Life Science Strategy Summit on IP & Exclusivity

The Bolar Exemption and Safe Harbor: Discover the Latest Regulatory Challenges in Application

Panel:
Brian Coggio, Takanori Abe, Ina Bürck, Bea McDonald, Christoph Rehfueß

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The Bolar Exemption and Safe Harbor: Discover the Latest Regulatory Challenges in Application

Agenda

- Overview Europe
  - Research exemption (incl. research tools)
  - Bolar-type exemption (incl. 3rd parties)
- Overview US
- Overview JP
- The unknown: UPC and proposed EU Directive
  - SPC manufacturing waiver
- Case studies
Research exemption in Europe

- There is no common basis in European law
  - Article 27 Community Patent Convention 1975
    - Article 27 Limitation of the effects of the Community patent
      - The rights conferred by a Community patent shall not extend to: ...
        - (b) acts done for experimental purposes relating to the subject-matter of the patented invention; ...
  - Article 30 of the TRIPS Agreement
    - "Members may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties."
- Provided in national law by national statutes
- Excludes scientific research from patent infringement
- Not harmonized at EU level: Significant differences at Member State level in the precise activities that are excluded
  - Research “on” or “with” the patented subject matter (e.g. as research tool)?
  - Does this exemption allow for the conduct of clinical trials and other tests necessary to obtain a marketing authorization?
## Research exemption in Europe

<table>
<thead>
<tr>
<th>Countries</th>
<th>Research</th>
<th>Scope</th>
<th>Research tools</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>Yes: Section 60(5)(b) Patent Act 1977 “… done for experimental purposes relating to the subject-matter of the invention;”</td>
<td>- research “on” the invention - finding out something unknown about the invention - ultimate commercial aim not harmful but preponderant purpose must be to find out something new</td>
<td>No, unless it is to learn something new about the research tool itself</td>
<td>Key case law: Monsanto vs. Stauffer RPC (1985)</td>
</tr>
<tr>
<td>DE</td>
<td>Yes: §11 Nr. 2 PatG (&quot;Experimental use privilege&quot;) “…acts done for experimental purposes relating to the subject matter of the patented invention;”</td>
<td>- research “on” the invention - new information or resolving uncertainties - commercial interest not harmful (if not only market information) - clinical trials for regulatory approval included (but not bioequivalence)</td>
<td>Not decided; likely not exempt</td>
<td>Key case law: FCJ Clinical Trials I (1995) &amp; II (1997)</td>
</tr>
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<td>FR</td>
<td>Yes: Article L.613-5(b) FIPC “…acts done for experimental purposes relating to the subject matter of the patented invention;”</td>
<td>- research “on” the invention - gain new information about the invention - no commercial use - clinical trials for regulatory purposes accepted by first instance courts</td>
<td>Not decided; likely not exempt</td>
<td>Key case law: TGI Paris, Science Union v. AJC Pharma (2001)</td>
</tr>
<tr>
<td>IT</td>
<td>Yes: Article 68(1)(a) Italian Code of IP “…actions carried out … as experimentation;”</td>
<td>- research “on” and “with” the invention to acquire knowledge and thus promoting scientific research</td>
<td>Probably exempt</td>
<td>Key case law: Supreme Court n. 2538 (1970); Supreme Court n. 240 (1976)</td>
</tr>
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<td>ES</td>
<td>Yes: Art. 61(1)(b) Spanish Patent Act 24/2015 “…acts done for experimental purposes relating to the subject matter of the patented invention.”</td>
<td>- research “on” the invention - improving or consolidating the inventive technical rule</td>
<td>Not decided; likely not exempt</td>
<td></td>
</tr>
<tr>
<td>NL</td>
<td>Yes: Art. 53(3) Dutch Patent Act 1995 “…acts solely serving for research on the patented subject matter, including the product obtained directly as a result of using the patented process.”</td>
<td>- research “of” the invention - research “on” the invention or in commercial setting only allowed if intent is a purely scientific purpose or to advance science</td>
<td>No, unless it is to learn something new about the research tool itself</td>
<td></td>
</tr>
<tr>
<td>BE</td>
<td>Yes: Art. XI.34, §1.b &amp; Article XI.34, §1/1 BCEL “… acts done for experimental purposes relating to the subject matter of the patent invention;” “… all acts carried out for the evaluation of medicinal products are considered as acts … within the meaning of paragraph 1.b”</td>
<td>- until the recent adaptation in line with the UPC wording very broad scope (research “on” and with” the invention) - commercial interest not harmful - Previously unclear whether clinical trials for regulatory approval could be covered (common opinion, no), recent amendment clarified (yes)</td>
<td>Until amendment; yes; now likely not exempt</td>
<td>With the UPC entering into force, provision adapted to UPCA wording; formally exempt in 1.b “acts done for scientific purposes on and/or with the subject-matter of a patented invention”</td>
</tr>
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Bolar exemption of EU Directive 2001/83/EC relating to medicinal products for human use


• Purpose was to address uncertainty about the scope of the experimental use exemption to clinical studies

• Only applicable for pharmaceutical products

  Article 10(6) of Directive 2001/83/EC:
  “Conducting the necessary studies and trials with a view to the application of paragraphs 1, 2, 3 and 4 and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products.”

• No uniform implementation of Directive 2001/83/EC in national law create significant differences between Member States
  ➢ Varying applicability regarding innovative drugs
  ➢ Varying applicability regarding country requirement for MA approval outside of the trial country
  ➢ Varying applicability regarding third party supply of API and other acts performed by third parties
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### National implementations of Bolar exemption provided by EU Directive 2001/83/EC

<table>
<thead>
<tr>
<th>Countries</th>
<th>Bolar-type exemption</th>
<th>Applicability</th>
<th>MA applications</th>
<th>3rd party supply</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>Section 60(5)(i) Patent Act 1977 (&quot;Bolar-type exemption&quot;)</td>
<td>Generic</td>
<td>UK or EU only</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td></td>
<td>Section 60(6)(D)-(G) Patent Act 1977 (&quot;Clinical trial exemption&quot;)</td>
<td>Generic and innovator</td>
<td>Anywhere</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td>DE</td>
<td>§11 Nr. 2b PatG (&quot;Regulatory approval privilege&quot;)</td>
<td>Generic and innovator</td>
<td>Anywhere</td>
<td>Possibly</td>
<td></td>
</tr>
<tr>
<td>FR</td>
<td>Article L.613-5(d) FIPC</td>
<td>Generic and innovator</td>
<td>Anywhere</td>
<td>Uncertain</td>
<td></td>
</tr>
<tr>
<td>IT</td>
<td>Art. 68(1)(b) Italian Code of IP</td>
<td>Generic and innovator</td>
<td>Anywhere</td>
<td>Uncertain</td>
<td></td>
</tr>
<tr>
<td>NL</td>
<td>Art. 53(4) Dutch Patent Act 1995</td>
<td>Generic</td>
<td>NL or EU only</td>
<td>Uncertain</td>
<td>Conor vs Angiotech</td>
</tr>
<tr>
<td>BE</td>
<td>Article XI.34(d) BCEL (referring to Article 6bis, §1 Belgian Medicinal Products Act)</td>
<td>Generic</td>
<td>BE or EU only</td>
<td>Uncertain</td>
<td>Henogen v Theravectys (not published)</td>
</tr>
</tbody>
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Other countries with broad implementation: DK, EE, FI, IS, LT, LV, MT, NO

Other countries with narrow implementation: CY, GR, IE, LU, SE
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<td>AT</td>
<td>Section 22 (1) Patent Act 1970</td>
<td>Generic</td>
<td>Anywhere</td>
<td>Possibly</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td>BG</td>
<td>Article 33 MPHMA</td>
<td>Generic and innovator</td>
<td>BG or EU/EEA only</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td>CH</td>
<td>Article 9(1)(b) and (c) SFAP</td>
<td>Generic and innovator</td>
<td>Anywhere</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td>CZ</td>
<td>Act No. 527/1990 (the &quot;Patents Act&quot;) and Act No. 378/2007 (the &quot;Pharmaceuticals Act&quot;). Generic and innovator (??)</td>
<td>CZ only</td>
<td>Possibly</td>
<td>Not yet litigated</td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>Art 98 (1) (2) the Patent Act</td>
<td>Generic and innovator (??)</td>
<td>Anywhere (??)</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td>HU</td>
<td>Art. 19 The Patent Act 2002</td>
<td>Generic and innovator (??)</td>
<td>Anywhere (??)</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
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# National implementations of Bolar exemption provided by EU Directive 2001/83/EC

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<td>PL</td>
<td>Act of 30 June 2000 – Industrial Property Law</td>
<td>Generic</td>
<td>Anywhere</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>PT</td>
<td>Article 19, No. 8 of the Medicines Act</td>
<td>Generic</td>
<td>Unclear</td>
<td>Uncertain</td>
<td>Extensively litigated</td>
</tr>
<tr>
<td>RO</td>
<td>Article 708(6) of the Health Law</td>
<td>Generic and innovator*</td>
<td>BG or EU/EEA only</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td>RS</td>
<td>Article 21 of the Serbian Law on Patents</td>
<td>Generic and innovator</td>
<td>Anywhere</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td>SI</td>
<td>Art. 45 Paragraph 9 Medicinal Product Act</td>
<td>Generic and innovator</td>
<td>SI or EU/EEA only</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
<tr>
<td>SK</td>
<td>Article 49 of Act No. 362/2011 Coll. on Medicines and Medical Devices</td>
<td>Generic and innovator</td>
<td>SK and EU/EEA etc.</td>
<td>Uncertain</td>
<td>Not yet litigated</td>
</tr>
</tbody>
</table>

* Experimental use exemption extends to innovator medicinal products.
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UPC

The UPCA has both Research and Bolar exemption codified in Art. 27

The rights conferred by a patent shall not extend to any of the following:

…

(b) acts done for experimental purposes relating to the subject matter of the patented invention; … [→ Research Exemption]

…

(d) the acts allowed pursuant to Article 13(6) of Directive 2001/82/EC* [veterinary medicinal products] or Article 10(6) of Directive 2001/83/EC* [medicinal products for human use] in respect of any patent covering the product within the meaning of either of those Directives; …

*including any subsequent amendments

Article 10(6) of Directive 2001/83/EC:

“Conducting the necessary studies and trials with a view to the application of paragraphs 1, 2, 3 and 4 [generics, hybrids, biosimilars] and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products.”

Scope:

- Bolar exemption only for the purpose of abridged application procedures for marketing authorizations according to Art. 10 (1)-(4) of Dir. 2001/83/EC
- Research exemption may cover (early?) clinical trials with innovative medicinal products – case law to clarify limits of this exemption; similar to DE case law?
- Bolar exempted applications must be for obtaining marketing approval in the EU
- Bolar exemption applies to SPC-protected products (Art. 30 UPCA)
Extending the Bolar Exemption and Research Exemption to third Parties

Development dependent on third party services, e.g., contract manufacturing by CMOs, testing by CROs

Dependent on national law, overall situation unclear, hardly any case law

DE: OLG Düsseldorf in a case 2 U 68/12, 2013 (Polpharma vs. Astellas)

- Polpharma manufactured (and advertised) a drug for a different party conducting experiments and studies under the Research and Bolar Exemptions
- 1st instance had issued prelim. injunction as not falling under research and Bolar exemptions;
- OLG Düsseldorf lifted injunction: whereas experiments and studies carried out do not fall within the research exemption, they may fall under Bolar exemption; the 1st instance did not distinguish between Research and Bolar exemptions, and did not elute on why a third party manufacturer should be treated differently
- Referral to ECJ: whether/under which conditions third-party supplier covered by exemption, but did not decide since the case was settled

From considerations of the court:

- A CMO manufacturing and delivering a drug to a party, whose activities fall under Bolar exemption, should also fall under it in case it is ensured that receiving party will act only within exemption
- Could be ensured by contract clauses, or be indicators such as business model of receiver, amount of drug to be delivered, expiry of patent/development plan
- Contractual precaution could be: use limitation with adequate penalties in case of breach to minimize the risk that receiving party acts outside of the exemption

OR

- Include manufacturer into development risk, e.g., milestone payments depending on development progress
Interplay between SPC waiver and Bolar exemption

SPC manufacturing waiver: further exemption permitting

- manufacture of **generics** and **biosimilars** (and related activities) in the EU to allow for **exporting goods to territories outside of the EU** (i.e., where there is no patent or SPC protection) and
- stockpiling products for launch in the EU for last 6 months prior to expiry of SPC for launch at day 1
- requires series of notifications, due diligence and labelling

→ **Covering real commercial activities**

Ineffective/insufficient to allow for launch at day 1?

- **six-month** exemption period for biosimilars and complex products appears to be insufficient - 9-12 months would be a more realistic period
- **reimbursement procedures** that need to take place ahead of a launch are not permitted under either the waiver or the Bolar exemption
- waiver does not extend to **intra-EU transportation**, which delays distribution ahead of or in time for a Day 1 launch
- Uncertainty about third party manufacturers and service providers
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Reform of the EU pharmaceutical legislation


- **Art. 85** of proposal aims to extend/clarify the scope of the Bolar exemption to include:
  
  a. studies, trials and other activities conducted to generate data for an application, for:
     
     i. a marketing authorisation of **generic, biosimilar, hybrid or bio-hybrid medicinal products and for subsequent variations**
     
     ii. **health technology assessment** as defined in Regulation (EU) 2021/2282 [health-economic approval]
     
     iii. **Pricing** and reimbursement.
  
  b. the activities … (a) … may cover the **submission of the application for a marketing authorisation** and the offer, manufacture, sale, supply, storage, import, use and purchase of patented medicinal products or processes, **including by third party suppliers and service providers**.

- ‘hybrid’/‘bio-hybrid’: similar as generic/biosimilar but with different strength, indication or pharm. form

**Commissions proposal**

- clarifies that activities relating to health technology assessments, and pricing and reimbursement are exempted (“waiver criticism”)
- includes third party suppliers (CMOs) and service providers (CROs)
- Likely includes test batches
- Leaves open: marketing authorization in the EU or anywhere?
- All limited to generics and biosimilars, i.e., **innovative medicinal products appear to be excluded from Bolar exemption**
Reform of the EU pharmaceutical legislation

But – are/will innovative medicinal products be covered under the research exemption? Dependent on national law/UPC

- **BE** recently amended research exemption to “all acts carried out for the evaluation of medicinal products”
- **UK** in 2014: anything carried out in or for the purpose of a “medicinal product assessment”
- **DE**: FCJ Clinical Trials I (1995) & II (1997) clarifying applicability of the research exemption to clinical trials on the subject matter, but likely excluding (established) research tools
- **UPC**: “acts done for experimental purposes relating to the subject matter of the patented invention” – scope to be clarified by case law

How far in the clinical development to marketing approval are activities covered by the research exemption?

Where are research tools included in the research exemption, *i.e.*, biomarker analysis during clinical development?

- First UPC preliminary injunction granted in 10x Genomics vs. NanoString (ACT568963/2023) preventing NanoString from selling or providing services;
  details not known yet, *i.e.*, whether NanoString tried to rely on services in the context of clinical development/Bolar exemption
- With increased focus on targeted drugs and patient stratification: dominating research tool patents may become more relevant for clinical development strategies
THANK YOU

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Case Studies
Scenario 1

- X produces Y’s drug (for example, an antibody or chemical entity) using information taken from a patent held by Y.

- X then uses Y’s drug as comparator with X’s product candidate.
Scenario 2

- X uses a compound patented by Y as a reagent in an assay that is used in the clinical development of a new drug.

- Alternative 1: X engages a third party to do the assay.

- Bonus: Does it make a difference where X or the 3rd party conduct their activities?