

Major legal developments affecting the generic medicines industry

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Five major hurdles to generic competition

- Patent law
- Data exclusivity
- Essential similarity/changes to reference product
- Vertical disharmony in MRP
- Pricing/reimbursement

Patent law

- Key issue: what can be done pre-patent expiry
 - Submitting a dossier
 - Submitting samples
 - Studies (stability, bio-availability)

Bolar vs. TRIPs

- Art. 28.1 TRIPs: exclusive rights
 - for *making, using, offering for sale, selling or importing* patented drugs
- Art. 30 TRIPs: limited exceptions allowed, provided
 - They do not unreasonably conflict with normal exploitation, and
 - Balance legitimate interests of patent owner and third parties

WTO panel report 17.3.00

- Regulatory review exception allowed
 - no unreasonable harm to innovator
- Stockpiling not TRIPs-compatible
 - affects pre-expiry rights of *making and using*, and is therefore unreasonable
- Conclusion: TRIPs not a barrier to balanced *Bolars* in EU or CEEC

Experimental Use (Germany)

- Clinical Trials I (1995)
 - finding out a new use is covered by research exemption
 - confirmed by *Bundesverfassungsgericht* 2.5.2000
- Clinical Trials II (1997):
 - if research is “real”, commercial purpose does not matter
- NB: bio-equivalence testing not addressed

Munich Convention Review proposal

- Second medical use (“Swiss claim”) to be protected:
 - *Where the subject-matter of the invention is a substance or composition for use in a method*
 - *... the substance or composition shall be deemed to be new ...*
 - *provided that use is not comprised in the state of the art*
- An end to divergent jurisprudence

Regulatory developments

- The starting point: Article 4.8(a)(iii) of 65/65/EEC
- Three conditions for generic MA:
 - No data exclusivity (6/10 years passed since first MA for reference product)
 - Essential similarity to reference product
 - Reference product “is marketed”

Essential Similarity

- Definition ECJ in *Generics* (3.12.98):
 - Same qualitative and quantitative composition in terms of active principles
 - Same pharmaceutical form
 - And bioequivalent
 - Unless it differs significantly in terms of safety or efficacy (because of excipients)

May 2000 Draft NtA

- Broad view of “same composition”:
 - Same active substance
 - “different salt, ester or derivate etc. ...should be regarded as essentially similar”
 - unless safety or efficacy concerns
- Broad view of “same pharmaceutical form”
 - “All oral forms for immediate release *must* be regarded as same ...”

Change of reference product

- Two solutions possible:
 - Keep using old version as reference product (interpretation of “is marketed”)
 - e.g. France: “has been marketed”
 - May 2000 NtA: “Is marketed” must be understood as “is authorised”
 - Or create link to new version

Omeprazole

- Losec changed to Losec MUPS
 - Different salt, smaller granules
 - Change in “active substance”?
 - Enterotablets vs. enteric coated capsules
 - Change in “pharmaceutical form”?
 - Losec MUPS bio-equivalent to Losec
 - Marketed as exchangeable
- Courts heading generics’ way?

Cyclosporine

- Sandimmun / Neoral
 - Different formulation (micro-emulsion)
 - 30% difference in bio-availability
- MCA approves Sangstat's hybrid application for generic cyclosporine
- UK court rejects Novartis appeal
 - press release Sangstat 31.3.00
- NB: US oral solution recalled for lack of bio-equivalence with Neoral

What if old version can be parallel imported ?

- RPR changes formulation of *zopiclone* (different excipient)
- ECJ case C-84/98 (16.12.99): Product with old formulation can be parallel imported where authorities
"are convinced that the product, in spite of differences relating to excipients, does not pose a problem for public health"
- Also relevant for *omeprazole* cases

How to strike a balance?

- Regulatory angle: determine how new product was approved (abridged procedure)?
- Competition law angle: determine if product change is market partitioning or real public health improvement (see A-G opinion in *RPR*)
- Points to consider:
 - generic MA dependent on subjective assessment of innovator choices
 - Difficult to fit in current legislation

MRP and vertical disharmony

- MRP requirement: all SmPCs identical
- CMS requirement: vertical harmony
- Solutions
 - Limit possibilities to base MRP refusal on vertical disharmony
 - Or harmonise innovator SmPCs (arbitration)
- Several Article 11 arbitrations said to be pending

Post-MRP issues

- Post-MA *refusals*
 - National case law: deleting MA because of sample requirements
- Reimbursement problems
 - If generic has less reimbursement than innovator: no sales
 - Important EC law question: what real marketing rights do generics have?

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