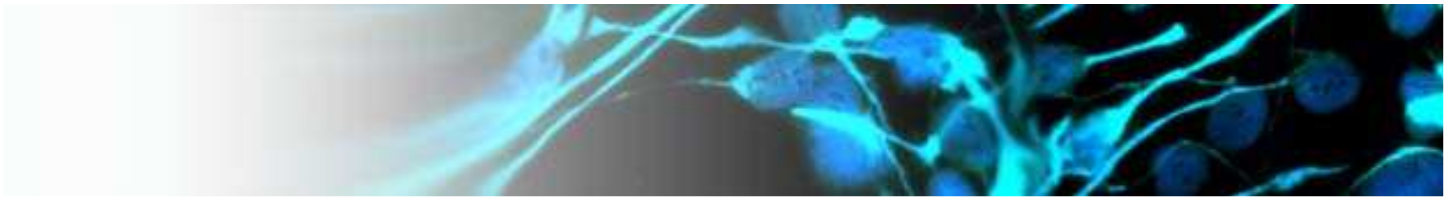
Implications of the EU Pharmaceuticals Inquiry: A few Issues

Adrian Towse,
Office of Health Economics

A few Issues

- Findings on generic entry and competition
- Some interesting economic issues
  - Patent thickets in the context of a changed innovative process
  - Distinguishing between an acceptable and unacceptable agreement
  - “Evergreening” ‘- abuse or payer incompetence?
- The search goes on…….
  - What is the purpose of a Sector Inquiry?
  - A successful EU pharmaceutical policy



Core findings

- Variable period of delay between loss of exclusivity and generic entry
  - Average **12 months** (whole sample of 219 INNs)
  - **7.9 months** weighted
  - **4 months** for 50 best selling products
- "Savings could have been €3 billion [in 17 countries]…if generic entry had taken place without delay" "The findings suggest that the practices under investigation contribute to this"
- Overlapping patents cause a "significant potential" for blocking research
  - Only two blockages found in 8 years

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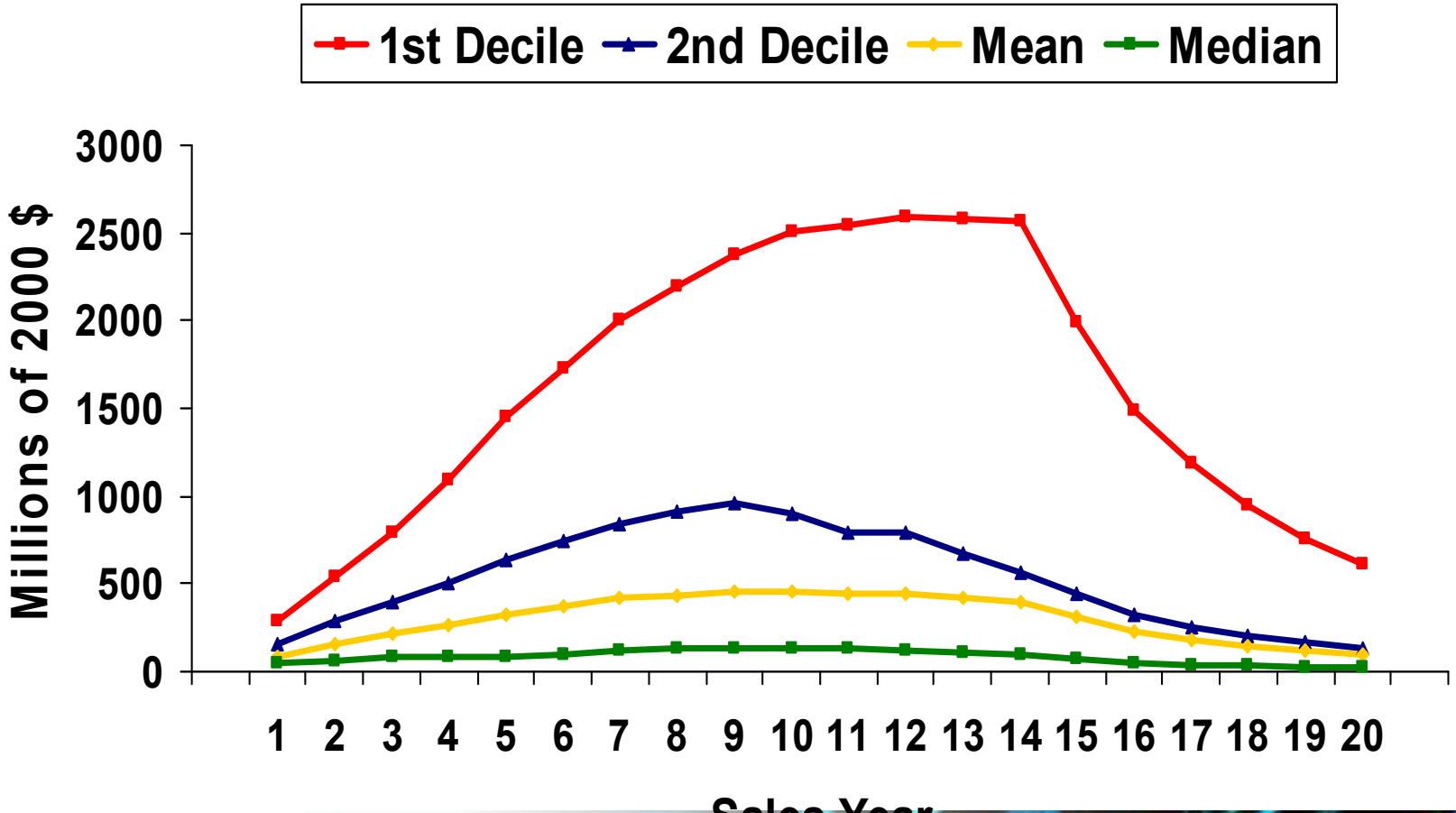
WW Sales Profiles of 1990-94 NCEs



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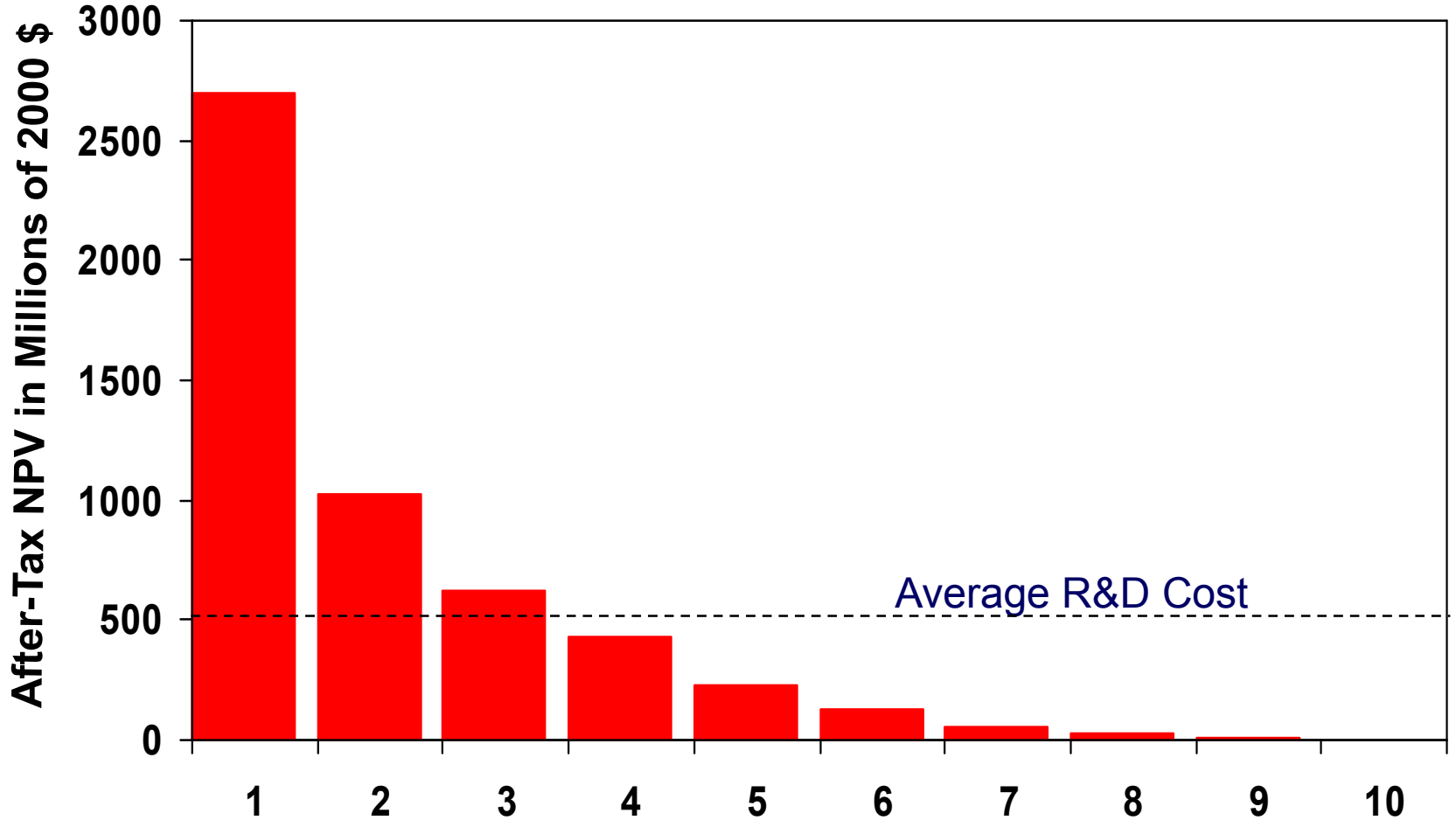
Present Values by Decile:1990-94 NCEs



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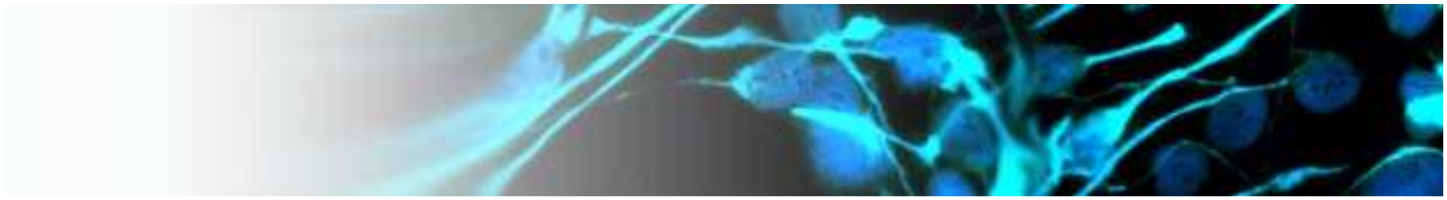
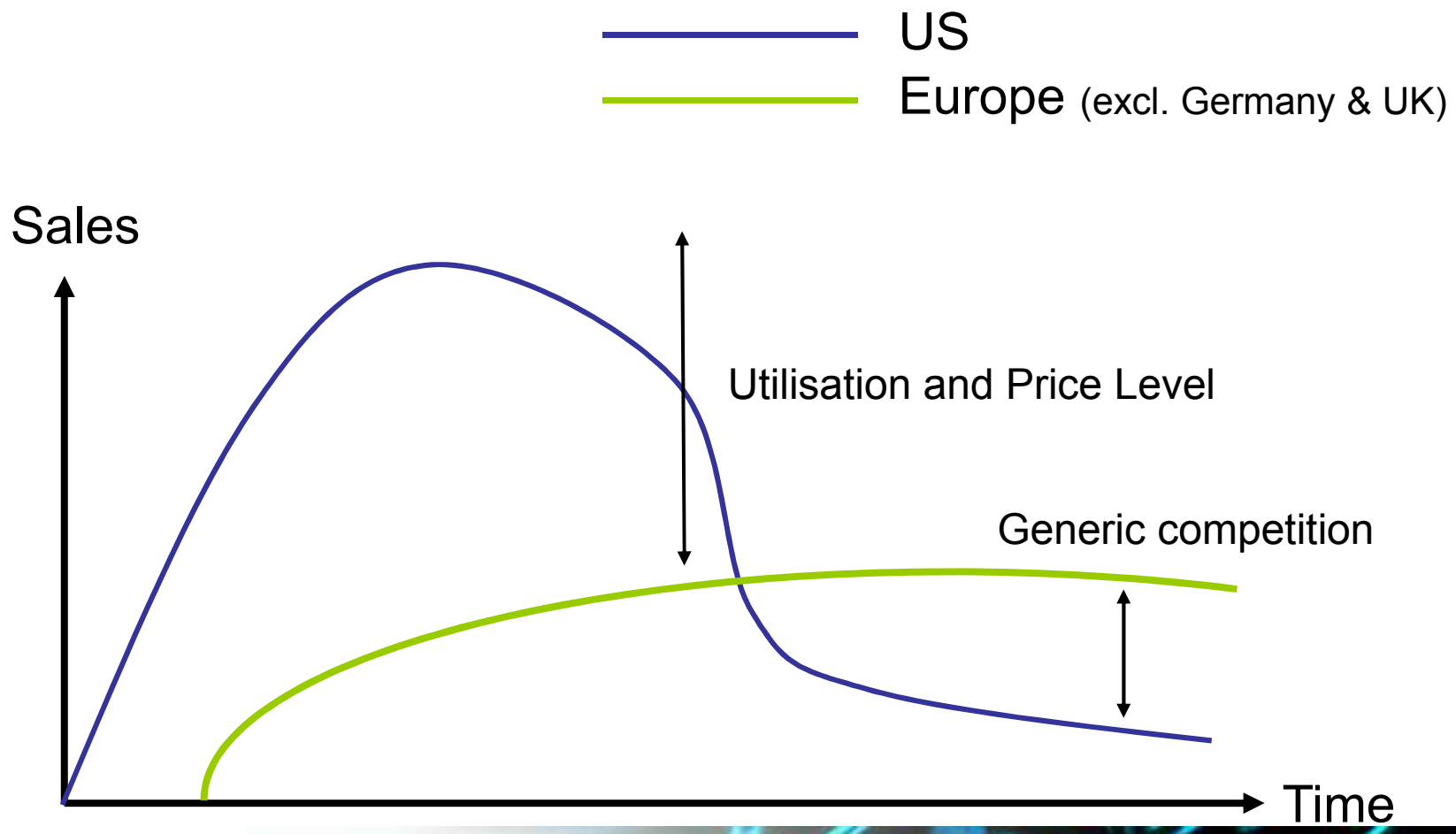
The importance of generic savings

- The importance of generic savings cannot be overstated. In the US, the biggest pharmaceutical market in the world, generics account for over 60 per cent of prescriptions filled but only about 10 per cent of drug expenditures, reflecting their low prices.
- The rapid generic erosion of originator market shares in the US reflects legislation authorizing pharmacists to substitute generics for originator drugs (unless the doctor states “brand required”) and incentives for them to do so. In the UK 80% of prescriptions are written generically with doctors and pharmacists incentivised to use generics.
- In parts of Europe and in Japan there is little generic use as there are no incentives and originator prices are low.
- Empirical studies of generic entry have shown, not surprisingly, that generic prices are inversely related to number of generic competitors (Grabowski and Vernon, 1992); generic entry is more likely for compounds with large markets, for chronic diseases (repeat use) and in oral-solid (easy to make) pill form (Scott Morton, 1999, 2000).



Product Life Cycle in US and Europe (excl. Germany & UK)



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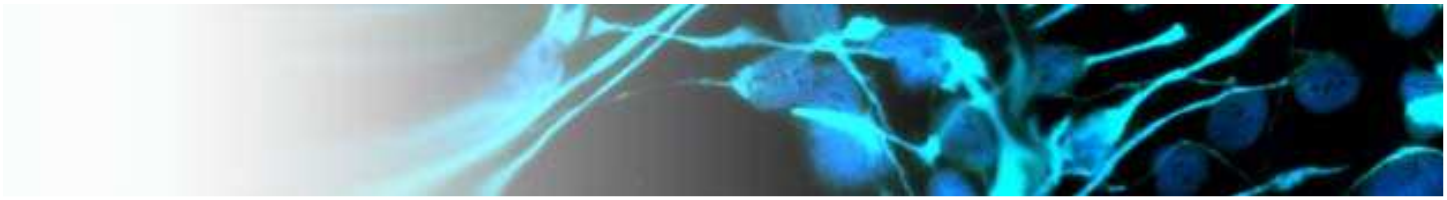
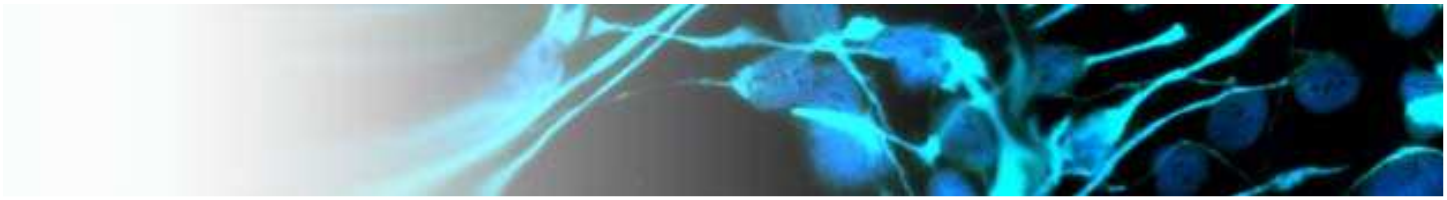


Patents I

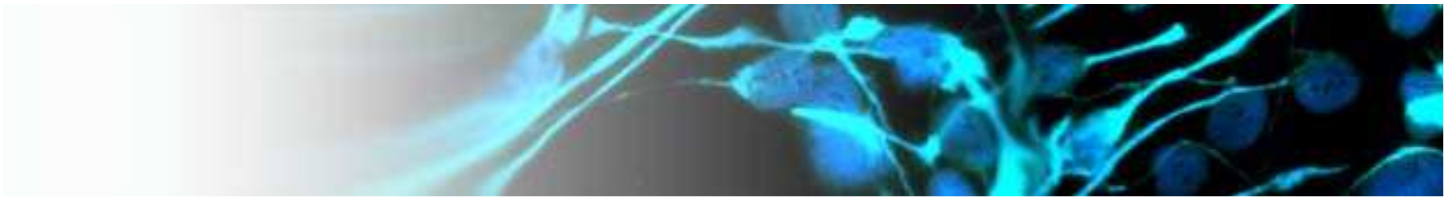
- The first is patent scope. Patents perform a dual role, enabling researchers to capture a reward for an innovation of value and putting information about the discovery into the public domain enabling others to learn from it.
- Broader patents and patent clustering increase the incentive to invest in finding them, but increase the danger that follow-on research is discouraged in two ways.
  - A rival approach to exploit an advance in basic science may be caught up in the patent, or
  - It may be hard to exploit the scientific discovery. Patents on “upstream” (targets) and platform technologies may reduce the incentive and ability of those wishing to undertake “downstream” research using these patents. Research to date (Walsh, Arora, Cohen, 2003) suggests that licensing and other workable solutions are almost always found but that the position needs to be monitored.



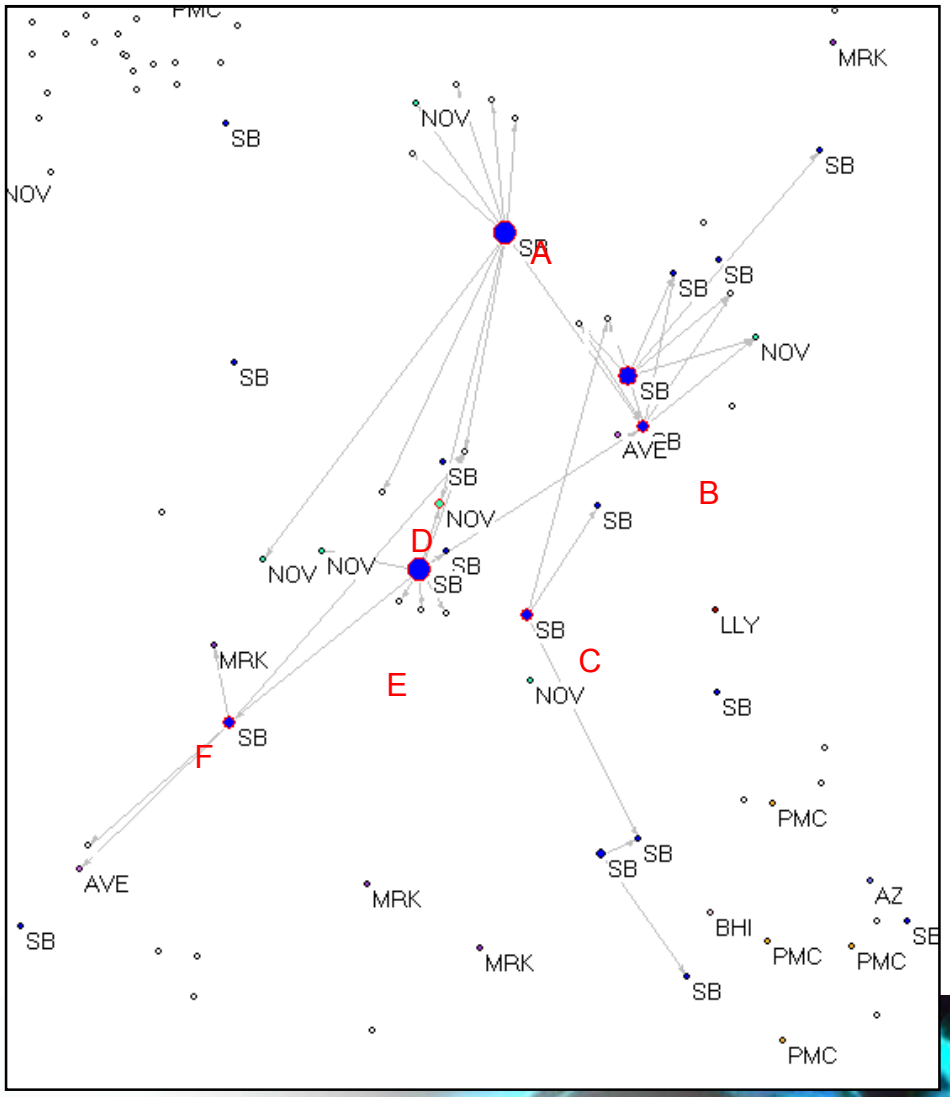
New industry structure?

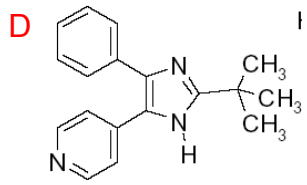
Pammolli and Riccaboni (2000) conclude that:

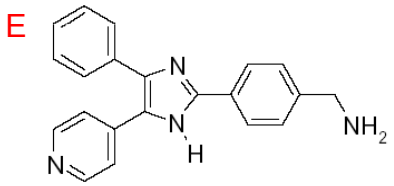
- the molecular biology revolution screening) has led to a new division of innovative labour between established large companies and new small companies;
- the network of R&D collaborative agreements is based on this division of innovative labour.
  - The biotech companies are active in the early stages of R&D as “originators” (those selling a technology).
  - The established pharmaceutical companies are specialised mainly in downstream development and commercialisation activities as “developers” (those buying a technology);

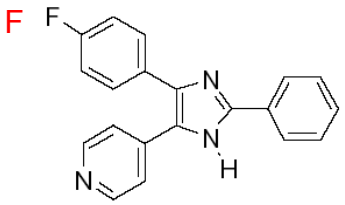


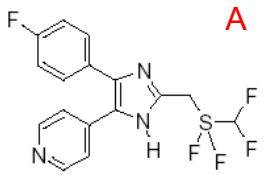
Patent Citation Network, 1995

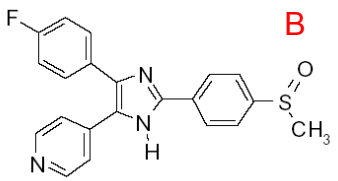


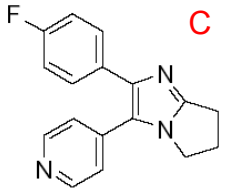












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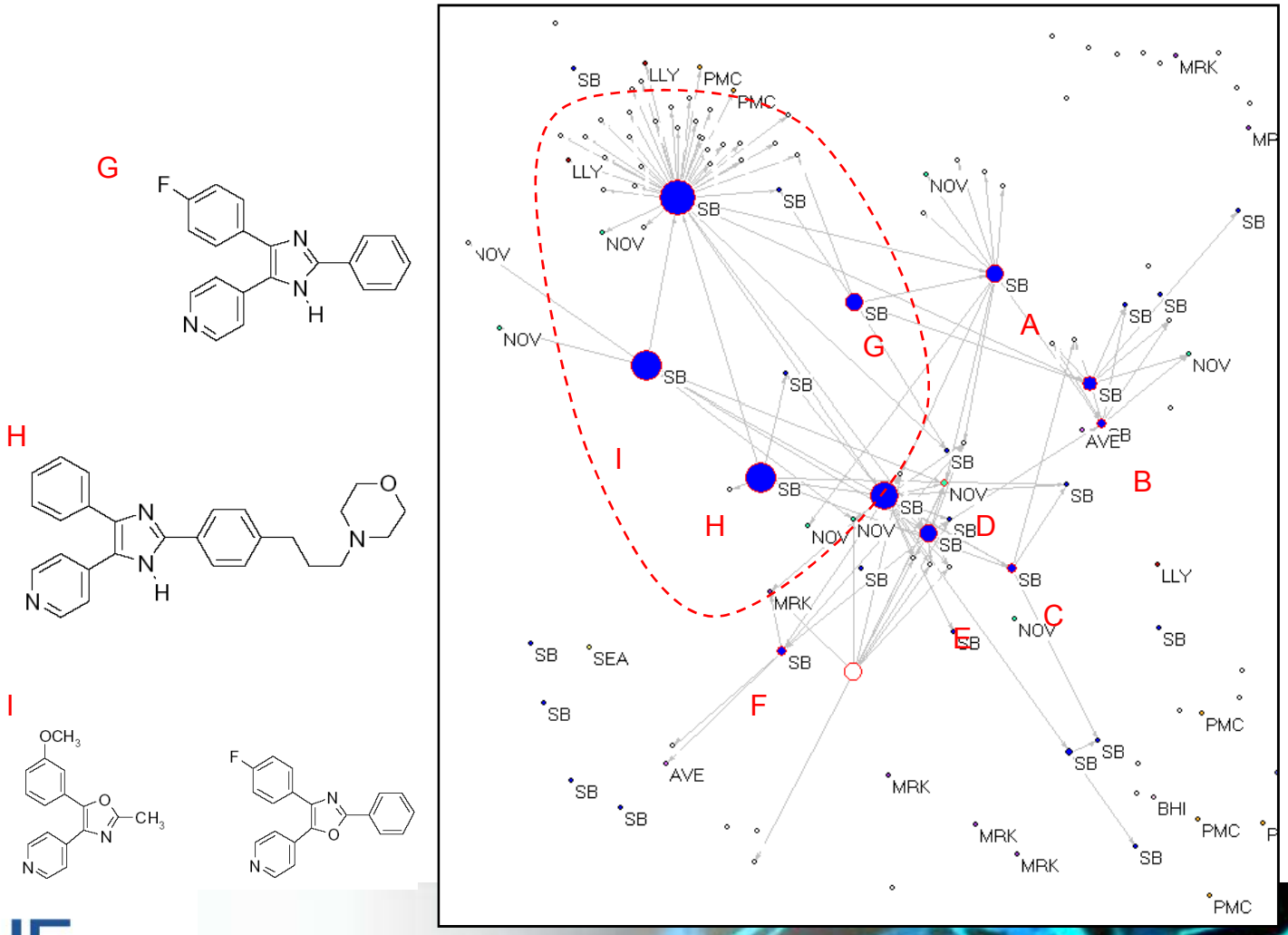
Patent Citation Network, 1996



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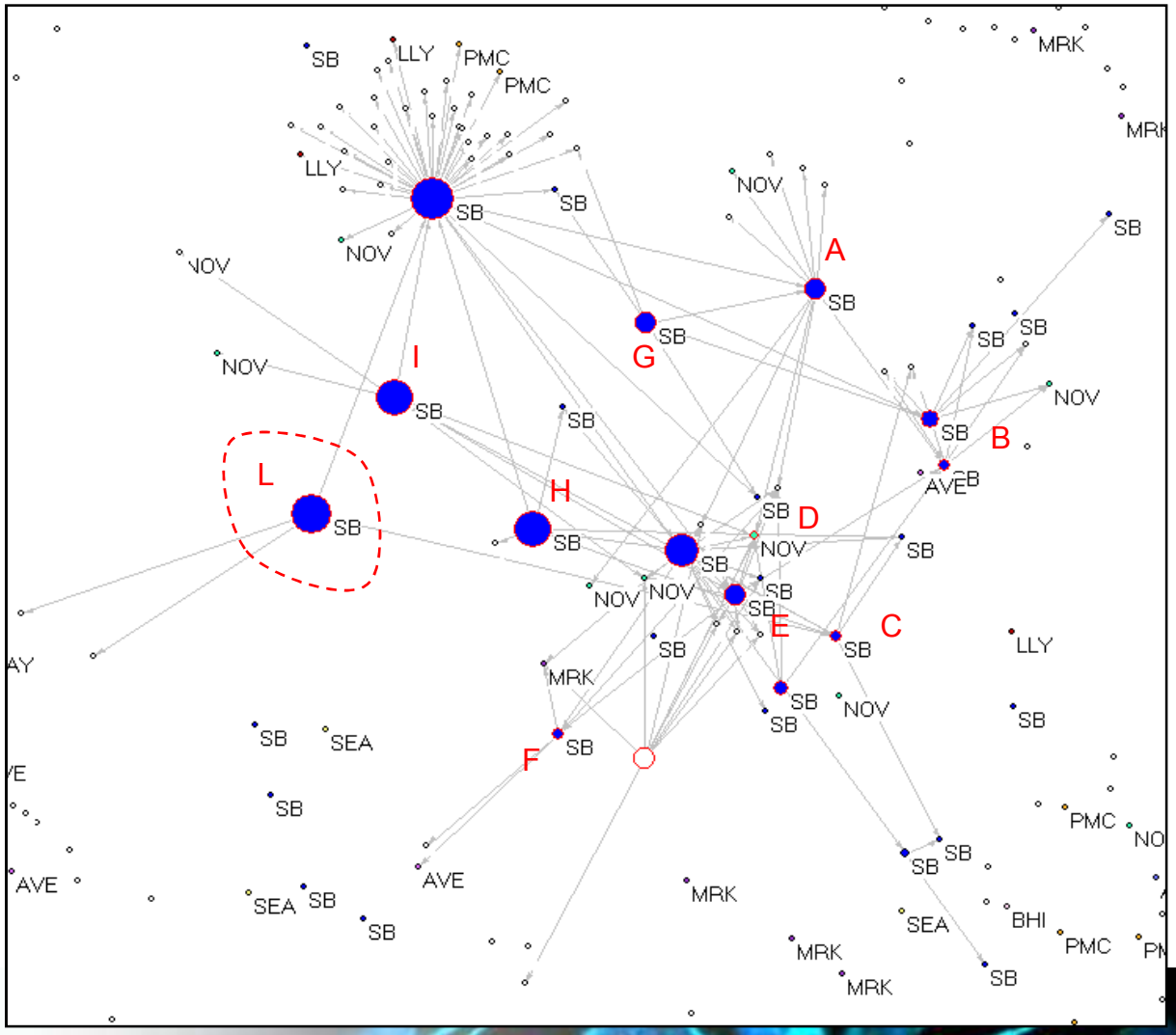

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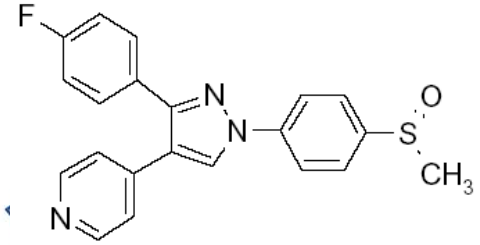

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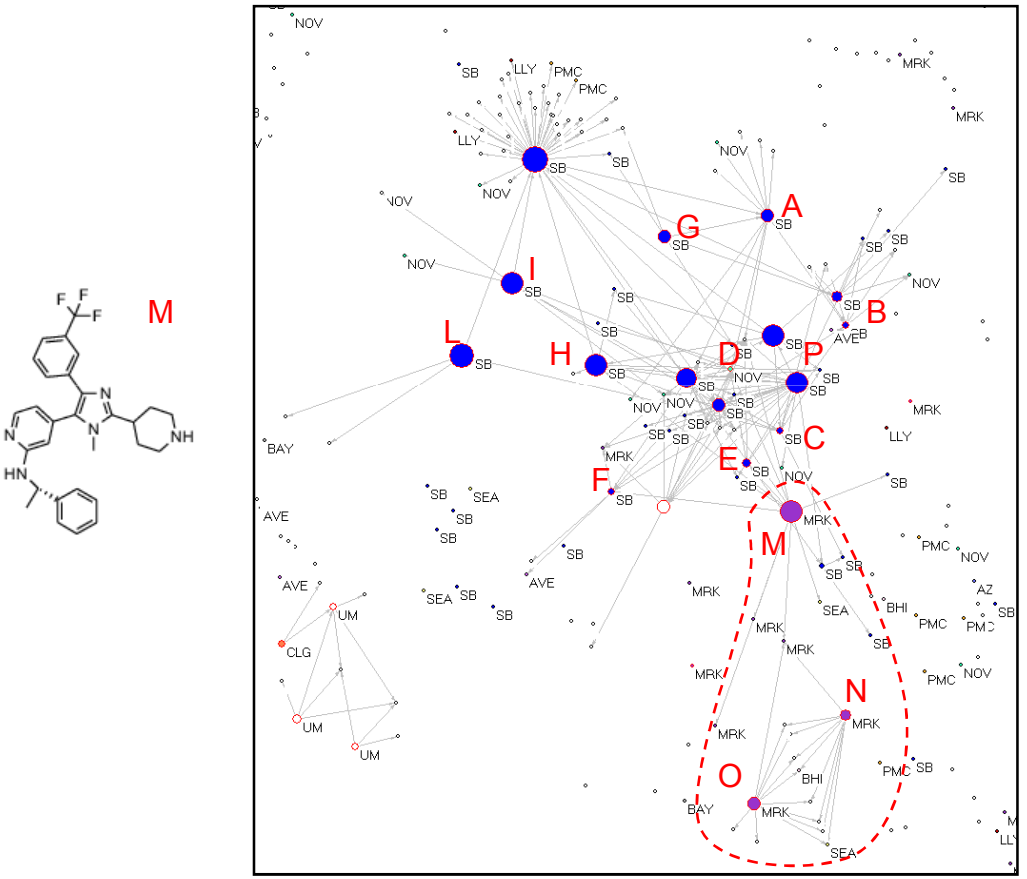

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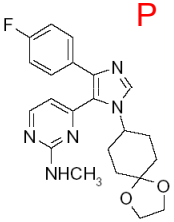

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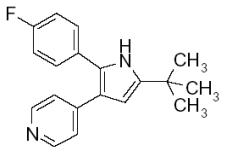

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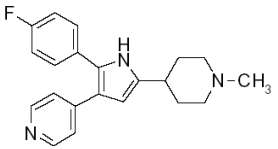

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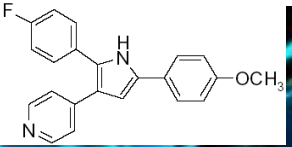

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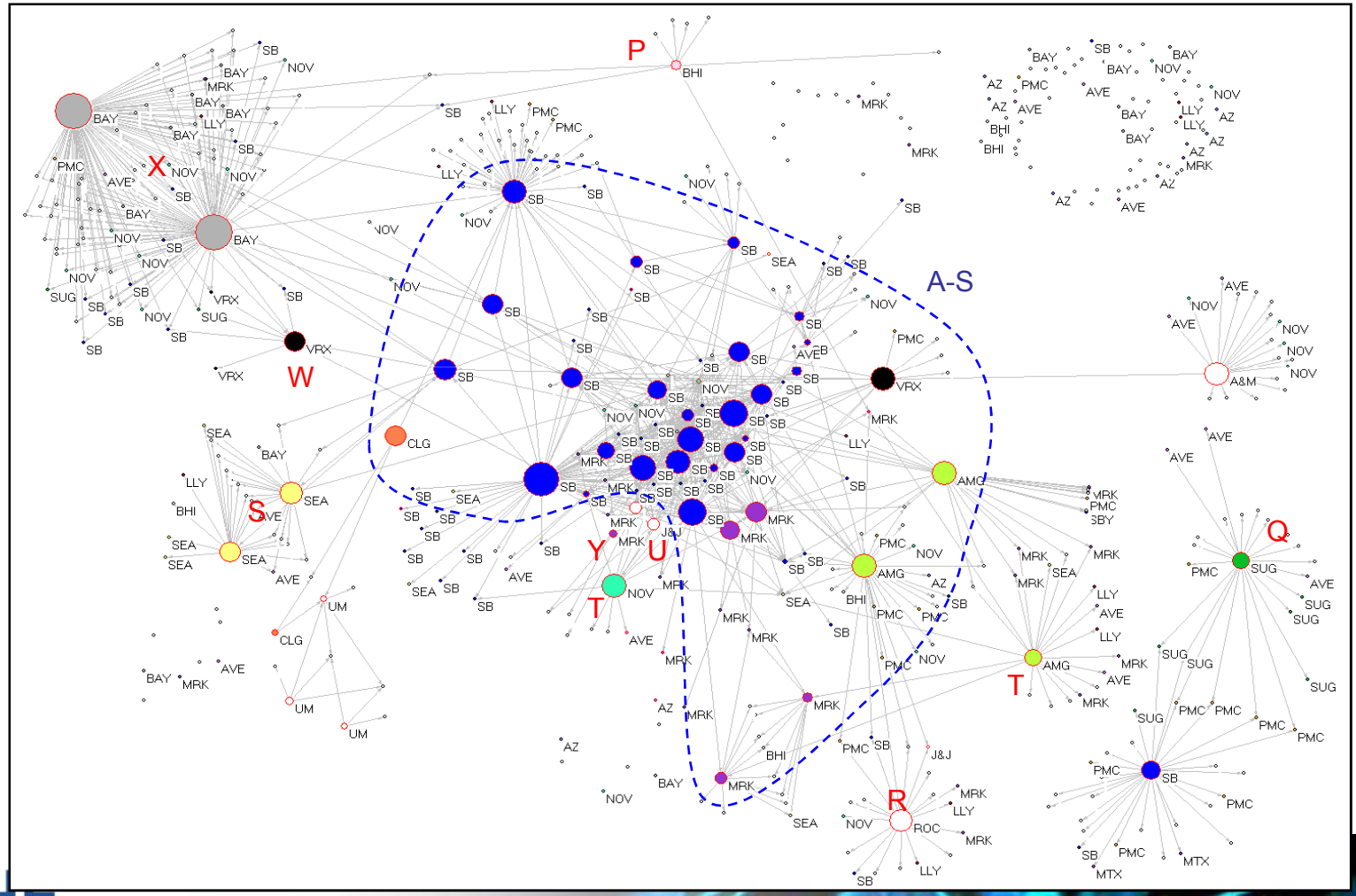

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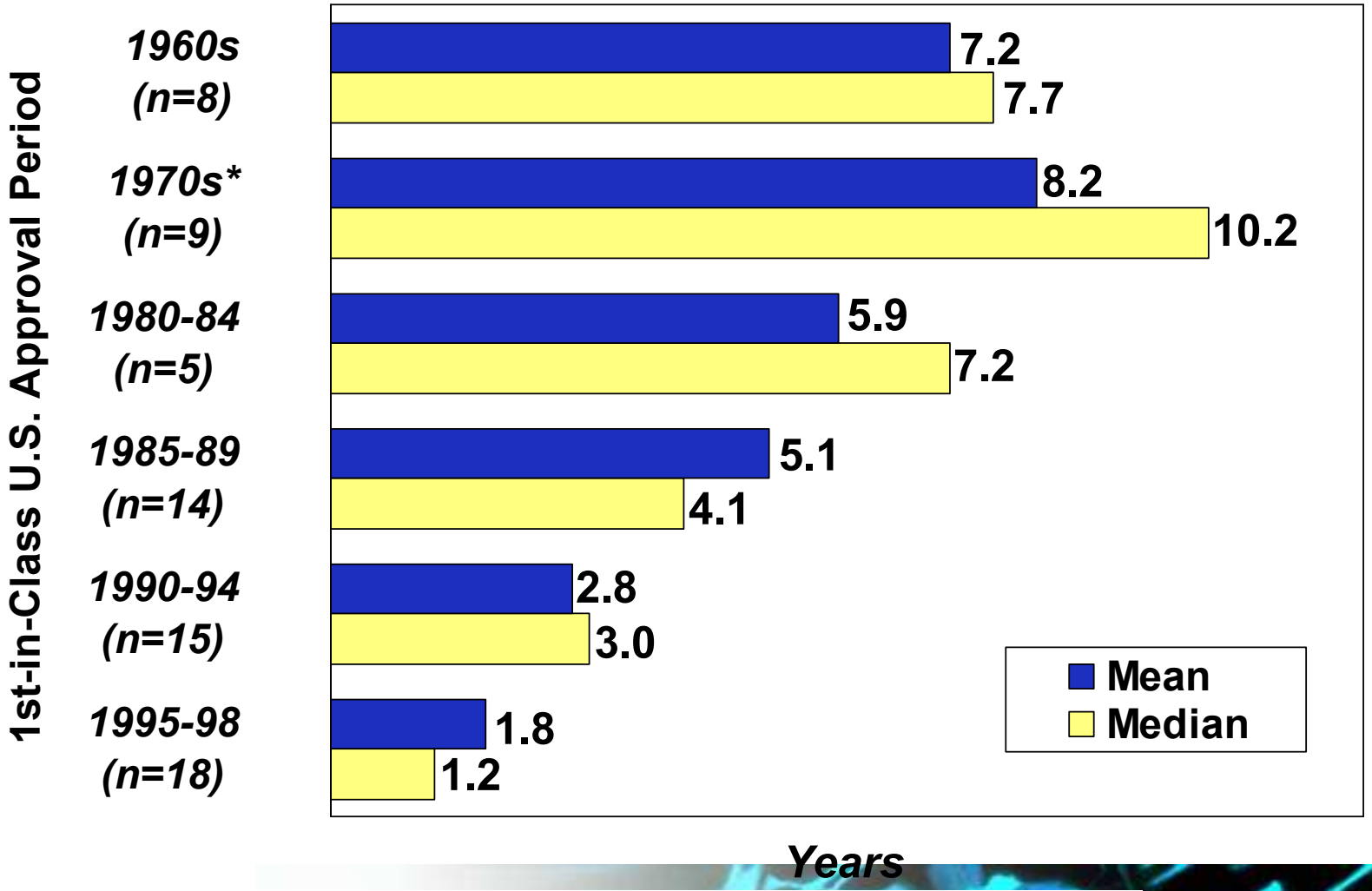
Marketing Exclusivity for Subclasses: Time to First Follow-On



* Two extreme outlier classes were excluded (SERMs and rifamycin antibiotics)

Source: DiMasi and Paquette, Pharmacoeconomics 2004;22(Suppl 2):1-14.

Patent Clusters and the nature of R&D

- The nature of pharmaceutical R&D competition has changed fundamentally
  - Driven by scientific breakthrough and racing for commercialisation
- Pharmaceutical industry R&D is characterised by the large presence of externalities
- It is difficult for companies to capture the benefits of their R&D
  - Getting a product to market
  - Getting a return on that product

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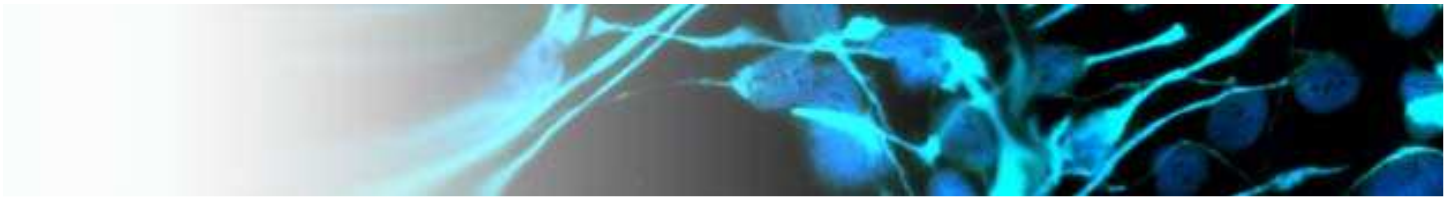
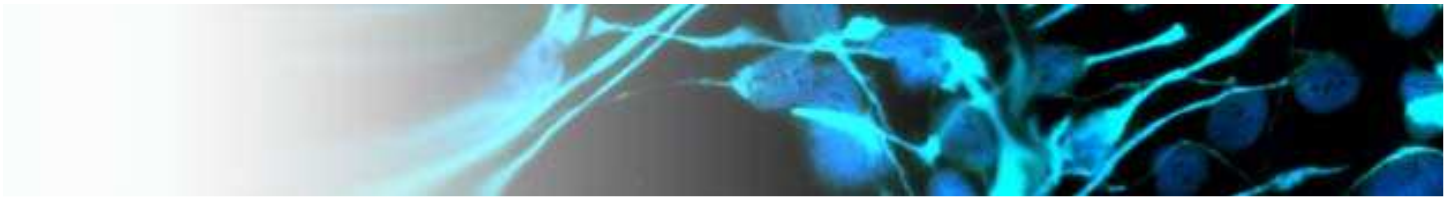


Patents II

- Secondly, whether *effective* patent life is enough to recoup R&D investment,
- US, Europe and Japan all introduced patent extensions in the late 1980s to apply where development times were particularly long.
- Analysis taking account of these extensions of 126 products introduced in the 1990-1995 period still only shows average "effective" patent life of 11.7 years, with a right skewed tail
- Intellectual property protection is also provided by "data exclusivity" periods and by "market exclusivity."
- The US Orphan Drug Act of 1983 (ODA) granted market exclusivity for seven years (that is, similar compounds will not be approved to treat the same condition). Japan and the EU followed the US and passed similar legislation.
- US and Europe have both introduced a six month paediatric patent extension for the larger *adult* market if they *undertake* clinical studies in children, i.e. whether or not the results indicate that the drug can be used in children.

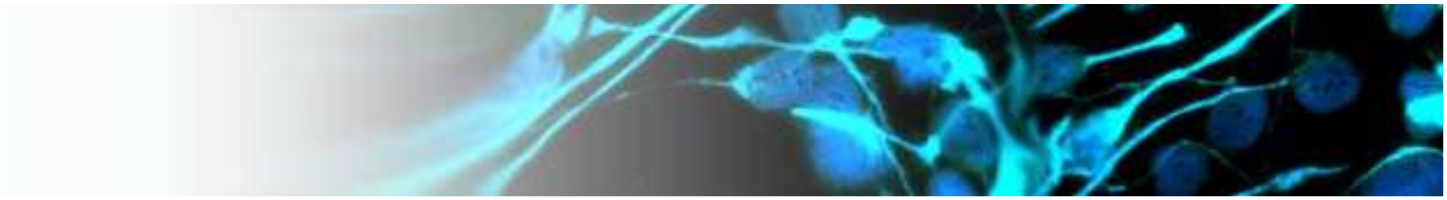
Patents III

- Thirdly, the regulatory criteria for admitting post-patent generic entrants are contentious. For chemical compounds the issues are around competition. For generic versions of large molecule, biotechnology products such as proteins and monoclonal antibodies, the challenge is to determine the conditions for safe approval.
- Generic manufacturers can work on the active ingredient before patent expiry (the Bolar exemption) and generics can be approved with an abbreviated application requiring only bioequivalence and chemical equivalence, without new safety and efficacy trials.



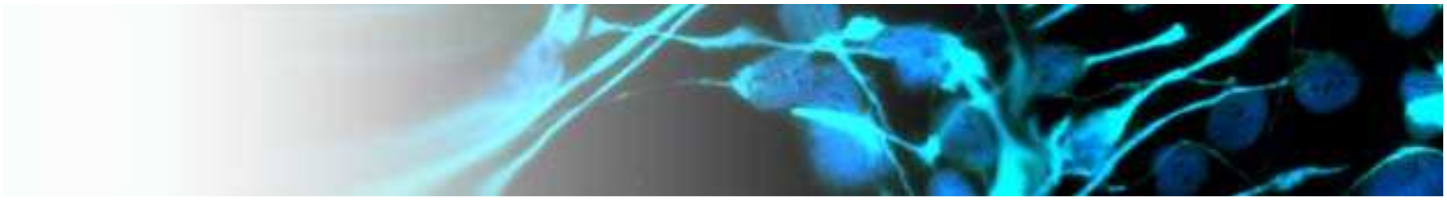
Patents III - generics

- Controversy has focussed on:
  - the period of data exclusivity. The US confers a five year maximum whereas the EU allows 10 years.
  - exclusive entry periods. The US grants the first successful generic firm to challenge a patent 180 days as the only generic in the market). This provides a strong incentive to be first to challenge patents, but may encourage excessive litigation. The EU has no such provision;
  - collusive agreements between originators and generic manufacturers to delay the launch of generics. The US 180 day exclusivity provision significantly increases the potential gains from these
  - “evergreening” In recent years, originator firms have been accused of “evergreening” their drugs by filing follow-on patents on minor aspects of the compound or by developing follow-on products that resemble the original product except for minor changes suffice for a new patent.



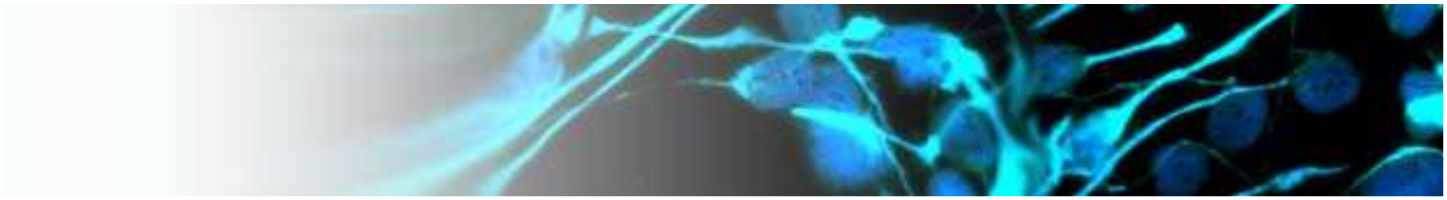
Collusive agreements?

- …between originators and generic manufacturers to delay the launch of generics.
- The 180 day exclusivity provision significantly increases the potential gains from these in the USA. The EU does not have 180 day exclusivity.
- The FTC views such settlements as anti-competitive and has taken enforcement action against originator and generic firms
- However, settling patent disputes with payments can be a legitimate and efficient means to resolve costly uncertainty as to an ultimate court decision.
- The EU Sector Inquiry found:
  - more 200 settlement agreements between 2000 and June 2008
  - 49 medicines, 31 were “best selling”
  - 48 per cent restricted generic market access with 10 per cent involving direct payments.
  - No conclusions were drawn.



Some interesting but unanswered questions

- To what extent should competition law promote copying over innovation? Can we contrast theories of harm in Magill, IMS & Microsoft with the sector enquiry?
- Can intention can ever be relevant to allegations of anticompetitive use of patents given that a patent creates a lawful right granted by a public authority, capable of being challenged before a court, and the purpose of the patent is to exclude the competitor?
- Under what circumstances can settlements of genuine disputes contravene competition rules?



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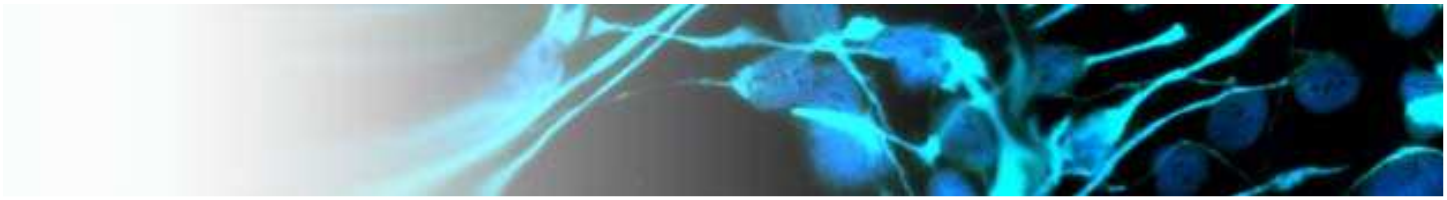

Reasons for and objectives of the Sector Enquiry

- "In order to establish the extent of [the commercial practices by pharmaceutical suppliers …which may cause market distortion] and to assess them fully in their proper factual and economic context, the use of formal investigative powers such as those granted to the Commission for sector inquiries is required" - Commission Decision of 15 January 2008 initiating the Inquiry para 6
- "the inquiry's main focus is company behaviour …The behaviour needs to be assessed in the context of the regulatory framework" - Executive Summary of Final Report, pp3-4

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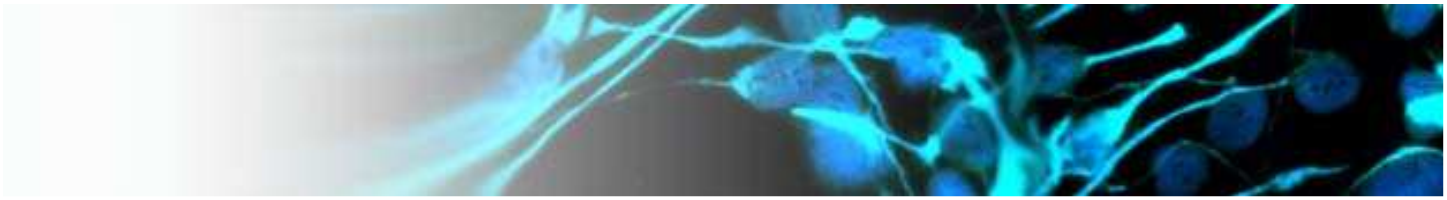
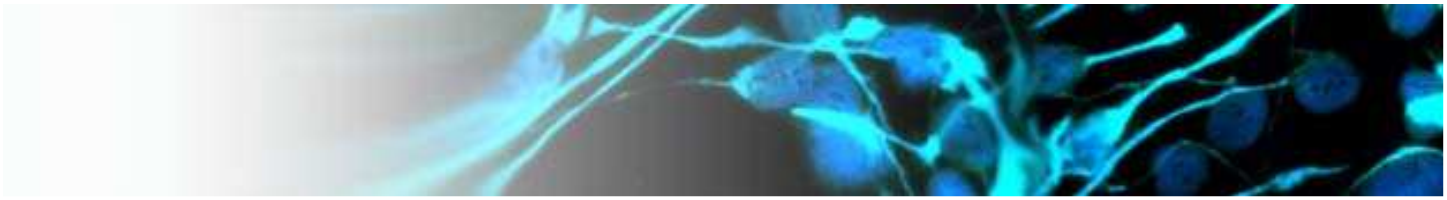


The conclusions, policy recommendations

- Conclusions are qualified e.g.
  - "results…suggest that the behaviour of companies contributes to delay" and "suggests that a variety of other conditions might play also an important role"
  - enquiry "points to certain company behaviours that might, amongst other factors, contribute to" the decline of novel medicines reaching the market
- Sensible but not new policy recommendations:
  - need for unified patent litigation system and Community Patent
  - need to streamline marketing authorisation process at EU and national levels
  - improved pricing and reimbursement procedures for innovator and generic products.
  - desirability of joint action on Health Technology Assessments
  - development of an environment which promotes generic uptake



Conduct of the Inquiry

- First use in sector inquiry of unannounced inspections
  - "The kind of information the Commission will be examining...is by its nature information that companies consider highly confidential….[it] may be may also be withheld, concealed or destroyed" Commission FAQs 16 January 2008
- Extensive questionnaires every week (the "Friday questions") for several months with 7 day deadlines
- Sir Christopher Bellamy (author, former judge of CFI and former Chairman of UK Competition Appeals Tribunal)

  "It came across at the outset as a prosecution, not an inquiry."

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Presentation of the Preliminary Report

- “Preliminary report on pharmaceutical sector inquiry highlights cost of pharma companies' delaying tactics”
  - DG Comp Press Release 28 November 2008
- The facts to some extent are shocking”
  - Dr H Ungerer (Deputy DG, DG Comp) 28 November 2008
- “You may be surprised how far they [R&D companies] will go to extend the depth and duration of patent protection.”
  - Commissioner Kroes 28 November

Presentation of the Final Report

- "The sector enquiry … does not exclude other factors such as shortcomings in the regulatory framework" – Press release
- Delays cost "20% in extra spending" – Press release
- "Makers of original medicines are actively trying to delay the entry of generic medicines onto their markets" – Commissioner Kroes
- "Overall it is indeed a conclusion that there is something rotten in the state" – Commissioner Kroes
- Some implicit thinking that extra "easy money" at the back end of the cycle is reducing incentives to find genuine new innovation

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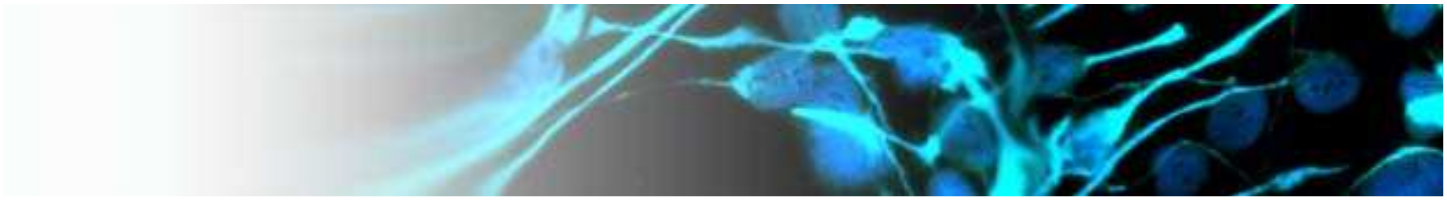
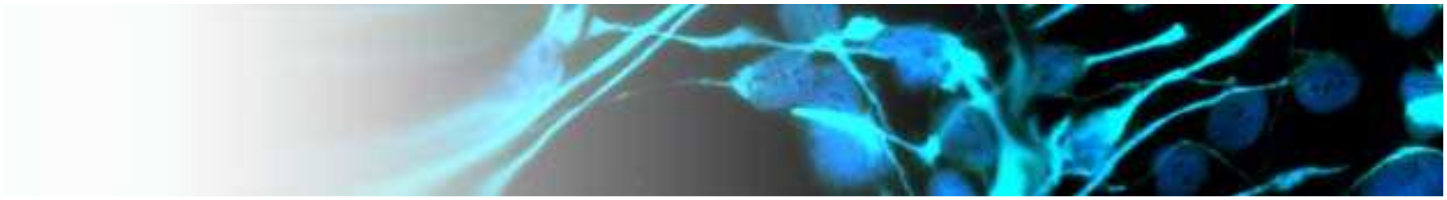


Pammolli et al Competitiveness Reports

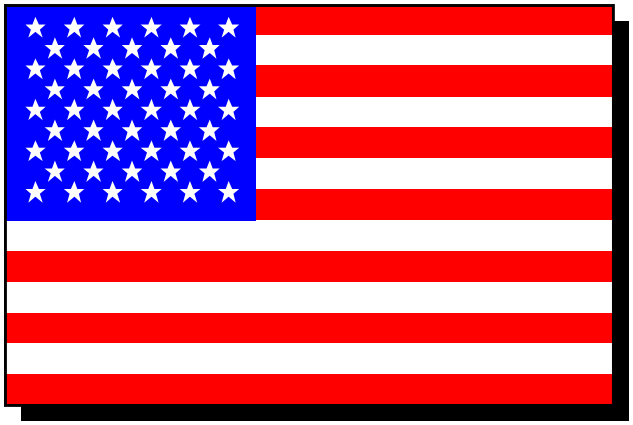
- **The US is not only by far the largest national pharmaceutical market, but has also grown rapidly since the middle 1990s. The US market is now almost twice the size of the EU-15 market in terms of revenue.**
- **The US market for pharmaceuticals is both more concentrated and more volatile than markets in Europe. In other words, the higher concentration of the US market does not mean that it is less competitive. On the contrary, the US market is highly contestable; product turnover is much more frequent than in the EU and Japan; and competition from generic producers is substantial. US market behavior is consistent with that of a market characterized by Schumpeterian competition**
- **There is too little market-based competition in some of the European countries, resulting in a less-efficient industry, as reflected in productivity indicators and market performance**
- **By artificially constraining prices of innovative medicines while failing to stimulate a robust and competitive market for generic medicines, European governments are missing the opportunity to create "headroom" for innovation. There are some exceptions, for example the UK and Germany have strong generic markets.**



R&D Investment 1990 - 2001

- Between 1990 and 2001, R&D investment in the US rose fivefold, while in Europe it grew 2.4 times

2.4 x



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