

Crop protection: Generics, Patents and Parallel trade Summit

Time for a Bolar-Type exemption to Patent Infringement in the Agrochemical industry?

Kristof Roox
Crowell & Moring (Brussels)
kroox@crowell.com

I. Regulatory approval vs. patent infringement

Background

- Successful products (chemicals, agrochemicals, pharmaceuticals, etc.) are protected by a patent portfolio
- Generic competition is only possible if a product is off patent (as a result of successful invalidity proceedings or the expiry of the patent/SPC)
- However, generic market entry requires a marketing authorisation
- A lot of acts (development, testing, etc.) have to be performed prior to patent expiry to obtain such regulatory approval
- Does this constitute a patent infringement?

II. Experience from the pharmaceutical sector

- Obtaining a MA for a generic medicinal product entails (bio-equivalence) studies and testing, and thus the use of a medicinal reference product for regulatory purposes;
- Development and testing is done before patent expiry to be able to market immediately upon patent expiry. Does this constitute a patent infringement?
- Until recently, pre-patent- expiry development and testing was not regulated at EU level
- National courts in different Member States applied their own national rules to determine whether these preparatory acts amount to a patent infringement : application of the so-called “research exemption” or “experimental use exception”
- Solution: the Bolar-exemption

II.1 The research exemption in the US

Overview of US experimental use exemptions

- Common law

- *Whittemore v. Cutter* [1813]:

- “*It could never have been the intention of the legislature to punish a man who [dealt with the patented invention] for philosophical experiments, or for the purpose of ascertaining the sufficiency of the [invention] to produce its described effect*”

- *Roche Products v Bolar Pharmaceutical* [1984] (narrow interpretation):

- Studies on a patented pharmaceutical a few months prior to patent expiry for the purposes obtaining regulatory approval was not experimental use under the *Whittemore v. Cutter* exemption. Bolar’s activities were regarded as solely for business reasons and not for “*amusement, to satisfy idle curiosity or for strictly philosophical inquiry*”

Overview of US experimental use exemptions

- Statutory exemption
 - Hatch-Waxman Act 1984
 - *Bolar exemption* : 35 U.S.C. § 271(e)(1) : limited industry specific experimental use exemption for testing drugs and medical devices for purposes reasonably related to regulatory data gathering . Exempted acts:

“make, use, offer, or sell within the US or import into the US a patented invention solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs, (...)”
 - Ambiguous language, resulting in disputes such as Merck v. Integra Lifesciences

The research exemption in the US

Merck v. Integra Lifesciences (2005)

- Issue
 - Whether uses of patented inventions in preclinical research, the results of which are not ultimately included in a submission to the Food and Drug Administration (FDA), are exempted from infringement by 35 U. S. C. §271(e)(1).
 - Could the Bolar exemption apply to the upstream development and identification of new drugs that will in turn be subject to FDA approval? (Experiments → approval v Experiments → drug → approval)

Merck v. Integra Lifesciences (2005)

- Decision of the Supreme Court
 - Broad interpretation of the research exemption
 - Preclinical studies of patented compounds may be exempted from patent infringement under 35 U.S.C. § 271(e)(1)
 - * Exemption requires a reasonable basis to believe that the studies will produce information relevant to an application to be filed with the FDA.
 - * It does not cover other research or research outside the industry sector
 - Pharmaceutical companies now have more freedom to research and experiment with patented compounds

The research exemption in the US

Merck v. Integra Lifesciences (2005)

- **Phase of Research Irrelevant:** “[T]here is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included.”
- **Identified Pharmaceutical Candidate Not Required:** The exemption is not limited to situations in which a pharmaceutical candidate has already been identified and is being tested in order to obtain FDA approval. It also applies to developing such candidate.
- **Application Need Not Be Filed:** Because “*scientific testing is a process of trial and error*”, the exemption extends to research for which a new drug application is not ultimately filed.
- **No Exemption Where Reasonable Belief Lacking:** Basic scientific research on a particular compound, performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce, is surely not reasonably related to the development and submission of information to the FDA.

II.2 Research Exemptions in Europe

Traditional exemptions in (national) patent law

- e.g. research exemption for experimental purposes relating to the subject matter of the invention
- Inspired by the Community Patent Convention
- No clear and consistent legal application of ‘experimental use’ provisions:
 - * UK : *Monsanto v Stauffer* [1985] (case regarding agrochemicals)

In this case Stauffer carried out field trials of a variant of Monsanto's patented herbicide in order to obtain data for regulatory approval. The court ruled that "trials carried out in order to discover something unknown or to test a hypothesis or even in order to find out whether something which is known to work in specific conditions [...] will work in different conditions can fairly be regarded as experiments, but trials carried out in order to demonstrate to a third party that a product works or, in order to amass information to satisfy a third party, whether a customer or a regulatory body, that the product works as its maker claims are not [...] to be regarded as acts done for 'experimental purposes'" ([1985] RPC, 542). Consequently, Stauffer's field trials were found to be outside the experimental use exemption.

II.2 Research Exemptions in Europe

Traditional exemptions in (national) patent law

- * Germany : *Clinical Trials I and II*
- * France : *Wellcome v Paraxel; Parienti v Peugeot ; AJC Pharma Expanpharm v Servier*
- * Italy : statutory provision ; *Squibb & Sons v Testaguzza*
- * The Netherlands : *ICI v Medicopharma ; ARS v Organon*
- * Belgium:
 - Clinical trials : *Fabricom v ABB* , legal doctrine
 - Filing of samples (Brussel 10 November 2000 – *fluoxetine*)
 - Filing of a request for a MA (diverging views : Rb. Brussel 1 april 2003 – *paroxetine* and Rb. Brussel 13 mei 2005 - *clarithromycine*)

Research exemptions in Europe

Traditional exemptions in (national) patent law

* Belgium:

- Transposition of the Biotech Directive resulted in a very broad research exemption: *“The exclusive rights deriving from a patent do not extend to acts **on and/or with** the patented invention for scientific purpose”* (Article 28 Belgian Patent act)

1. *“with”*: e.g. protein is used as an instrument for research which aims at developing a medicinal product.
2. Interpretation in Parliament : the research exemption should not only cover activities which are carried out on a purely scientific basis, without any commercial affinity, but can cover mixed activities, with both a purely scientific and commercial goal, provided that such activities have a certain goal, which is to "collect further knowledge"

II.3 The European Bolar exemption

Patent infringement exemptions in pharmaceutical law: Article 10(6) Directive 2001/83:

- *“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 as or supplementary protection certificates for medicinal productst”*
- European “Bolar”-provision
- General and ambiguous wording – Scope of Bolar-provision
- * *Studies and trials?* Type of studies and trials have been discussed but no list has been agreed upon at EU level

The European Bolar exemption

- * *with a view to the application of paragraphs 1, 2, 3 and 4*
 - Generic abridged applications (10.1/10.2), hybrid applications (10.3) and biosimilar applications (10.4). Not for bibliographical applications or applications for new combinations.
 - Limitation to applications in the European Union
 - no exemption for all activities: e.g. use of trial information or production in Europe in support of applications outside the EU ; acts done for export (rejected by the European Commission) ; production for trials in support of applications outside the EU;
 - Not applicable to experiments with the aim of proving product yield or a new variant of the patented product?
 - What if the application for a MA fails?
- * “*and the consequential practical requirements*” (application for a MA, filing, samples, P&R, production of commercial batches, stockpiling, publications and marketing, taking pre-orders, etc.)
- * more narrow than US provision (not for developing new drugs)

The European Bolar exemption

Implementation in national legislation

- UK : implemented (17 October 2005)
- * Amendment of section 60(5) of the Patents Acts 1977: *An act which, apart from this subsection, would constitute an infringement of a patent for an invention shall not do so if (...) it consists of:*
 - (i) an act done in conducting a study, test or trial which is necessary for and conducted with a view to the application of paragraphs 1 to 5 of Article 13 of Directive 2001/82/EC or paragraphs 1 to 5 of Article 10 of Directive 2001/83/EC, or*
 - (ii) any other act which is required for the purpose of the application of those paragraphs”*
- * Literal transposition (incorporation by reference)
- * MHRA consulting document with view on how the exemption should be construed

The European Bolar exemption

Implementation in national legislation

– Belgium : implemented (May 1, 2006):

* Article 6bis, §1 Medicines Act

Het uitvoeren van de noodzakelijke studies, testen en proeven met het oog op het voldoen aan de voorwaarden en de modaliteiten bedoeld in de leden 1 tot en met 7 van deze paragraaf en alle daaruit voortvloeiende praktische vereisten worden niet beschouwd als een inbreuk op octrooien of aanvullende beschermingscertificaten (...)

* “Studies, testen en proeven” v. “studies and trials”

* Almost literal transposition (subtle differences)

* Pres. Brussel 21/06/2006 (Filing applications for pricing and reimbursement falls within the scope of the Bolar-exemption)

The European Bolar exemption

Implementation in national legislation

- The Netherlands : no implementation yet
- * Proposal for a literal implementation into the Medicines Act (Geneesmiddelenwet article 42, § 10) : *“Het uitvoeren van de noodzakelijke studies, tests en proeven met het oog op het toepassen van het vijfde lid onder a, zesde en zevende lid, alsmede van de daaruit voortvloeiende praktische vereisten, worden niet beschouwd als een inbreuk op octrooien of aanvullende beschermingscertificaten”*
- * Literal transposition

The European Bolar exemption

Implementation in national legislation

- Germany : implemented and in force as from September 6, 2005
 - * Article 3 of the Drug Act adding a new paragraph 2b to section 11 of the German patent act:
 - “The effect of a patent shall not extend to (...)*
 - 2. Acts done for experimental purposes relating to the subject matter of the patented invention (...)*
 - 2b. Studies and trials and the consequential practical requirements necessary for obtaining an authorisation according to the Drug Law for the marketing in the European Union or an authorisation according to the Drug Law for the marketing in the Member States of the European Union or in third countries”*
 - * Broad implementation : not limited to generics and not to the European Union !

The European Bolar exemption

Implementation in national legislation

- Italy : implemented (4 March 2005)
- * Amendment of the new Industrial Property Code (art. 68 (1) a):
'Whatever the subject of the invention is, the exclusive right granted by the patent does not extend to:
 - a) *acts performed privately and for non-commercial purposes, or for experimental purposes even if aimed at obtaining, in any country, an authorization to market a finished dosage form and at accomplishing the consequential practical requirements, including the preparation and the use of the active pharmaceutical ingredients which are strictly necessary*
- * Not limited to generics, nor to the European Union.

The European Bolar exemption

Implementation in national legislation

- France : no implementation yet
- * Proposal to amend Article L.613.5 CPI (IP Code) by introducing a new paragraph d): *“The rights afforded by a patent shall not extend to:*
 - (b) acts done for experimental purposes relating to the subject matter of the patented invention;*
 - (d) the studies and trials necessary in order to obtain a marketing authorisation for a medicinal product in any Member State of the European Community or any Member State of the European Economic Area, as well as any acts necessary for their performance”*
- * Broad implementation : Not limited to generic applications, not limited to EU (also EEA)
- * Proposal to amend article L.5121 of Public Health Code (CSP)

The European Bolar exemption

Implementation in national legislation

- Spain : Implemented in Article 52 (b) Patents Act (26/07/2006):
 - * *Rights conferred by the patent do not cover (...): b) actions for experimental purposes in relation to the objective of the patented invention; particularly studies and trials carried out for the authorization of generic medicines and the consequential practical requirements, including the preparation, obtaining and use of the active ingredient for these purposes”*
 - * Not limited to the European Union ; some guidance regarding “consequential practical requirements” (limited view)
 - * Provincial Court Madrid 5 May 2006: *“preparation of samples, performance of bioequivalence studies and filing of authorisation applications, etc. by an applicant for generic medication, before the expiry of the patent, cannot be considered infringement of it. Furthermore, procedures carried out with the Ministry of Health to include a generic pharmaceutical product in the National Health System would also not infringe the patent”*

The European Bolar exemption

Conclusions:

- Some degree of certainty by introducing a Bolar-clause : Europe is a safe harbour where testing can be done
- Again too late and too limited in view of US developments (also applicable for development of new drugs)
- Ambiguous wording and different transposition in national law : ECJ-ruling necessary?
- Continued forum shopping (studies and trials in jurisdiction with the broadest exemption)
- Lawyers paradise!

III. A Bolar-exemption for the Agrochemical Industry?

Is there a need for a Bolar-type exemption in the Agrochemical industry?

- Similar markets and economical principles
- Similar regulatory framework (Directive 91/414/EC vs. 2001/83/EC as amended by Directive 2004/27) :
 - prior regulatory approval before marketing;
 - pharmaceutical, pre-clinical and clinical trials vs. studies on efficiency, physical-chemical properties, toxicology, environmental impact, ecotoxicology, analytical methods, residues, etc.
 - mutual recognition
 - data exclusivity regime (article 10 Directive 2001/83 vs. article 13 Directive 91/414)

III. A Bolar-exemption for the Agrochemical Industry?

Is there a need for a Bolar-type exemption in the Agrochemical industry?

- Same question : can field trials, toxicology tests, studies regarding identity and impurities of generic active substances, etc. be performed when an active substance is still protected by a patent or SPC?
- No Bolar-exemption for agrochemicals
- Application of national research exemption will lead to divergent judgments and legal uncertainty