A New Scenario for Infringement of Second Medical Use Patents: Are Generics Liable when They Participate in Discount Contract Tenders?

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Recent decisions in the Netherlands, the UK, Denmark and Germany have shed light on the enforcement of second medical use patents.[1] One issue considered by the courts in their infringement analysis was the regulatory reimbursement practice of public health insurance companies under the different national laws. Courts in the Netherlands and Germany now held generics liable for indirect infringement of second medical use claims because they had participated in public tenders of health insurance companies, even though they had carved out the patented indications under a so-called "skinny label".[2] The ruling of the German court is of particular interest as it deviates from a (criticized but widely accepted) ruling of another German court which had *de facto* denied indirect infringement in case of second medical use claims.[3] This article focuses on the German perspective and outlines the new liability generics potentially face in particular in Germany, but potentially also in other jurisdictions that may take this approach as a guideline for developing their case law.[4]

1. Background

In cases where no patent for the compound or any first medical use exists or has already expired, second medical use patents provide for protection of a new (second) medical use of the compound, i.e. normally a new indication for treatment. The protection of such invention is problematic under the European Patent Convention (EPC) because (i) protection over the compound cannot be granted since it is already know and thus lacks novelty and (ii) the EPC prohibits patent methods of treatment of human by therapy[5]. The EPO initially established the practice of granting second medical use claims in the form of "Swiss-type" claims, i.e. "use of compound X for the manufacture of a pharmaceutical compound for the new therapeutic application Y".[6] The EPC has since been amended to allow purpose limited product claims also for the second (and further) medical use which are referred to as "EPC 2000 claims".[7] While these EPC 2000 claims replaced Swiss type claims which will no longer be granted,[8] there are still many years where Swiss-type claims will exist for infringement considerations. For national German patent, a "German-type" claim for the second medical use claim had been endorsed which claims the "use of compound X for the new therapeutic application Y".

Cross-label use of drugs comes into play when generic companies market their generic drug under a "skinny label" on which the patented indication is explicitly carved out.[9] Then, patent infringement is discussed when the generics undertake additional advertising activities for promoting the product also for the patented (but off-label) indication.

Apart from advertising, the turnover with generic drugs is also highly influenced by discount contracts between public health funds and generic companies. German law encourages negotiating such discount contracts for drugs.[10] Importantly, pharmacies are even legally obliged to *substitute* a drug or active substance prescribed by physicians with one of the drugs listed in a discount contract of the respective public health fund.[11] Pharmacists use special software enabling them to correctly comply with all rebate contracts. The substitution applies as long as the discounted drug and the original drug *overlap in at least one* indication for which a marketing authorization exists.[12] That means substitution of the originator drug against the discounted generic takes place for all indications, not only the indication where the databases show an overlap. This regulatory system of rebate contracts and mandatory substitution gives generics a backdoor for marketing their drugs for

1 Warner-Lambert Company, LLC v. Actavis Group PTC EHF, UK Court of Appeal, 2015 EWCA Civ 556; Novartis AG v. Sun Pharmaceutical Industry (Europe) B.V., The Hague Court of Appeal, 27 January 2015, Case No. 200.1 50.713/01; Maritime und Commercial Court Copenhagen, Judgement of 26 June 2015, Case no. A-6-15; Warner Lambert LLC v. Hexal AG et al., District Court of Hamburg, 2 April 2015, Case Nos. 327 O 67/15 (Hexal), 327 O 143/15 (1A Pharma), 315 O 24/15 (Ratiopharm), 327 O 132/15 (Glenmark) and 327 O 140/15 (Aliud Pharma).

2 Novartis AG v. Sun Pharmaceutical Industry (Europe) B.V., The Hague Court of Appeal, 27 January 2015, Case No. 200.1 50.713/01; Warner Lambert LLC v. Hexal AG et al., District Court of Hamburg, 2 April 2015, Case Nos. 327 O 67/15 (Hexal), 327 O 143/15 (1A Pharma), 315 O 24/15 (Ratiopharm), 327 O 132/15 (Glenmark) and 327 O 140/15 (Aliud Pharma).

3 District Court of Düsseldorf, 24 February 2004, Case No. 4a O 12/03, GRUR-RR 2004, 193 (196) – Ribavarin; District Court of Düsseldorf, 19 April 2011, Case No. 4a O 236/09.

4 In the US, for instance, the Hatch-Waxman Act provides generics with the possibility to carve out indications in the label to be approved by the FDA for which no approval is sought. Cf. 21 U.S.C. § 355(j)(2)(A)(viii). State law often requires that the cheapest product has to be handed out by pharmacies. The US Court of Appeals for the District of Columbia has confirmed this regulation, even though the court acknowledged that this law interferes with the interest of protecting the manufacturer of a pioneer drug. Bristol-Mayers Squibb Co. v. Shalala, 91 F.3d 1493 (D.C. Cir. 1986).

5 Art. 52 (4) EPC 1973; EPO Enlarged Board of Appeal, G 5/83.

6 The name "Swiss-type" goes back to the practice of the Swiss Patent Office which was later endorsed by the EPO.

7 Art. 54 (5) EPC 2000.

8 EPO Enlarged Board of Appeal, G 2/08.

9 Sec. 11a(1e) German Medicinal Products Act.

10 Sec. 130a (8) German Code of Social Law V.

11 Sec. 129 (1) sentences 1-3 German Code of Social Law V.

12 Sec. 129 (1) sentence 2 German Code of Social Law V.

the patented indication. Depending on the protected indication, this may significantly impact the turnover of both generics and originators.

2. German Law Prior to the "Lyrica" Case

Second medical use claims, *i.e.* Swiss-type and German type claims, are classified as method claims under German law, even though there has been tendency to regard them as a separate category of product claims.[13] When it comes to the question of infringement, however, courts leave this strict classification and treat them *de facto* as product claims with the limitation to the claimed use (*i.e.* the patented indication). Courts shift the acts relevant for infringement considerations to an earlier point in time, *i.e.* prior to the sale of the drugs by pharmacies.[14]

2.1 Direct Infringement

According to established case law, a drug manufacturer can be held liable for direct patent infringement if it produces and sells its generic drug with label instructions describing the patented use. Such instructions are typically laid out in the package leaflet. Under German law adding such label constitutes a so-called "manifested arrangement" (*sinnfällige Herrichtung*).[15] The reasoning for considering this as an infringing act is that the manufacturer has fulfilled all relevant acts for patent infringement by labeling the drug for the patented medical use. The final infringing act performed by the patient will occur more or less automatically, as the patient will follow the label instructions. According to the case law, the "manifested arrangement" for the claimed use can also happen in other ways, for instance, by confectioning, ready to use preparation or dosage of the drug.

If there are no label instructions but only separate advertising acts which promote the drug for the patented use in marketing materials, flyers and statements by sales people, it becomes more difficult for the patentee. In these scenarios, courts have been reluctant to find for direct patent infringement.[16] The advertisement measures have been regarded as insufficient to be a manifested arrangement of the drug for the patented use. The courts stated that it were uncertain whether the recipient of the marketing material would take notice of the advertised second medical use and thus, it were similarly uncertain whether infringement will actually take place.

13 Cf. Federal Supreme Court, 2005 GRUR 135 – Arzneimittelgebrauchsmuser; Bopp, in: Festschrift for Reimann, p. 13 (16); Kaess, in: Festschrift for v. Meibom, p. 191.
14 Federal Supreme Court, 1992 GRUR 305 – Heliumeinspeisung; Federal Supreme Court, 1990 GRUR 505 – geschlitzte Abdeckfolie.
15 Most recently Düsseldorf Court of Appeal, 7 August 2014, Case No. 2 U 8/14; Federal Supreme Court, 1983 GRUR 729 – Hydropyridin; Federal Supreme Court, 1977 GRUR 652 – Benzolsulfonylharnstoff); Hufnagel, 2014 GRUR 123 (125); Königer, Kompter, Ludwig, Lunze, Prinz zu Waldeck und Pyrmont, Schüssler, Wiegeleben, in: 2014 GRUR Int. 906 and Question 238 of AIPPI.
16 Most recently Düsseldorf Court of Appeal, 7 August 2014, Case No. 2 U 8/14; Düsseldorf Court of Appeal, 31 January 2013, Case No. 2 U 54/11 – Cistus Incanus.

Courts have not yet decided whether and how these principles apply to EPC 2000 claims which are not method but purpose-limited product claims. Given their character as product claims, a less concrete relation between the product and the intended purpose might be regarded as sufficient which could mean a different outcome regarding advertising acts. The German Federal Supreme Court, however, does not seem to distinguish between the different kinds of claim language as indicated in a decision related to patentability of a purpose-limited product claim.[17]

2.2 Indirect Infringement

Indirect infringement requires that the drug manufacturer must have known or it must have been obvious from the circumstances that the drug is (i) suitable and (ii) intended to be used for the patented second medical use. Given that the production of the drug as such is in the public domain because there is no longer patent protection for the compound or the first medical use and the patented use is not indicated in the label instructions, this subjective requirement is different to establish in practice. A mere potential cross-label use of the drug for patented indications is normally not sufficient. Rather, infringement considerations depend on the facts of the case and the evidence the patentee can present (e.g. information material provided to physicians, statements by sales persons on the cross-label use, increased amount of prescriptions and sales, etc.).

Apart from this subjective requirement, the question of liability of the drug manufacturer for indirect patent infringement depends on whether the seized court would follow the Düsseldorf "Ribavirin" decision.[18] The Ribavirin case-law says that only the offer or supply of a compound *for the purpose of being prepared for* the patented purpose may constitute indirect infringement. According to this decision, the supply of the drug *for immediate use* could not be considered as indirect infringement. In a later decision, the Düsseldorf Court of Appeal explicitly left open whether it might consider indirect infringement in such scenarios and thereby deviating from "Ribarvirin". Given some criticism in the literature, a change of the Düsseldorf case-law does not seem to be unlikely.[19]

3. The "Lyrica" Case

The recent German Lyrica cases so far been decided concern various preliminary injunction proceedings initiated by Warner Lambert against several generics.[20] The preliminary injunction proceedings have been decided and the

17 German Federal Supreme Court, 25 February 2014, Case No. X ZB 6/13 - Kollagenase II.
18 District Court of Düsseldorf, 24 February 2004, Case No. 4a O 12/03.
19 Haedicke, 2004 Mitt. 145 (147); Brandi-Dohrn, in: Festschrift for König, p. 33 (42).
20 *Warner Lambert LLC v. Hexal AG et al.*, District Court of Hamburg, 2 April 2015, Case Nos. 327 O 67/15 (Hexal), 327 O 143/15 (1A Pharma), 315 O 24/15 (Ratiopharm), 327 O 132/15 (Glenmark) and 327 O 140/15 (Aliud Pharma).

appeal is pending. The cases provide a typical procedural scenario for PI requests: Price erosion of the original product takes place due to the market entry of the generics and therefore the patentee has to fear that it cannot compensate its losses in the course of lengthy main proceedings. In addition, the validity of the patent at issue had been confirmed in an opposition before the EPO which is a further criterion supporting PI proceedings.

The patented indication was not mentioned in the package leaflet. In addition, the generics made use of the possibility to carve out the patented indications in the expert information which is directed to physicians and pharmacists. The German Medicinal Products Act provides generics explicitly with such option if patent law protection exists at the time of placing the drug on the market. Warner Lambert argued indirect infringement and attacked the generics for two behaviors: (1) participating in public tenders for discount contracts conducted by public health insurance companies without notifying the health insurance companies that the generics could not market their products for the patented indication and (2) notices in software for pharmacies and wholesalers without notifying them that the drug cannot be marketed for the patented indication.

The Hamburg court granted the preliminary injunction with regard to the participation in public tenders for rebate contracts. The court put emphasis on the fact that these tenders do not state the specific indication of the drug but only refer to the active substance (active pharmaceutical ingredient, API). Pharmacies handing over the drug to patients derive their information only from these rebate contracts, which similarly also only refer to the active substance. Neither the pharmacies nor the patients will consider patent infringement, and obviously do not even have the opportunity to do so. In fact, German public regulations even *mandatorily* require pharmacies to substitute a drug or active substance prescribed by physicians with one of the drugs listed in the discount contract of the individual public health fund. A substitution will take place as long as there is an overlap in one of the indications. The court concluded that taking part in these tenders without limiting the offer to the patent-free indications would constitute indirect infringement: An unlimited tender will result in an unlimited discount contract and thus in an unlimited entry in the database. Then, the pharmacies will more or less automatically sell the drug also for the patented indication.

The Hamburg court deviated from "Ribavirin" without providing detailed reasoning. Apparently, the Hamburg Court focuses on the already prepared drug and regards this as being sufficient for the manifested arrangement, at least when the generics participate in discount contracts at the same time. The Hamburg court rejected, however, Warner Lambert's request that the generics would have to give notice in software for pharmacies and wholesalers. The court reasoned that it had not been proven that the generics are responsible for the appearance in the pharmacy software.

4. Conclusion

The Hamburg court decision has established a new scenario for patent infringement by generics. It can be welcomed that the court has rejected the standard defense of generics that they could not be liable for indirect patent infringement due to the carve-out which in fact ignores the regulatory practice of substitution. Instead, generics need now to review their marketing activities towards public health funds.

By the same token, the court has established a new angle for pharmaceutical companies in reviewing potential liability of generics, namely by monitoring the bidding process of public health funds.

It also remains to be seen how the Hamburg Court of Appeal and the Düsseldorf courts will deal with this new approach. The first instance Hamburg court has applied a deliberate analysis of the practice of discount contracts by taking a self-confident decision which may lead to increased liabilities of generics for the use of the public reimbursement system. This may also have implications on other areas, namely the public bidding process and the procedure of tendering discount contracts. Parallel to the Hamburg court decision a regulatory decision of the Procurement Chamber of the Federal Cartel Office has been issued which emphasized that patent law is not preempted by regulatory law.[21] Instead, public health funds have to ensure that their tender process complies with patent law.

21 German Federal Cartel Office, 16 March 2015, Case No. VK 2-7/15.