The Enforceability of Medical Use Claims in Germany

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Introduction

In an increasingly competitive pharmaceutical sector and in view of exploding medical prior art, obtaining broad product protection for medications is becoming increasingly difficult. Especially in highly competitive fields (e.g. recombinant antibody technology), in which patent protection for a biotechnological product class defined by function is in many cases no longer an option, applicants are often forced to restrict product claims to specific nucleotide and/or amino acid sequences corresponding to a particular single product of interest.

In this environment, second medical use ("Swiss-type") claims are becoming an increasingly important way of securing broad patent protection. Indeed, as the biopharmaceutical market matures and increasing numbers of potential biological medications enter clinical testing for specific indications, second medical use claims often represent an attractive option for obtaining commercially relevant patent protection of reasonable scope. Securing this patent protection is crucial for companies in attracting partnerships and investors needed to defray the substantial costs incurred in the course of clinical testing.

While the European Patent Convention ("EPC") provides a single legal framework for the central examination and grant of European patents, the EPC expressly leaves matters of infringement to the EPC member states. Despite the growing importance of second medical use claims in Europe, patentees and (potential) licensees are thus faced with the vexing situation that second medical use claims obtained before the European Patent Office ("EPO") may not be enforceable in the same way in different EPC member states.

The present article examines the enforceability of second medical use claims of European patents validated in Germany or German national patents before German courts. In view of recent developments in case law concerning the admissibility of second medical use claims before the EPO, special attention will be given to the enforceability of medical use claims in Germany where these medical use claims include features relating to treatment regimens and/or specific modes of administration.

Form of second medical use claims allowable before the EPO

In the landmark decision G5/83, the Enlarged Board of Appeal of the EPO held that a medical use claim of the form "*Use of compound X for treating disease Y*" contravenes the patentability exclusion for methods of treatment as laid out in Article 52(4) EPC. At the same time, the Board held that such a medical use claim may allowably be expressed in "Swiss-type" format (*"Use of a compound X for preparation of a medicament for treating of disease Y"*) without contravening Article 52(4) EPC. Since the rendering of G5/83, the Swiss-type claim has been a mainstay of biotechnological, pharmaceutical and medicinal claims and has become an invaluable tool by which methods of treatment may be protected in Europe.

For years, consistent case law of the Boards of Appeal of the EPO held that patentability of second medical use claims derived from a novel and inventive technical effect of a known product. This known product may have already been

used in the prior art to treat a disease other than Y, or may even have been used to treat disease Y, but by a different mode of administration or for a different patient group. What was not accepted by the Examining Divisions of the EPO as a feature for establishing the novelty of a second medical use claim was a particular timing of administration of the active agent. This was regarded as a feature excluded under Art. 52(4) EPC and, hence, was not seen as admissible for delimiting a second medical use claim against the prior art.

In late 2005, Technical Board of Appeal 3.3.4 expressly departed from this practice, holding in decision T1020/03 that:

> *"Any use to which Article 52(4) EPC first sentence applies in circumstances where the composition has already been suggested for some therapeutic use, allows a second medical use claim to the preparation of the composition for that second medical use,* ***irrespective of in what detail that use was specified****"* (emphasis added).

The case before the Board concerned the patentability of second medical use claims including a specific administration scheme entailing intermittent administration cycles. The Examining Division had refused the application in the first instance due to what they viewed as features in the claim pertaining to activities which would be part of the typical activities of a doctor in curing, preventing or alleviating an illness. As such, so the Examining Division, the claim comprised subject matter falling within the non-commercial and non-industrial medical activities excluded from patentability under Article 52(4) EPC.

In the course of a lengthy review of past decisions allegedly supporting the view of the Examining Division, the Board came to the conclusion that there is

> ***"…*** *no reason why the person who develops a novel therapy by looking for the most effective way in which a known composition can be administered should a priori be said to lack merit to such an extent that even the limited form of patent protection of the second medical use form can be denied without an examination of whether the therapy is indeed novel and inventive."*

Taken together in light of the facts of the case, T1020/03 makes clear that the patentability of a second medical use claim may be based not only on a new feature such as a new disease, a new mode of administration, a new patient group or a new dosing, but also on a new timing of administration of the active agent.

Form of medical use claims allowable before the German Patent and Trademark Office (GPTO)

§5(2) of the German Patent Act ("PatG") contains a provision corresponding to Article 52(4) EPC. However, in contrast to the EPO's interpretation of Article 52(4) EPC, the German Federal Supreme Court ("BGH") held in its 1983 decision *Hydropyridin* ("Hydropyridine") that §5(2) PatG

> "*… does not exclude from patentability an invention entailing the use of a known substance for the treatment of a disease*" (author's translation).

As such, before the GPTO an allowable medical use claim may be formulated either as a direct medical use or as a Swiss-type claim; according to existing case law (*Trigonellin,* BGH, 2001) the scopes of claims formulated in these two ways are to be interpreted in more or less the same way.

In addition, in the 1996 decision *Knochenzellenpräparat* ("Bone cell preparation"), the Federal Patent Court ("BPatG") held that:

> *"The use of an active agent for the treatment of a disease is deemed to be industrially applicable even in the case that it consists entirely of a therapy plan and/or a dose recommendation. … In such a case, the requirements of the therapy plan and/or of the dose recommendation are to be considered for the assessment of novelty and inventive step."* (author's translation)

As a result, a new timing of administration of the active agent can also establish the novelty of a second medical use claim before the GPTO.

Enforcement of medical use claims in Germany

German national case law has repeatedly held that the scope of a medical use claim, regardless of whether this claim is formulated as a direct medical use or as a Swiss-type claim, includes both the medical use itself, as well as the preparatory work required to put the compound used into a form in which it may be administered for the claimed purpose. In this context, German case law has developed and maintained the concept of the "evident preparation" ("*sinnfällige Herrichtung*") in *i.a.* landmark decisions *Benzolsulfonylharnstoff* (1977; "phenyl sulfonyl urea"), *Sitosterylglykoside* (1982; "Sitosteryl glycosides"), *Hydropyridin* (1983; "Hydropyridine") and *geschlitzte Abdeckfolie* (1990; "slitted covering film").

The concept of the "evident preparation" is important for understanding the enforceability of medical use claims in Germany. In its 1977 decision *Benzolsulfonylharnstoff* the BGH held:

> *"The use of a substance for combating a disease, in which the medicinal benefit of the substance is exploited, does not take place only by the doctor's use or prescription of the medication, but also routinely includes a number of activities which do not, like the doctor's activities, exist outside the scope of commercial use, for instance the formulation and the confectioning of the medication, its dosage and its packaging in a form ready for use. All these medical activities are embraced by the filed use claim."* (author's translation)

The "evident preparation" denotes all forms of preparation of the substance used which, in contrast to the abstract intention to administer a particular compound for a particular purpose, may be perceived as such by any of the human senses. The evident preparation of an active agent for a claimed medical use may for example include: formulation, confectioning, dosing, packaging for use, written instructions for use of the medicament containing a particular compound, or, especially, a package insert containing information as to the intended medical indication, suitable dosing and/or timing of administration. The description of the package insert is especially important to a Plaintiff contemplating initiating a patent infringement suit, as the package insert will often be the only physical proof which the Plaintiff can provide to the court to demonstrate that the claimed use is infringed.

This interpretation of medical use claims in Germany effectively shifts the protection afforded by a medical use claim to a time point prior to the actual administration of a substance for the claimed use. As such, infringement of a medical use claim in Germany may already be found when a third party puts a medicine on the market which is accompanied by a product description referring to the features of the use claim.

For such a finding of infringement of a medical use claim, it is crucial that the Plaintiff proves that the *purpose* of the Defendant's allegedly infringing actions is to treat precisely the disease in precisely the same way as recited in the medical use claim in suit. As held in the 1987 BGH decision *Antivirusmittel*, it is not enough

that the Defendant's proposed use is merely *suitable* for the claimed purpose:

> *"A final element, namely a particular attainment of purpose, is inherent in "purpose-specific product protection", which makes up an essential component of the protected invention. If this purpose is neither striven for nor purposefully attained, but rather another purpose than that claimed is attained, then no use of the subject matter of the patent exists."* (author's translation).

In other words, in order for an action to be found infringing of a medical use claim, the Defendant must have realized the claimed use, which means that the purpose as taken from the package insert of the allegedly infringing product must be the same as the purpose recited in the claim.

The importance of establishing that the Defendant's purpose is identical with the purpose of the claim is illustrated in the 2004 *Ribavirin* decision rendered by the District Court of Düsseldorf. In the case before the court, the Plaintiff's claim covered the use of the antiviral drug ribavirin for preparation of a pharmaceutical composition for treatment of HCV infections. The claim in suit read as follows (with numbering indicating the individual features as discerned by the court):

1. The use of ribavirin for the manufacture of a pharmaceutical composition for treating a patient having chronic hepatitis C infection to eradicate detectable HCV-RNA;

2. by a method comprising administering an effective amount of ribavirin in association with an effective amount of interferon alpha;

3. for a time period of 40-50 weeks;

4. wherein the patient is one having failed to response to a previous course of interferon alpha therapy, characterized in that;

5. the patient has a viral load of greater than 2 million copies per ml of serum as measured by HCV-RNA quantitative PCR;

6. of a HCV genotype type 1 infection.

The Plaintiff's arguments were based in large part on a package insert of the Defendant, presented as proof of making use of the patentee's claim. However, this package insert specified ribavirin administration as part of a co-therapy regimen with alpha interferon (as required by the claim) merely as a *possible* administration. Based on the package insert, the court viewed that the primary mode of ribavirin administration envisioned was monotherapy in patients who have not responded to treatment with alpha interferon due to a contraindication or intolerance. Further, the court found that the package insert provided no specific reference to the patient groups defined in features 5 and 6 of the patent in suit (see above). In view of these findings, the court held that the claim in suit was in fact not infringed, even though

> "*… it cannot be excluded that with the help of the embodiment in suit patients belonging to the special subgroup described in the patent in suit are also treated*" (author's translation).

The court concluded:

> *"For the direct infringement of a patent conferring protection for the use of a pharmaceutical composition for the treatment of a patient with a particular infection … it is necessary that the pharmaceutical composition is not just generally offered and sold for patients with the particular infection, but also that the composition is evidently prepared for specifically those patients with the further infection-specific features."* (author's translation)

The *Ribavirin* decision illustrates how important it is for a Plaintiff to make a strong case based on the specific purpose recited in an asserted use claim. The burden of proof is a heavy one for the Plaintiff to discharge, since it is incumbent on him to convince the court not only that the claimed medical use is practiced by the Defendant, but also that the underlying purpose of this practice is congruent with the claim in suit.

Medical use claims are therefore enforceable in Germany. The Proprietor of such medical use claims is entitled to block activities in Germany directed to the evident preparation of an active agent for a claimed use, to block import of the evidently prepared agent from countries where no patent protection exists, and to block export of the evidently prepared agent from Germany to another country. This requires, however, that he is able to demonstrate that the purpose of the Defendant's actions is to treat the same patients or patient subgroups as claimed and in the same manner as claimed.

With regard to the enforceability of medical use claims which, in addition to an active agent and the indication to be treated, also include features relating to specific dosage regimens modes of administration and/or treatment regimens, such claims are likely to be interpreted by German courts by the same standards as claims lacking these features. This is because the enforceable scope of medical use claims has already been repeatedly and consistently interpreted at the highest level of German case law based on criteria entirely independent of such methodological features. It is therefore to be expected that the scope of medical use claims including dosage regimens, modes of administration or treatment regimens would likely include the effective shift of enforceable protection to the time point at which an evident preparation of an active agent is effected, *i.e.* prior to the actual administration of this agent.

The success of a Plaintiff in enforcing second medical use claims including treatment regimens is likely to depend in large part on his ability to prove that the claimed treatment regimens are not only possible under the treatment regimen suggested by the Defendant, but that this specific treatment regimen is specifically mentioned in the package insert.

Who can be sued for infringement of a medical use claim?

Any party producing, offering and/or selling the evidently prepared product for the claimed use may be sued for direct infringement (§9 PatG).

In Germany it is even possible, albeit uncommon, to sue a doctor for patent infringement, as discussed in the 1995 District Court of Hamburg decision *Patentverletzung durch ärztliche Verschreibung* ("Patent infringement by doctor's prescription"). That the activity of doctors may be restricted by patent protection was made clear in the earlier 1977 decision *Benzolsulfonylharnstoff*, in which the BGH stated that the restriction of a doctor's freedom of treatment and prescription by a medical use claim does not go beyond that which already exists for a product claim. The decision of the District Court of Hamburg went one step further, saying that the doctor's prescription of a medication is a commercial activity and, therefore, a doctor making a prescription falling within the scope of a patent claim infringes this patent directly. Although likely commercially uninteresting to sue a doctor personally for infringement of a medical use claim, it is – contrary to widespread belief – nevertheless possible. Of potential greater interest for the Patentee of a second medical use claim may be to sue, besides the manufacturer of the medicament, the clinic or hospital in which the medical use claim is demonstrably and repeatedly infringed.

In summary, both direct medical use claims (allowable before the GPTO) as well as Swiss-type medical use claims

(allowable before the GPTO and the EPO) are enforceable in Germany. According to consistent and developed case law, their enforceable scope includes the evident preparation of a substance and therefore shifts the effective time point of infringement to a time prior to the actual treatment of a patient. In enforcing a medical use claim in Germany, great care must be taken to prove that the purpose of the Defendant's putatively infringing activity corresponds to all features of the asserted medical use claim.