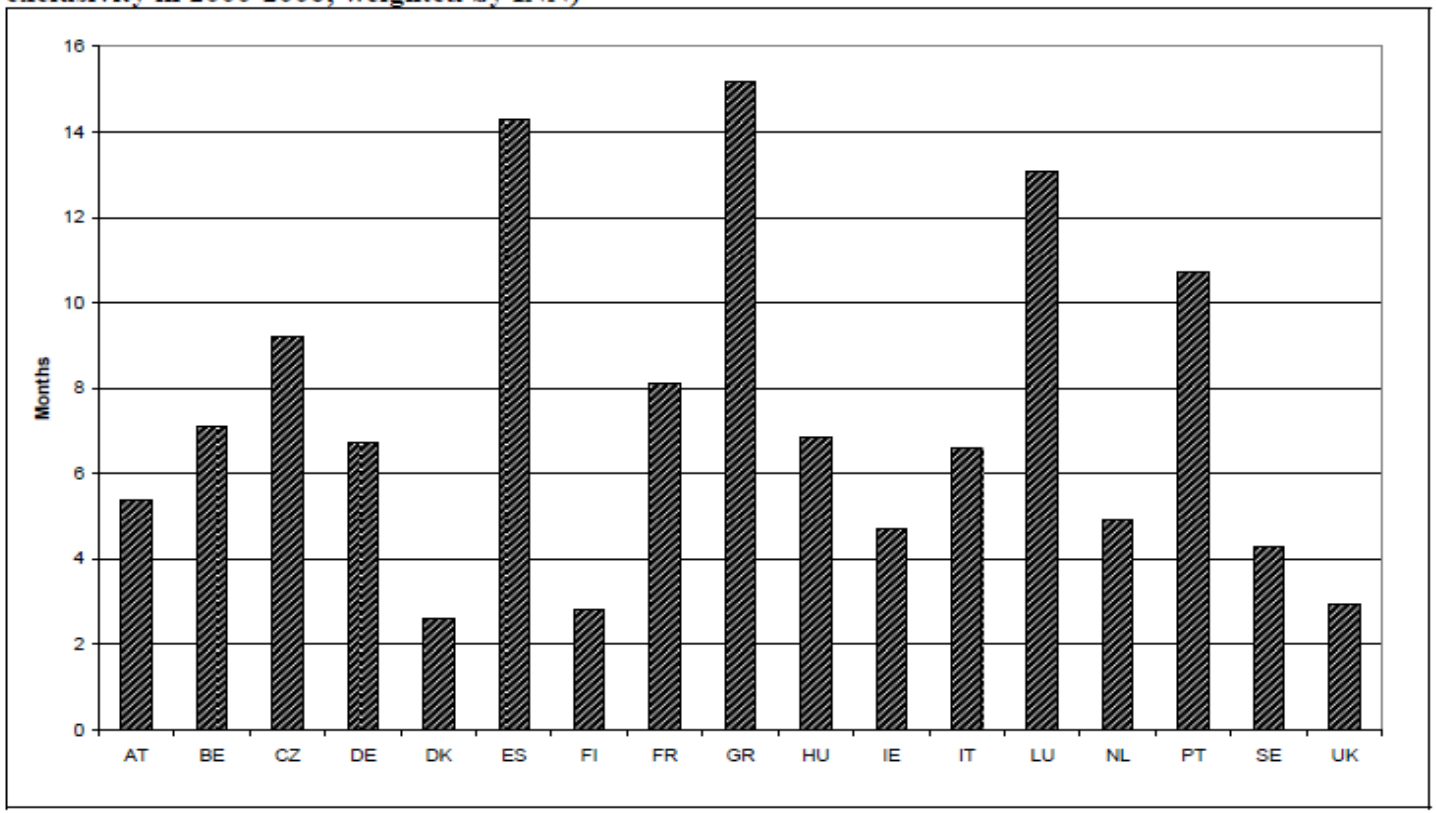
- Savings of EUR 14 billion occurred due to generic entry in the EU in 2000-2007
- A further EUR 3 bn could have been saved assuming (p. 74) generic entry had happened immediately in 2000-2007
  - This further saving is equal to €0.75 per patient per year compared to average spending on pharmaceuticals of €430 per patient per year
  - Not realistic to expect entry on day 1 given regulatory hurdles and commercial and technical issues –e.g. a drug with low sales that is complex to produce may never see generic entry
- Average time for generics to enter after loss of exclusivity was 7 months
  - Only took 4 months for the most valuable medicines
- "Toolbox" of practices used to prolong the life cycle of originator medicines
  - "may increase the likelihood of delays to generic entry" (p. 322) and
  - "may significantly increase legal uncertainty to the detriment of generic entry and can cost public health budgets ... significant amounts of money" (p. 322)

Was the toolbox the real issue?

- Report contains no assessment of how significant the toolbox was compared to other factors, nor indeed any concrete finding that the toolbox caused the delay cited ("may increase the likelihood")
- There are a number of other elements which suggest that the toolbox was not the cause (or not a significant cause) of the delay
- Main issue – the very significant variations between countries
  - No indication that toolbox used differently in different countries
  - Suggests other national (regulatory) reasons behind delay

National disparities as to generic entry (p. 68)

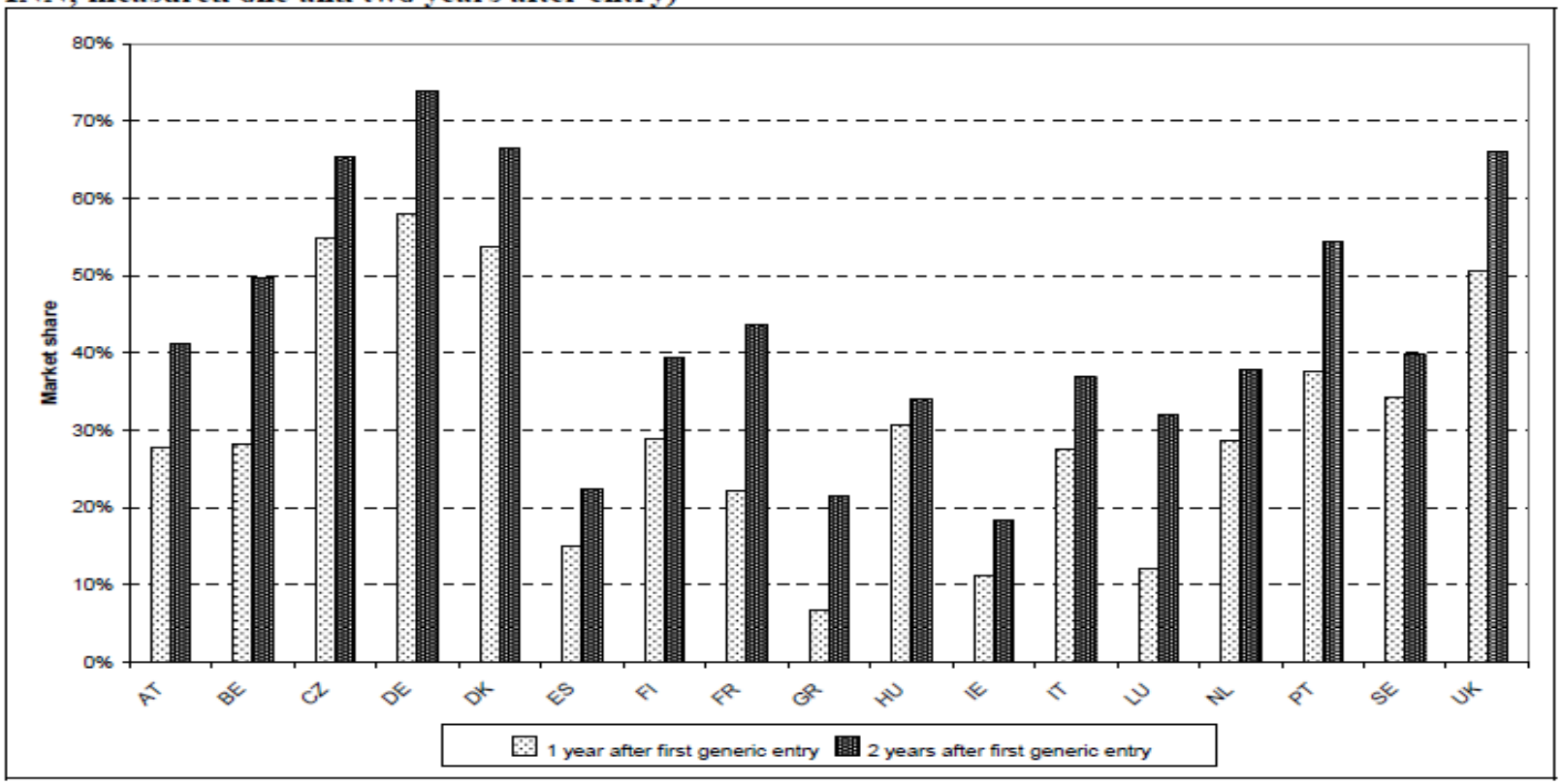
Figure 14: Average time to entry following loss of exclusivity, by country (sample: E75 list; loss of exclusivity in 2000-2006; weighted by INN)



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

National disparities as to generic entry (p. 81)

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).

Other reasons why toolbox may not be to blame

- Toolbox works less well for the most valuable products
  - Suggests that toolbox isn't the cause of delays: toolbox is most used for the best-selling medicines (p.322) yet generics enter faster (p. 85)
- Delays ascribed to toolbox elements listed in the report generally exceed a year, yet average delay is much shorter
- Entry has speeded up over the past 8 years, notably in France and Italy
  - Inconsistent with idea that tool box is being increasingly used
  - But consistent with changing regulatory approach in these countries (see Simeons and De Coster report, below)

Regulation as the cause of the delay

- Pricing and reimbursement delays
  - Can take >6 months for a generic to be given a reimbursement price in some countries
    - At 28 November hearing, EGA said P&R approval can take up to 13 months in Belgium
  - Significant factor compared e.g. to 4 months delay for most valuable medicines

- Differences caused by how "slow" countries incentivise generic entry
  - Generic entry faster where there are greater market opportunities and incentives
  - Generic entry driven by substantial price difference between branded and generic price: if price controls set at a low level, there may be insufficient margin to encourage generic entry
  - Generic entry quicker in countries without formal generic price controls
    - In markets such as UK or DE where no need to apply for pricing and reimbursement approval prior to launch, entry is almost immediate
    - By contrast France, Spain, Italy are significantly slower

- Marketing authorisation delays
  - Problems of backlogs described in the report

- The impact of these factors is not examined in the report

Simeons and De Coster report (2006), commissioned by EGA, confirms importance of differences in approach between different countries:

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

The Commission's findings on practices between originator companies allegedly hindering innovation

- Commission started inquiry because it felt there was a lack of innovative products on the market
  - 1995-1999 → average of 40 new chemical entities launched
  - 2000-2004 → average of 28 new chemical entities launched
- Commission identifies a number of practices, but no findings that they caused number of NCEs to drop – merely that there was a potential effect:
  - The overlap between patent of one company and patent/R&D programme of another "creates significant potential for originator companies to find their research activities blocked, with detrimental effects on the innovation process" (p. 350)
- Innovation is core of competition between originators
  - If no new products get to market, innovators will fail
  - Investment in R&D has remained high (17% of turnover)
- Suggests other factors may be behind fall in NCEs

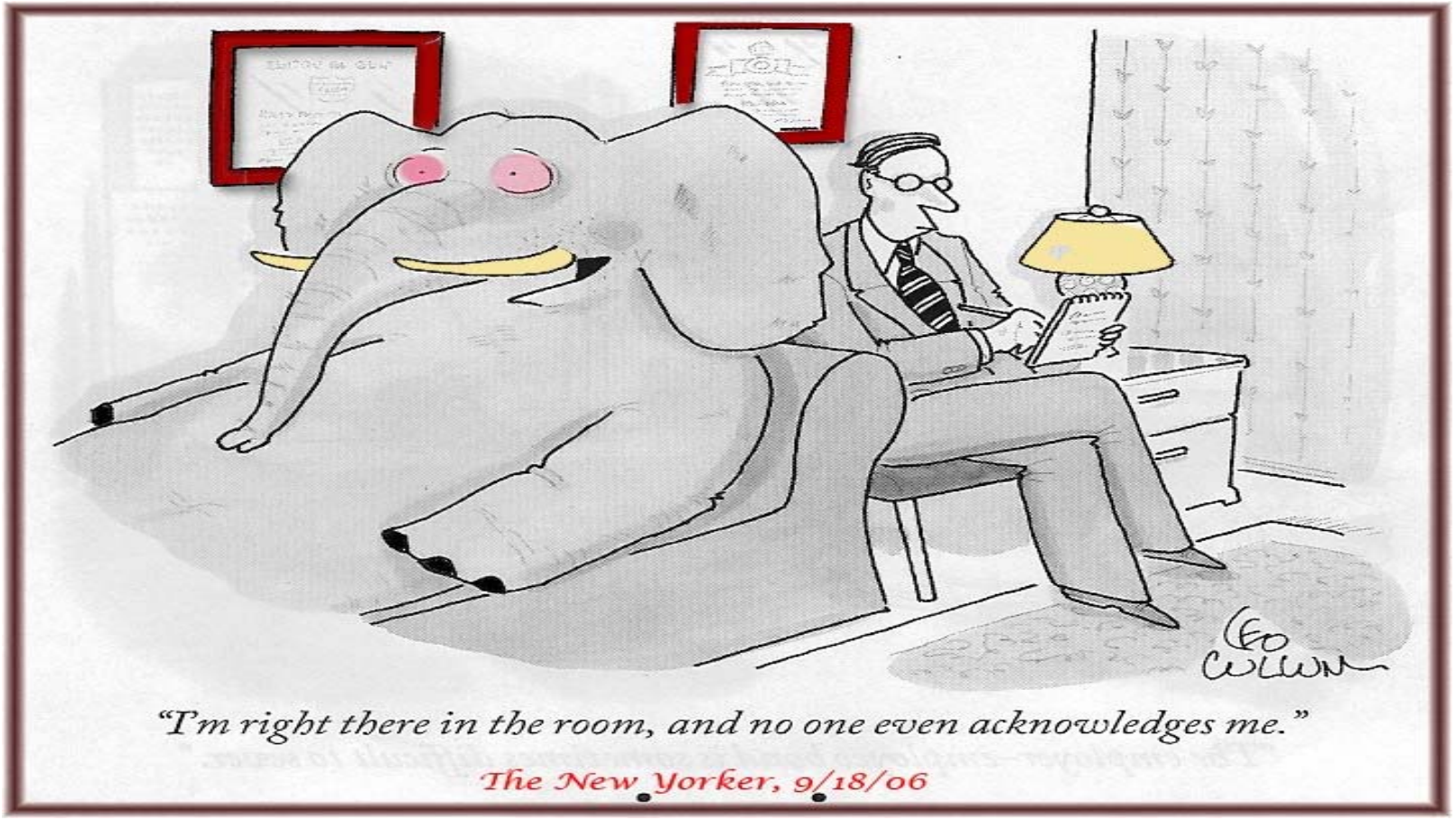
Possible regulatory reasons for drop in NCEs

- Pricing and reimbursement and cost containment strategies
  - For example, state buyers communicate unwillingness to fund innovative medicines in the same class as existing drugs (e.g. by reference groups)
  - Impact on research priorities, also impacts numbers of NCEs
    - Leads companies to try and differentiate themselves from existing products – more risky research projects – higher likelihood of failure
    - Termination of advanced projects (i.e. in Phase II and III) before incurring costs of trials and launching the product if there is a feeling state buyers will not pay
      - Particular issue for incremental innovation
      - Early stage R&D projects have continued to increase
- Other factors include increased costs of regulation and cost and complexity of trials
  - R&D budgets continue to grow (albeit at a less fast pace) but so do costs
  - Trials have become more complex: more complex to enroll patients; patients already have treatments for many diseases
  - More expensive trials increase attrition
- These factors are not analysed in the report

Conclusion

- Regulation is one of the most important elements in the pharma sector, yet it is little analysed in the report
- Not entirely a matter of choice for the Commission: its powers for sector inquiries under Reg 1/2003 are limited
  - Compare with e.g. the UK Competition Commission
- But the report cannot draw sound conclusions without looking at this topic, the missing element in the analysis

Questions?


"I'm right there in the room, and no one even acknowledges me."
The New Yorker, 9/18/06

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