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Infringement of second medical use patents in Europe

How to claim a second medical use

The European Patent Convention (EPC) precludes methods for therapeutic treatment of the human body from patentability. The intention of the legislator was to not unduly bar physicians from actually doing their job in the very interest of public welfare. However, this preclusion from patentability does not apply to products like substances or compositions: These may well be patented. Even if a substance or composition is already known in the art a patent can still be granted for the first medical use thereof, broadly claimed e.g. as ***"substance x for use as a medicament."***

Already in the early days of the EPC it was realized that the consequences of this legal framework were nevertheless unsatisfactory. Once a single therapeutic use of a substance had been known in the art there was no way to protect any further medical uses of the very same substance: The substance as such was not novel anymore, not even its first medical use. On the other hand, a claim on the new method of treatment was precluded by law. This dilemma was resolved by the Enlarged Board of Appeal in 1984 with the decision G 5/83. It was held that a European patent may be granted with claims directed to the ***"use of substance x for the manufacture of a medicament for the treatment of disease y"*** (provided, of course, that this treatment is new and non-obvious). Novelty of such a claim is derived from the new pharmaceutical use. The wording is renowned as Swiss-type claims. The wording has always been somewhat awkward, its conformance with material law has frequently been questioned, and it meanwhile is a relic of the past: Since a revision of the law enacted in 2007, second medical use claims may be formulated in more direct terms according to Art. 54(5) EPC, e.g. ***"substance x for use in the treatment of disease y."*** Consequently, the Enlarged Board held in 2010 (G 2/08) that the cause for the former praetorian approach had ceased, and that Swiss-type claims are no longer permitted to proceed to grant. But a lot of patents had already been granted over the years with such Swiss-type claims.

What's so new about it?

Healthcare costs are dramatically on the rise in many countries, with an increasing public awareness for it. There is a permanent price pressure on medicaments, i.e. it is a golden age for generic companies. European regulatory legislation facilitates access to generics in the European Union. This is aggravated by the fact that physicians frequently prescribe drugs with reference to international non-proprietary names (INN) only, without referring to the actual indication or the branded originator's product.

Now, assume that a generic product has received market authorization for a specific non-patented use. The market authorization may rely on the originator's prior authorization, while the summary of product characteristics and the patient information sheet are frequently silent on references to indications or dosage regimes which are still patented (so-called 'carve out', also frequently referred to as 'skinny labelling'). Sometimes, authorities require an explanatory statement to be included as to why certain indications or dosage regimes are missing; but the wording used in this 'blue box concept' is not very telling in most cases. Even express disclaimers for patented uses are sometimes seen. In any event, guess what is happening: The generic product is handed over by the pharmacist even for still patented indications. There are various incentives for pharmacists to do so, e.g. by national health care insurance acts or reimbursement regimes.

Evidently, any such 'cross-label' or 'off-label' use of drugs has the potential to render second medical use patents ineffective what makes it a big concern to originators.

Claim construction of Swiss-type claims

The preposition 'for' in a second medical use claim is of utmost importance. Is it to be interpreted as meaning only 'suitable for'? Or does it imply an element of subjective intention?

The *Warner-Lambert v Actavis* cases on generic *pregabalin* (marketed by Pfizer under the tradename Lyrica®) in the U.K. shed some light on this issue. High Court's Arnold J had decided that a subjective intent on the part of the manufacturer is required that their product be used for the respective indication. But the Court of Appeal held that a Swiss type claim was already infringed if it was foreseeable to the manufacturer that the product would be intentionally administered for the respective indication. This again requires some further interpretation by Arnold J. Whose intention is decisive? In first place, it is the physician's intent that counts. If the pharmacist actually knows about the doctor's 'off-label' or 'cross-label' prescription of the generic product (what is rarely the case), intention might also derive from him. In any event, the relevant intention cannot derive from the patient. The test now applied in U.K. is thus:

> *At the date of manufacture of the product, has it been foreseeable to the generic manufacturer that the physician and/or pharmacist intended administration of specifically that generic drug for the respective indication?*

How to establish / prevent infringement

In the U.K proceedings, Actavis had already notified superintendent pharmacists and medical associations that the generic product was not licensed for the respective indication. Thus, it was held that it was not foreseeable – at least not anymore – that the generic product would be intentionally administered for the patented indication.

A similar case is known from The Netherlands (*Novartis v Sun*). Novartis sought for injunctive relief against Sun. Novartis markets *zoledronic acid* under the tradename Aclasta®. The generic company had unconditionally registered for the tender of a health insurer for the supply of generic *zoledronic acid*, and committed itself to supply unlimited quantities of the generic product. In fact, the quantities of the generic product by far exceeded the required amount for the very rare non-patented indication in the country.

The court held that an email to wholesalers referring only to a 'formality' in the very first sentence of the email is not enough to prevent indirect infringement. Rather, it should have taken serious action in the tender process of the health insurance and in agreements with hospitals.

However, in main proceedings the Dutch court ruled otherwise: The claims were construed as purpose-limited process claims implying the essential element of preparation of a medicament. Consequently, the court ruled that Sun did not commit indirect infringement. Rather, the parties have been invited to present their arguments in relation to direct infringement.

These cases provide significant guidance for both originators and generic companies to assess individual cases.

Direct or indirect infringement: Why does it matter?

The aforementioned U.K. decisions dealt with the question of direct infringement of the generic manufacturer in any detail. Whether or not the conduct of the generic company could also

amount to an indirect infringement or not was only touched in passing. It was left undecided – but not in principle ruled out.

The case in The Netherlands firstly dealt with indirect infringement but now also focusses on direct infringement. To the contrary, a German court in *Warner-Lambert v 1 A Pharma* has ruled for indirect infringement in a case pertaining to the very same European patent of Warner-Lambert as in the aforementioned U.K. proceedings, yet against a different generic company (Regional Court Hamburg, 327 O 143/15). Like in the Dutch summary proceedings, the generic company had unconditionally joined a tender of health insurances, which in turn had explicitly incentivized physicians and pharmacists to prescribe / hand over the generic product for all indications.

Both the Dutch and the German patent act explicitly prohibit indirect infringement, i.e. that someone, without the consent of the patent proprietor, offers or supplies means relating to an essential element of the invention to a third party who is not entitled to use the invention, for the purpose of using the invention in that country, and the supplier knows, or it is obvious from the circumstances, that said means are i) suitable for using the invention and ii) intended by the customer for using the invention, i.e. the customer plans to apply the means in order to use the invention. But this is not necessarily the case in every country. In Switzerland for instance, indirect infringement is not independently prohibited but rather essentially depends on the actual occurrence of a direct infringement to which it contributed. In the absence of any direct infringement, no indirect infringement can be sanctioned.

It is important to note that a change to the Swiss Patent Act is currently in the pipeline to exempt physicians' and pharmacists' activities from patent infringement. This is a remarkably different approach compared to e.g. the situation in the U.S. where medical practitioners are only exempt from liability – but nevertheless their conduct may be infringing.

Generic companies may argue in countries like Switzerland (upon enactment of the new law) that in the absence of any direct infringement of a physician or pharmacist there cannot be any indirect infringement, either. Conduct of a generic company will thus likely have to be litigated as direct infringement in Switzerland in the future. It remains to be seen how this can be done in case of second medical use claims in the Swiss type form. Strategies may well depend on the actual construction of the claim. At the face of it, a Swiss type claim is directed to a use. In claim categories, this means it is a method claim. However, it is construed in some case law as a product claim: It has not been granted in view of a new and inventive method of manufacturing, but rather in consideration of its new and non-obvious second medical indication. The same reasoning applies to a first medical use claim like *"substance x for use as a medicament"* – which undisputedly is a product claim – and to second medical use claims according to the EPC 2000. Some practitioners argue that the crummy language of a Swiss-type claim as formerly required should not change anything in this respect. To the contrary, the Enlarged Board of Appeal in its decision G 2/08 held that the rights conferred on the patentee by the claim language under the EPC 2000 *"are likely broader, and could, in particular, lead to possible restrictions on the freedom of medical practitioners to prescribe or administer generics."* This might imply that the Enlarged Board of Appeal presumed this freedom still to be given over second medical use claims in the Swiss type form.

To date, there is still a significant uncertainty with respect to the extent of protection of Swiss type claims, as well as the requirements to prove or avoid an act of infringement.

What is next?

It is obvious from the above that a clear-cut solution of protecting the rights conferred by a second medical use patent while allowing lawful generic competition for non-patented indications is still lacking, especially in the case of Swiss type claims. Arnold J in the U.K. strongly advocated in favor of a separation of the markets by ensuring that prescribers write prescriptions for the patented indication by reference to the patentee's brand name and write prescriptions for non-patented

indications by mere reference to the INN. But physicians and pharmacists cannot be expected to know which prescription is when to be made, and they should not be required to take steps to find out. It appears to be common sense that centralized and authoritative guidance is necessary in this respect. To date any such authoritative guidance has only been given on a case-by-case basis when it is all too late like in the U.K. *Warner-Jenkins v Actavis* case. However, there is apparently no initiative to establish a systematic centralized and authoritative routine to prevent such conflicts between originators and generic companies.