



Application of Patent Litigation Strategies to Biosimilars: Is there a difference?

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I. Overview of strategies

Clearly identified in the EC Pharmaceutical Sector Inquiry Report (08/07/2009)

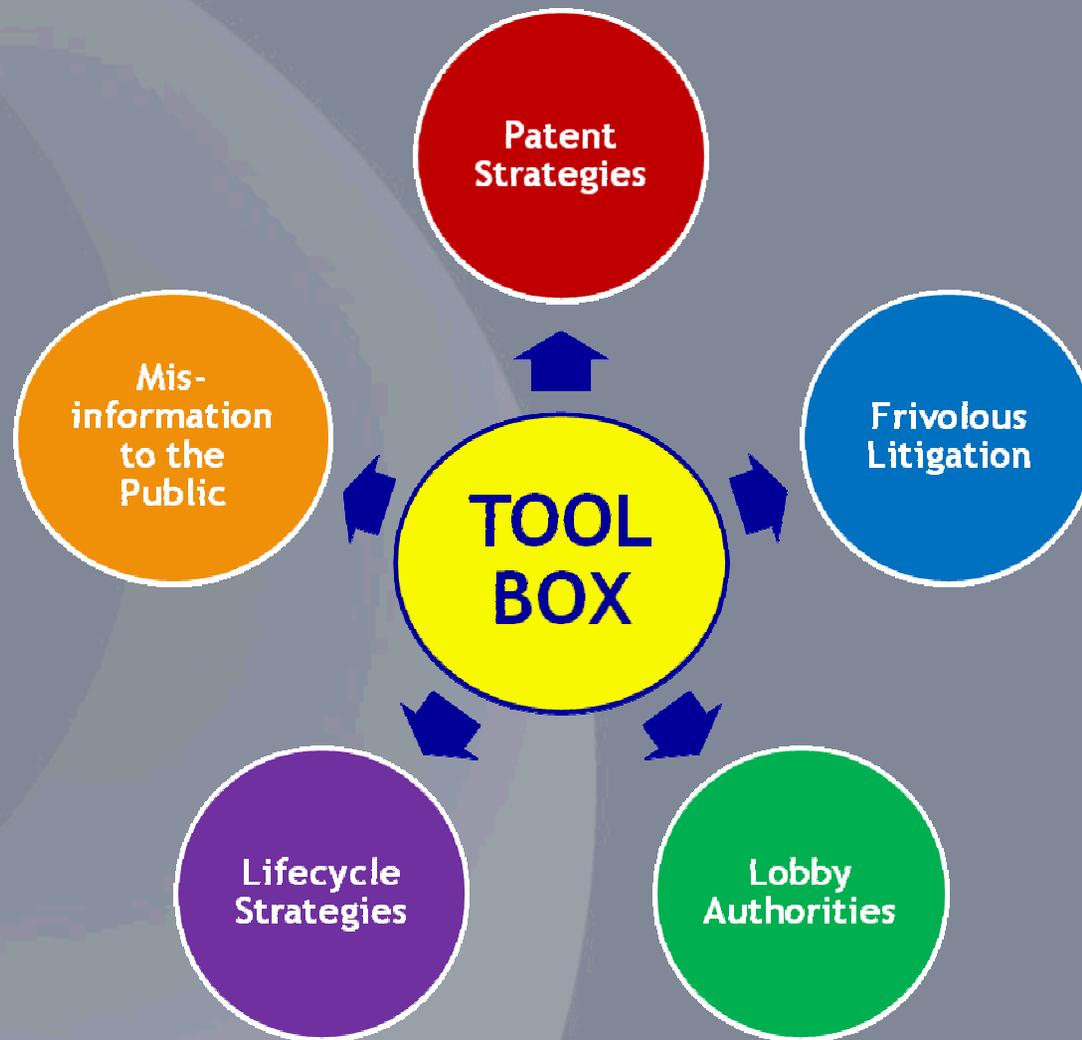
- Why a sector inquiry?
 - » Fewer new pharmaceuticals launched
 - » Kroes: 'Competition in this industry does not work as well as it should'
 - » Generic delay: more than 7 months on average

- Impact of generic entry = price drop:
 - » Generic price is on average 25% lower than originator product prior to the loss of exclusivity.
 - » Two years after entry, prices of generic medicines are 40 below the former originator price.

I. Overview of strategies

- Facts uncovered “shocking”
- There is more than patent litigation strategies
- “Toolkit” of tactics to delay generic entry:
 - » patent filing strategies (patent thickets)
 - » patent litigation
 - » life-cycle strategies (follow-on products)
 - » interventions before national authorities
 - » settlement agreements
 - » Cumulative of practices

I. Overview of strategies



II.2. Follow-on products

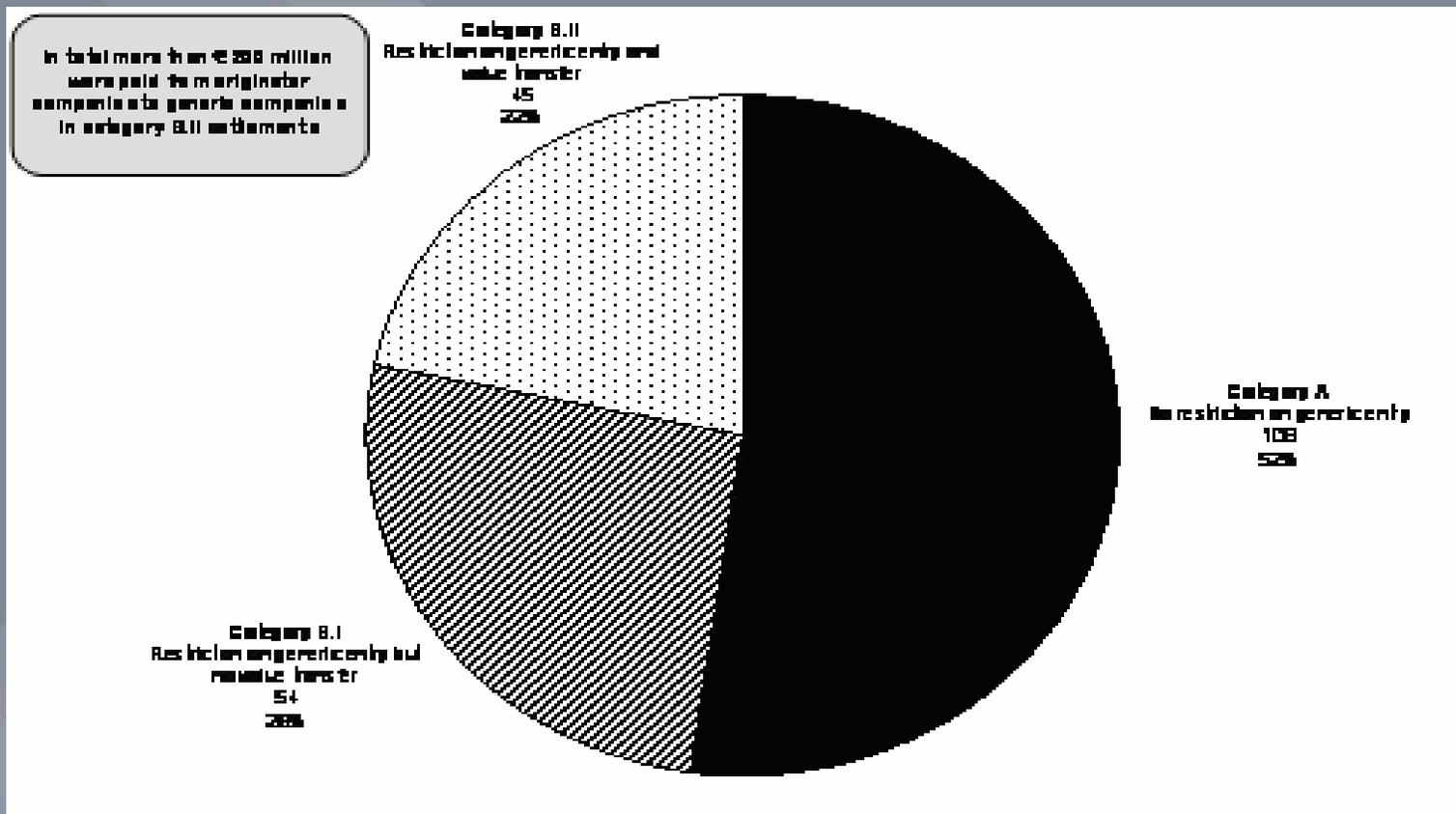
- “new” “better” product is launched before patent expiry
- through marketing campaigns shift from patients to “new” product
- small market is left for generic competition after patent expiry
- Examples:
 - » citalopram (Ciprmail) -> escitalopram (Sipralexa)
 - » alendronate (Fosamax) -> alendronate + vitamine D (Fosavance)

II.3. Patent linkage

- *The practice of linking the granting of a MA, the pricing and reimbursement status or any regulatory approval for a generic medicinal product, to the status of a patent (application) for the originator reference product” (sector inquiry report, § 278)*
- Originator companies “intervene” before national authorities (MA, P&R) raising alleged:
 - » alleged patent infringement (Bolar-exception)
 - » and safety issues
- Very limited success rates of originator companies in court (2% as regards MA), but on average procedures with intervention last four months

II.4. Settlement and other agreements

- More than 200 settlements: half of them restricted generic market entry, significant part of these contain value transfer (direct transfer: € 200 mio)



II.5. Patent filing strategies

- Strategy of filing numerous patents for the same medicine, forming so called patent clusters and patent thickets, to delay or block generic market entry;



“ a dense growth of shrubbery or small trees” ; something impenetrability

- Blockbuster medicines may be protected by up to 1,300 patents and/or patent applications EU-wide

II.5. Patent filing strategies

- Basic (compound) patent : New compound (NCE) ; active Ingredient
- Secondary or follow-on patents
 - *Products*
 - » Active Principle (Active substance/moiety)
 - » Metabolites of NCE
 - » Isomers/Enantiomers
 - » Salts, Crystalline Form, Hydration State, Polymorphic Form
 - » Formulation
 - » Combination (cocktail drugs)/Selection Inventions
 - » Purity/Purified form
 - » First medical use
 - *Processes*
 - » Manufacturing methods/Synthetic/Purification
 - » Second medical use
 - *Delivery Systems/methods of administration/Dosing Schedules/patient groups, etc.*

II.5. Patent filing strategies

- Thickets create legal uncertainty and may delay generic entry as generic may need to analyze the sum of all patents (applications)

- Patent quality issues:
 - » lack of rigorous assessment of patentability requirements
 - » lack of quality applications
 - » divisional applications
 - » not enough consideration of third-party observations

 - » Opposition rate for pharmaceutical patents is higher than in other sectors
 - » 60% of opposition cases led to revocation of the patent (in addition scope of patent was restricted in additional 15% + national litigation)

 - » length of opposition and appeal proceedings: almost 80% of procedures before the EPO took more than 2 years

II.6. Patent litigation strategies

- Very often weak follow-on patent, but enforced
- Some facts:
 - » the number of patent litigation cases increased by a factor of four between 2000 and 2007 (698 cases were reported)
 - » mainly based on follow-on patents
 - » average duration of cases to reach final outcome: 2.8 years
 - » generic companies won 62% of patent litigation cases
 - » average cost Euro 230,000
 - » interim injunctions were granted in almost half of the cases when they were requested (112 of 255 cases), average duration 18 months
 - » In 46% of the cases in which injunctions were granted, the subsequent cases on the merits were lost by the originators
 - » High total cost

II.6. Patent litigation strategies

- The issue: the national character of patent
 - » No Community instruments
 - » National patents
 - » European patents under the EPC, resulting in a bundle of national patent rights
- Infringement and/or to invalidity are therefore a matter of national courts: there is not (yet) a centralized European patent court
- Litigation has take place in each country
- Litigation strategies require a detailed knowledge of national procedures

The Netherlands

- Specialized patent court in The Hague
- Open for cross-border injunctions, even after recent ECJ-judgments:
 - » Injunction proceedings: Gatt/Luk does not seem to apply (Steur/Zilka; Fleuren/Ruvo)
 - » No cross-border in proceedings on the merits when invalidity is raised(Sandisk/Sisvel)

The Netherlands

- Very effective preliminary relief proceedings to obtain an interim injunction (*kort geding*)
 - » urgency (presumed in IP litigation)
 - » not always possible when the case is too complicated (rather exceptional)
 - » in-depth study of both validity and infringement issues
 - » a decision is usually obtained within 3 months

The Netherlands

- Proceedings on the merits
 - » permanent injunction
 - » damages (no punitive/treble damages)
 - » account of profits (bad faith)
 - » accelerated main proceedings (judgment in 10 to 14 months)

The Netherlands

- Judicial rules and costs
 - » No discovery, but new “*conservatoir bewijsbeslag*”
 - » Normally no court appearance of experts or witnesses
 - » No cross-examination
 - » Between 30,000 and 100,000 EUR (more expensive depending on various factors, such as complexity, validity issues, experts, etc.)
 - » No recovery of attorney’s fees until recently under the European Enforcement Directive

Germany

- Specialized patent courts
- Only European country with dual treatment of infringement and validity (no invalidity defense in infringement proceedings)
- Relatively open to grant cross-border injunctions (on the basis that invalidity arguments do not have to be dealt with in infringement proceedings)

Germany

- preliminary relief proceedings
 - » only in urgent matters (within one month after knowledge of infringement)
 - » strong case of infringement must be established + technically not too complicated cases
 - » less frequently granted because a judgment can be obtained in the main proceedings within one year
 - » even ex parte (*einstweilige Verfügung*) ; possible defensive strategy : *Schutzschrift* (protection letter to the court by the alleged infringer in order to make sure that defense arguments are heard)

Germany

- Proceedings on the merits
 - » permanent injunction
 - » damages (three methods of calculation: reasonable royalty, patentee's lost profit or the infringer's profit); recent development towards higher damages
 - » no punitive/treble damages
 - » infringement decision within one year (if no expert is appointed)
 - » invalidity decision: 1-5 years

Germany

- Judicial rules and costs
 - » Limited type of discovery under a recent ruling of the Federal Supreme Court
 - » Dual system (issues of infringement and validity are decided by separate courts; invalidity may not be raised as a defense in an infringement action)
 - » Stay of the infringement proceedings only if a clear-cut novelty attack is at issue in the nullity action
 - » National nullity proceedings cannot be started before the Federal Patent Court until the EPO opposition proceedings have been concluded or the opposition period has expired
 - » Preferred venue for patent enforcement litigation

Germany

- Judicial rules and costs
 - » Between 40,000 and 125,000 EUR (more expensive depending on various factors, such as complexity, validity issues, experts, etc.)
 - » Costs have to be paid by the losing party but they are calculated according to formal rules resulting in the *Streitwert* (value) of the proceedings.

United Kingdom

- Specialized patent courts
- Very critical towards (European) patents: high rate of invalidity judgments
- Reluctant to grant cross-border injunctions: A cross-border infringement question cannot be dealt with when issues of infringement and validity are so intertwined that it is not possible to judge one without the other, taking into account that a national court has no jurisdiction to invalidate a foreign patent

United Kingdom

- preliminary relief proceedings
 - » Only granted in exceptional circumstances, typically when irreparable harm for the plaintiff is likely and the defendant would not suffer irreparable damage from a temporary injunction
 - » Irreparable damage for both parties: court decides on the balance of convenience
 - » Also less frequently granted because a judgment can be obtained in the main proceedings within one year

United Kingdom

- Proceedings on the merits
 - » permanent injunction; other remedies available (e.g. delivery up of infringing goods)
 - » Damages are not awarded following the first instance trial which only deals with the liability of the alleged infringer. The judge will only order an inquiry as to either damages or the loss of profits which have been suffered
 - » Timing: up to 12 months

United Kingdom

- Judicial rules and costs
 - » documentary, but no oral, disclosure: defendant can be compelled to produce documents and/or description of product/process
 - » further specific discovery can be required, as well as the possibility of providing samples or allowing for an inspection of the product/process in question
 - » results can only be used for the UK proceedings (but court can give leave)

United Kingdom

- Judicial rules and costs
 - » No jury
 - » Real trial (up to two weeks) with very experienced judges
 - » Cross-examination of witnesses and experts
 - » Very expensive (ranging from US\$300,000 for a simple matter to millions in complex issues)
 - » English courts are inclined to award litigation costs at the expense of the losing party

Belgium

- No specialized patent courts
- Proceedings on the merits
 - » Rather slow proceedings – often appointment of a technical expert by the court
 - » Relatively inexpensive – no discovery/cross-examination
 - » In general, costs cannot be recovered (yet) from the losing party; rather low damages

Belgium

- Preliminary injunction proceedings:
 - » open for cross-border injunctions (Colgate/Unilever ; Altana Pharma ; ATMI/Praxair)
 - » *prima facie* of assessment of the patent rights: assumption that a European patent is *prima facie* valid. Invalidation defenses raised by the alleged infringer are very unlikely to succeed.
 - » urgency/balance of interests

Belgium

- Information gathering (saisie-contrefaçon/beslag inzake namaak):
 - » ex parte request – no urgency required
 - » prima facie assessment of patent rights
 - » court order appointing an expert, sometimes allowing confiscation of goods
 - » visiting of premises (“unannounced private search warrant”); pre-trial alternative
 - » sworn report with expert findings; information can be used in other proceedings in Europe (Belgian Supreme Court decision of 03/009/1999)

Conclusion

- Patent litigation requires a thorough knowledge of:
 - » Patent law
 - » Patent portfolio management
 - » Jurisdictional issues (forum shopping)
 - » National legal systems and the operation of national courts
- On the basis of that knowledge, a patent litigation strategy can be developed:

From Cipramil (citalopram) to Siplelexa (escitalopram)

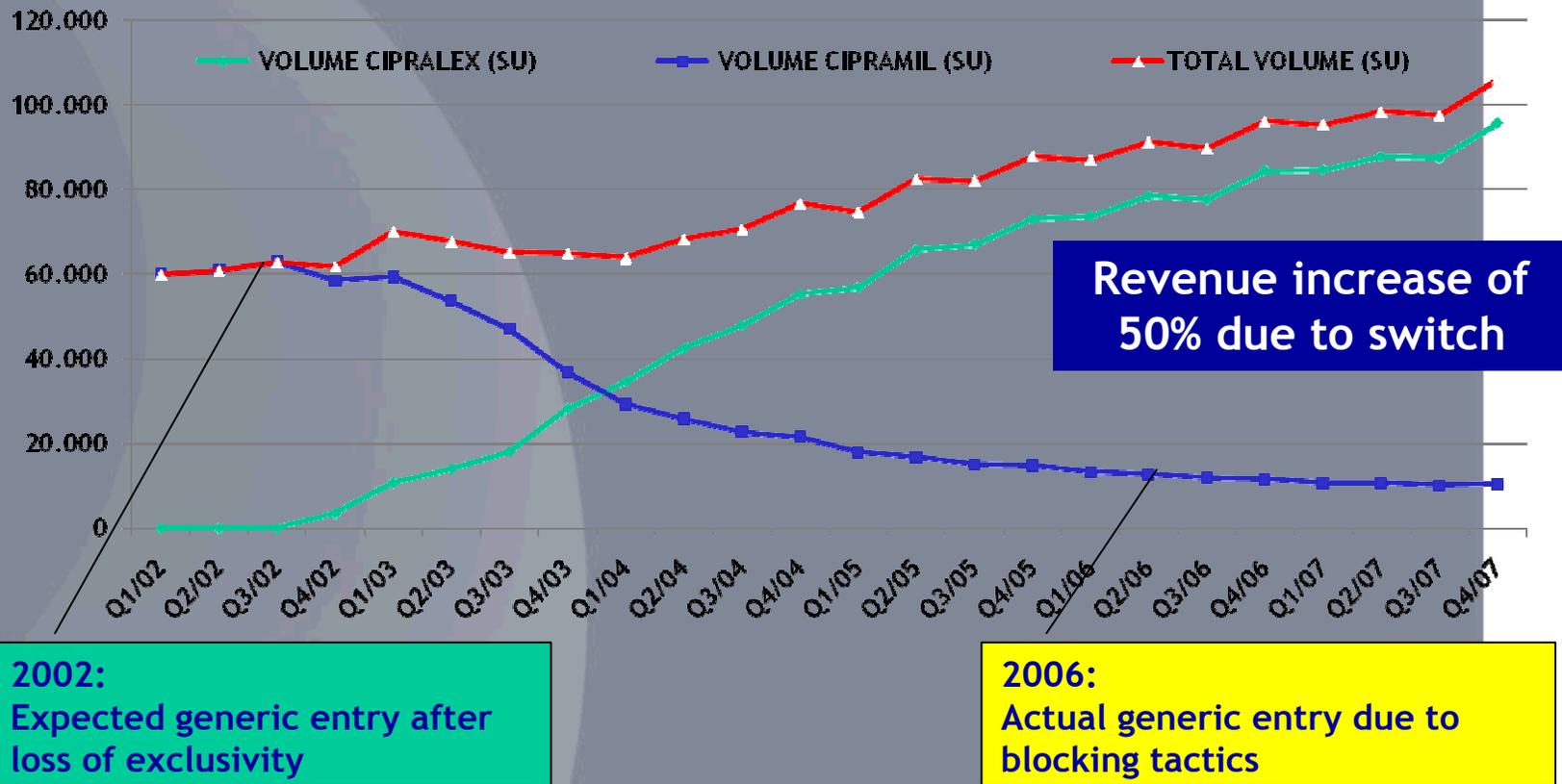
- Generic entry expected in 2002 (after patent and SPC expiry)
- 30 follow-on patents (including a crystalline base patent, which was clearly anticipated in the prior art), resulting in 30 court cases in 9 countries
- Lundbeck managed to prevent generic competition, but the patent was eventually revoked by the EPO in 2006!
- In the meantime switch but gigantic marketing campaign from Cipramil to Siplelex (which has as AI the enantiomere of the racemic citalopram)

From Cipramil (citalopram) to Siplalexa (escitalopram)

- Generic competitors develop escitalopram and apply for MA's, but Lundbeck intervenes with the MA authorities to oppose the use of public bridging data which are part of Lundbeck MA
- new patent granted for escitalopram, followed by new litigation.
- Result:

II.7. Example

From Cipramil (citalopram) to Siprolexa (escitalopram)



Source: IMS Data 2002-2007

III. Strategies/defences for biosimilars

- Can these strategies also be applied to biosimilars?
- Yes : very similar legal environment (patents relating to DNA and RNA sequences, polypeptide sequences, cell lines, monoclonal antibodies and other proteins, fermentation and purification processes, et.)
- So what to do?
 - » Use the sector inquiry as a policy documents : lobby for changes in the system on the basis of the recommendations of the EC (e.g. better and faster patent system ; unified patent and patent litigation system, no patent linkage, etc.);

- So what to do (2)?
 - » Develop launch strategies depending on the national situation:
 - launch at risk? (UK and The Netherlands)
 - send protective letters to avoid ex parte action (Germany, Belgium)
 - start national invalidity or non-infringement proceedings (it can help to avoid preliminary injunction proceedings)
 - » Gather as much information to prepare a possible competition law argument as a defence in patent litigation or to file a complaint with the EC