Time for a new tool in EPC's box?

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ask what the future holds for second medical use claims in Europe

The term second medical use refers to new therapeutic uses of known compounds and substances and may be the second or any subsequent new therapeutic use of a known compound or substance. Second medical uses provide solutions to unmet medical needs and bring significant benefits to patients. They require extensive and risky investments in research and development, albeit facilitating a safer access for patients to already tested substances with known or no side-effects. They represent socially, medically and economically valuable innovations and are as such protectable in several national European jurisdictions.

However, in the wake of socio-economical desires to lower the cost of existing drugs on the market, research on second medical uses has become much less attractive for pharmaceutical companies.

In many jurisdictions, regulatory frameworks allow generic applicants for marketing authorisation to exclude references to patented second medical uses from the product information, which is referred to as skinny-labelling, or carving-out patent protected indications.

In addition, in many jurisdictions, the regulatory framework provides incentives for the generic substitution of a branded pharmaceutical, even for indications that are unauthorised and patented.

For second medical uses, conventional remedies, such as injunctions and damages, face significant challenges. Infringement actions have proven to be difficult in practice and have often only been successful when the infringing party has mar-

keted the drug with explicit instructions for the patented use. A recent decision from the High Court of England and Wales, however, (*Warner-Lambert Company v Actavis Group* 2015) has potentially granted the owners of second medical use patents a new legal means against infringers in the UK.

Justice Arnold took the unprecedented measure of ordering the National Health Service (NHS) in England to at least issue a guidance note on the prescription of the drug, recommending that the drug be prescribed under the brand name of the originator when being prescribed for the patented indication. While only a guidance note, this could be a sign of a trend to favour of the originator industry, or at least a first step in the right direction.

Paradoxically, the serious lack of incentive to invest in and develop new medical uses for existing drugs is not only a problem for the originator industry. In the end, this leads to lack of incentive for the generic industry to copy a drug with a lesser market-value.

One particular problem is that the permissible claim format for a second medical use is inconsistent between jurisdictions, laying an important cornerstone to the dubious protection conferred by a patent granted.

First and second medical use claims before the EPO

New substances or compositions found to have a medical use have always been patentable under the EPC (European Patent Convention). For a known pharmaceutical substance, the EPC dictates two general possibilities for seeking patent protection: the first or second medical use format.

The first medical use format can be used when the substance as such is already known but has not been used in medicine. Under Article 54(4) EPC, these patents confer strong and desirable protection for a purpose-limited product claim 'product X for use as a medicament'.

Further medical inventions are patentable under Article 54(5) EPC in the second medical use format, a narrower purpose-limited product claim 'product X for use in the treatment of pathological condition Y'. G2/08 sets an official stop to the formerly prevalent use of the Swiss-type claim format for second medical use, and T0067/94 rules for the first time that a new technical effect can be considered to lead to a new medical use.

However, according to the Examining Guidelines of the EPO (European Patent Office), a defined, real treatment of a pathological condition is explicitly required in order to transform a scientific contribution into an invention eligible for patent protection (G-VI, 7.1), the existence of which is left to be decided on by the individual examiner. The mere explanation of an effect does not render a medical use novel (T0060/04). According to the Guidelines (G-VI 7.1 and based on T 241/95), it is clear that a pharmaceutical effect in itself does not imply a therapeutic application. Also, the Boards interpret G5/83 such that a new technical effect can only confer novelty to a medical use if it is also linked to a new industrial commercial application or activity (case law of the Boards of Appeal of the EPO, 5th Edition, 2006).

According to the same Guidelines (F-IV 4.22), a further therapeutic application may be defined in functional terms provided that 'instructions, in the form of experimental tests or testable criteria, are available from the patent documents or from the common general knowledge allowing the skilled person to recognise which conditions fall within the functional definition' (T 241/95). No clear guidance is provided, however, as to how such tests should be designed in order to fulfill this requirement.

The requirement by the EPO for an acknowledged pathological condition creates an unnecessary hurdle to the patenting process for further medical uses. Modern medicine places considerable importance on understanding the biology of a disease, since this allows the development of optimised treatments with a minimum of side effects. When seeking new pharmaceutical compounds to treat a particular disease, the skilled person would therefore almost always focus on identifying the biological pathway of the disease.

When drafting patent applications on further medical indications, to avoid losing claim scope, patentees today tend to list a wide plethora of diseases, of which many are not yet proven to be treatable by the drug in the description. This tendency effectively prevents any future inventors from being able to obtain patents on traditional further medical indications, once shown to share the same underlying molecular pathway, because the new treatment is often already revealed in the better-safe-than-sorry lists.

However, the grouping of diseases based on clinical symptoms has been changing towards also taking into account the underlying molecular causality, as can for example be seen in the World Health Organisation's international classification of diseases (ICD-10).

Therefore, it appears that the EPO needs to align the patentability criteria for medicinal inventions with modern pharmaceutical research. Such a goal may be achieved by introducing a further medical use claim category: the first molecular use claim. This claim format could read as follows: product X for use in molecular pathway Y for treating a pathological condition. However, it may be reasonable to require that, in order to obtain such a claim, at least one disease or disorder should be linked to said molecular mechanism and made plausible to be treatable by effecting the claimed pathway, even if this specific disease or disorder need not explicitly be part of the claim language.

In fact, the EPO has allowed second medical use claims where the same substance is used for treating the same disease as previously known, but via a newly identified pathway (see for example T 1642/06 and T 836/01). If a first molecular indication patent could give full protection for treating each and any disease with the same underlying molecular pathway with the same drug, a third person (or the same inventor) could subsequently still file for a traditional further medical indication

patent. Today, this is often made impossible due to the apparently accidental revelation of the said same disease.

It therefore appears that the necessary legal basis for a molecular use claim is basically in place.

The question then arises whether a molecular use claim will give an unduly broad scope of protection. That is, will researchers be discouraged from developing treatments for new pathological conditions using the known compound that may be linked to the patented molecular use? Bearing in mind that scientific progress in the life sciences is predominantly based on accumulative knowledge, it is doubtful that this would be the case. Also, a similar situation already pertains to product claims, which confer protection against infringement by any future use of the patented product. The subject matter of a molecular use claim may in fact be narrower and clearer in comparison to the current attempts of applicants trying to cover speculatively related groups of pathological conditions.

Another question that may arise regarding the proposed claim formulation relates to whether it would be difficult for a potential infringer to know if a molecular indication patent is infringed or not. However, as described above, when developing new drugs, most often the molecular pathway is targeted first. Screening for substances affecting the mechanism follows heels. To the scientist, identifying infringing actions might not be as burdensome as it may first seem to the legal practitioner.

So what about further second medical uses drawn to treatment of different diseases, based on affecting the same molecular pathway? Such inventions could still be protected via regular second medical use claims based on defined, real pathological conditions treatable. However, they should be dependent on the molecular indication patent, just as a new use of a product is patentable but will be dependent on the product patent. With regard to the opposite situation, where patent protection is obtained for a second medical use defined as a pathological condition, and the affected molecular pathway is later revealed, it should be possible to obtain a patent for this molecular indication, if it is linked to at least one further pathological condition. The patentee for the first patent could then obtain a prior use right for the previous pathological condition.

A comparison with the US

Claims for first and second medical use inventions are handled differently in the US than in Europe. First, the patentability of methods of treatment of the human or animal body is not prohibited. Instead, medical practitioners are exempt from liability for performance of a medical activity that would otherwise be infringing. The exemption does however include some explicit exclusions, such as the use of a patented composition.

In the US, purpose-limited product claims are not patentable. New uses of known compositions, however, are comprised under the term 'process', one of the statutory categories of patentable subject matter. Therefore, first and second medical use claims are patentable under a 'method of treatment' category, which must include a number of steps. In agreement with this, methods drawn to manipulating molecular pathways with known compounds are in principle patentable.

A further particular challenge that this type of claims faces, bearing in mind that they revolve around a known compound, is a rejection based on inherency. A prior art reference may be relied upon in the formulation of an anticipation or obviousness rejection, not only for its explicit disclosure, but also for its implicit, and inherent disclosure. To be inherent, a feature must be 'the natural result of the combination of elements explicitly disclosed in the prior art', and to establish that may not be that immediate (*Par Pharmaceutical v Twi Pharmaceuticals* Fed Cir 14-1391 2014)

In the US, the enforcement of second medical use claims faces similar challenges to those in other jurisdictions. While the statute provides protection for patentees not only from direct

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Prior to joining Valea AB in 2002, Ylva gained a PhD in medical research at Biomedicinska Centrum in Uppsala. She has worked in the IP field since 1999, acquiring broad experience in patenting medical and biotechnological inventions such as medicaments, vaccines, diagnostics and medical or dental devices, biomaterials, and applied nanotechnology in these areas. Ylva is a sought-after specialist in handling worldwide portfolios and IP strategies built on protein pharmaceuticals, including their formulation and production, as well as on patenting of transgenic animals and plants. She has broad expertise in exceptions to patentability under the European Patent Convention, as well as in the patenting of new medical uses of known compounds. Ylva is a senior partner at Valea AB and is key account manager for several multinational companies. She assists clients from small biotech start-ups to global companies and technology transfer units with devising IP strategies, drafting and prosecuting applications worldwide, including applications for supplementary protection certificates, freedom-to-operate evaluations, oppositions, litigations, due diligence and licensing issues. Ylva gives EQE training lectures and she also lectures on a broad range of IP topics regarding patenting of biotechnological and pharmaceutical inventions. She has published several articles on recent IP law developments.

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Isabel specialises in prosecuting patents in the areas of software, business methods, telecom, life sciences and medical devices. Isabel started her career in IP in 2002, first as a technical consultant, and later as US patent agent, at Clifford Chance US LLP (New York, US). During her time in the US, Isabel worked drafting and prosecuting patent applications, as well as in US patent litigation, invalidity and infringement opinions, due diligence and transactional operations. Prior to joining Valea AB in June 2012, Isabel also worked as US patent agent at Baker & Hostetler LLP (New York, US).

Isabel has a master of science in neurobiology and physiology and a PhD in neuroscience, both from Northwestern University (Illinois, US). She also has five years of postdoctoral research experience in neuroscience (biotechnology) at Cold Spring Harbor Laboratory (New York, US). Isabel has numerous scientific publications and has contributed as referee to several scientific journals.

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infringement, but also from indirect infringement (induced or contributory), potential infringers may escape infringement liability by skinny-labelling.

A first step

In a resolution adopted in September of last year, the AIPPI (International Association for the Protection of Intellectual Property) resolved that each jurisdiction should recognise at least one claim format that provides patent protection for second medical uses, commensurate with, for example, that second medical uses should not be limited to uses that treat disease but should include uses directed at alleviating or preventing disease or otherwise improving health. The first molecular use claim format proposed here may just be the first step on the path to such a goal and a sought-after complement to the EPC's present tool box.

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