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Personalised medicine, medical indication patents and patent infringement: emergency treatment required

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***151** Abstract

This contribution provides for the first time an in-depth analysis of the scope of protection of medical indication claims. This analysis leads to the inevitable conclusion that virtually all players in the chain, i.e. the generic drug manufacturers, the drug wholesalers, the physician and the pharmacists, run a credible and documented risk of committing patent infringement in the case of an off-label use by producing drugs for the use in medical treatment, by prescribing them and by dispensing those drugs. The introduction of a therapeutic freedom exception for clinicians and pharmacists is advised. Such an introduction is not sufficient to guarantee full therapeutic freedom at a reasonable cost for both patients and the healthcare system at large. It is evidenced that medical indication patents do not only come very close to the therapeutic activities of the clinician, and present serious risks from that perspective; other players in the pharmaceutical product chain also run the risk of committing patent infringements which they cannot necessarily control. It is likely that under the current state of the law, generic manufacturers will be liable for patent infringement, knowing that their drugs, which are not authorised and offered for sale for patented medical indications, will be used off-label by physicians for the use in the treatment of a patented medical indication. Such a situation is not desirable, as it will expel generics from the pharmaceutical product market, even in markets which are no longer patent protected. This can come at a potentially very high cost for the healthcare system, which is already under financial pressure in most countries. This article puts forward a number of solutions to prevent this from happening.

Introduction

Medical indication patents have for a very long time led a somewhat quiet existence. The law pertaining to these types of patents is not very easy to understand, and it has never attracted much attention from most scholars. Medical indication patents cover a new use of an existing drug, and constitute as such an exception to the absolute novelty rule prevalent in the patent system. That new use can reside in the treatment of a new medical condition, a new mode of administration, a new patient group, a new dosage regime, etc.

Since the inception of the European Patent Convention, there are largely two moments in time when these types of patents have taken centre stage. The first was the decision of the Enlarged Board of Appeal in the G5/83 [Eisai](#) case, where it was held that despite an at first sight contrary provision in the Convention, second and further medical indication patents deserved protection. ¹ In the period immediately prior to and ***152** after that decision, medical indications patents were widely discussed, as we will see in a separate contribution in a subsequent issue of this Journal, ² but then it went rather quiet. A second surge in attention originated when the European Commission launched a sector inquiry into

pharmaceuticals on 15 January 2008. The so-called *Pharmaceutical Inquiry Report*³ which emanated from that inquiry provides interesting if not always pleasant reading. The European Commission concluded that there are a number of so-called patent strategies used in the pharmaceutical industry with a view to extend patent protection for drugs or in any event to keep generics off the market.⁴ Medical indication patents play a not unimportant role in achieving that goal, according to the European Commission.⁵

This knowledge has created a renewed interest in medical indication patents, also by the present author. This contribution is very timely in a world of growing demand for what is called personalised medicine, a medical model using molecular profiling for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and stratified prevention. It may also involve imaging and other technologies.⁶ This modelling will lead in many cases to so-called stratified medicine, where populations and sub-populations of patients will be treated in such a manner which fits their genetic make-up best. That will imply in many cases that existing drugs may be used for treating a different disease in certain patients, that different dosages or other means of administration may be required, etc. In other words, personalised medicine is likely to lead to an explosion of what we call medical indication treatments and consequent patents.

There is a substantive body of literature covering the non-patentability of medical treatment methods and the patentability of further medical indication patents.⁷ What the literature lacks is an analysis of one of the core aspects of second medical indication claims, which is their scope. The English literature is virtually entirely silent on this matter. That is somewhat surprising, as we are now faced with a situation in which we realise that, even though the (non-)desirability of medical indication claims has been well documented, very few have ventured an analysis of the scope of protection of those claims and the issue of infringement.

It is an aim of this contribution to provide for the first time an in-depth analysis of the scope of protection of medical indication claims.⁸ As will be demonstrated, this analysis leads to the inevitable conclusion that virtually all players in the chain, i.e. the generic drug manufacturers, drug wholesalers, physicians and pharmacists, run a credible and documented risk of committing patent infringement by producing drugs for the use in medical treatment, by prescribing them and by dispensing those drugs. It is striking *153 to see that even though so many words have been spent on determining whether medical indication patents conflict with the therapeutic freedom and activity of the physician, very few have examined what consequences the scope of those patents could have on therapeutic freedom.

The introduction of a therapeutic freedom exception for clinicians and pharmacists is advised. Such an introduction is not sufficient to guarantee full therapeutic freedom at a reasonable cost for both patients and the healthcare system at large. It will be evidenced that medical indication patents do not only present a serious infringement risk for the clinician, but other players in the pharmaceutical product chain also run the risk of committing patent infringements which they cannot necessarily control. It is likely that under the current state of the law, generic manufacturers will be liable for patent infringement, knowing that their drugs which are not authorised and offered for sale for patented medical indications will be used off-label by physicians for the use in a treatment of a patented medical indication. Such a situation is not desirable, as it will expel generics from the pharmaceutical product market, even in markets which are no longer patent protected. This can come at a potentially very high cost for the healthcare system, which is already under financial pressure in most countries. To that effect, this article attempts a number of solutions to prevent this from happening. Not all of these solutions have the same viability, but the present author wishes to contribute to the discussion and the search for a remedy for this serious problem by providing a range of possible solutions.

In the second section, some introductory elements of personalised medicine will be explained. In the third section we will explain what medical indication patents are. The fourth section will provide an in-depth critical appraisal of the various infringement scenarios which are possible and we will identify which players in the "chain" could be held liable for infringement and whether that will be under the concept of direct or indirect (contributory) infringement. The players

of interest to us will be the generic drug manufacturers, the medical professionals, the pharmacists and the patients. In the fifth section, we will provide policy considerations and make a number of proposals to resolve the current problems, which are in our view unsustainable. We will finally draw some conclusions in the sixth section.

Personalised medicine—what is it?

Personalised medicine (PM) has become a common denomination for a variety of techniques and technologies that do not necessarily all relate to the treatment of patients. In fact, most of the techniques and technologies understood to fall within the denomination of personalised medicine do not pertain to the treatment of an individual patient, but are based on so-called stratification strategies, i.e. technological strategies which aim at categorising patients into a variety of patient groups, on the basis of which treatments targeted at those groups can be developed. The term "personalised medicine" hence encompasses a number of technologies that are in fact ancillary to the effective treatment of patients.

A useful definition is to be found in a Report from the European Alliance for Personalised Medicine:

"Personalised medicine most frequently refers to a medical model using molecular profiling for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and stratified prevention. It may also involve imaging and other technologies." ⁹

It includes the prediction of disease risk, treatment response and safety profile based on genomic sequence data, but is much wider than that. It includes also what is called stratified medicine. The latter refers "to the identification of subgroups of patients with a particular disease who respond to a particular drug or, alternatively, are at risk of side effects in response to a certain treatment". *154 ¹⁰

Biomarkers play a crucial role in personalised medicine. A biomarker can be defined as

"a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention". ¹¹

A biological marker (biomarker) is simply a molecule that indicates an alteration in physiology from the normal. For example, any specific molecular alteration of a cancer cell on a DNA, RNA or protein level can be referred to as a molecular marker. Applications of biomarkers relevant to personalised medicine are the following: the biomarker could specifically and sensitively reflect a disease state and could be used for diagnosis, for predicting response to drug, and for disease monitoring during and following therapy; biomarkers can be used as drug targets in drug development; biomarkers might serve to integrate diagnostics and therapeutics. ¹²

Pharmacogenomics, another crucial part of personalised medicine, promises to enable the development of safer and more effective drugs by helping to design clinical trials such that non-responders would be eliminated from the patient population, which would take the guesswork out of prescribing medications. It will also ensure that the right drug is given to the right person from the start. In clinical practice, doctors could, before prescribing, test patients for specific single nucleotide polymorphism (SNPs) known to be associated with non-therapeutic drug effects to determine which drug regimen best fits their genetic makeup. ¹³

Pharmacogenetics, the study of the linkage between the individual's genotype and the individual's ability to metabolise a foreign compound, will equally play a very important role in personalised medicine. The pharmacological effect of a drug depends on pharmacodynamics (interaction with the target or the site of action) and pharmacokinetics (absorption, distribution and metabolism). It also covers the influence of various factors on these processes. Drug metabolism is one

of the major determinants of drug clearance and the factor that is most often responsible for inter-individual differences in pharmacokinetics. Pharmacogenetics links genotype and phenotype.¹⁴

Personalised medicine has developed out of the shortcomings of traditional medicine, which started from the identification of lead molecules. These were then tested in vivo. Based on those results, and after clinical trials, a drug was brought on to the market. This approach has quite a high number of inefficiencies built in. First of all, it ignores the specific circumstances of patients. One patient reacts better to a certain drug than another. Indeed, a certain drug has in certain situations no effect at all for a specific patient. The use of drugs in the traditional manner also ignores side effects that may occur in certain patients, as apart from dosage and testing of allergic reactions, no further filtering takes place prior to the administration of a drug. Such methods obviously present further inefficiencies in the treatment of medical conditions.

With the advent of gene technology, that has all changed. The growing strength in computational power allowed technology to make genetic profiles of patients, thus presenting a first step in the process towards personalised medicine. On the basis of a genetic profile of a patient, it is first of all possible to derive some diagnostic conclusions, such as, e.g., the predisposition to certain genetic conditions. The genetic profile of a patient also allows targeting medication in a far superior personalised fashion. Access to genetic profiles of patients also has important consequences for future drug and therapy development. Genetic profiling can be used to study the distribution of certain mutations in (parts of) a population, thus allowing the provision of a more targeted approach towards drug development. For example, certain mutations seem to be prevalent in certain populations. That knowledge allows one to target a diagnostic and/or therapeutic treatment towards that population. *155

Applications are multiple. It was recently reported that certain people with a certain genetic make-up react much more seriously to the flu virus and run a higher risk if contracting it. One in 400 people carries a variant of a gene called IFITM3¹⁵ that makes those people more likely to suffer seriously from flu. Genetic testing can test people for the presence of the gene variant. That in turn can prioritise those patients for flu jabs as they run a higher risk of complications, and in a more distant future, could allow the development of new drugs specifically targeted at that group of patients.¹⁶

It will become clear from what follows that patent claims filed for inventions in the area of personalised medicine as defined above will predominantly be in the format of further medical indication claims. That is why the present contribution is so important.

Medical indication patent claims—quid?

Introduction

Knowing what personalised medicine encompasses, we can also appreciate that a vast array of techniques and technologies are used, not all new and untested, but most definitely a large variety of them. For the present contribution, we will limit ourselves to only one issue, the patentability of medical indication patents. Indeed, one of the areas of personalised medicine is the application of existing drugs to a variety of medical indications, be it for the treatment of a different condition from the one the drug was originally known for, for the use in a new mode of administration, or by using a different dosage regime from the one(s) known in the state of the art, etc. All of the aforementioned techniques can be used to provide treatment that not only targets stratified patient groups, but which is also shown to be effective where the standard treatment would not be.

In what follows, we will give an overview of what medical indication patents are.

Medical indication claims—what are they?

In Europe, the patentability of inventions relating to known molecules is subject to the rules pertaining to second and further medical indication patents. An understanding of the law relating to second and further medical indications requires distinguishing between the legal regime until recently prevailing and the current statutory regime.

Some concept of patent law will need to be clarified, albeit concisely, with a view to reaching a good understanding of the concept of medical indication claims.¹⁷ The reader is warned, though, that this is not perceived as an easy subject, as Jacob J eloquently said in *Bristol-Myers Squibb v Baker Norton* when he was called to evaluate a second medical indication claim:

"I must now say something about the general structure of the claim. I daresay that an ordinary skilled man (to whom it is notionally addressed) would find it puzzling, unless he had been initiated in some of the Byzantine logic of patent law and jurisprudence. *156 " ¹⁸

A first basic principle of patent law is that one can patent a new chemical entity as such as long as it does not form part of the state of the art. Under the concept of absolute novelty in patent law (for the EPC, see art.54), i.e. anything which forms part of the state of the art can no longer be the subject of a patent, it would normally not be possible to obtain patent protection for a chemical entity or molecule once it forms part of the state of the art. For years, the pharmaceutical industry had argued that, absent protection for further medical uses of an already patented or known substance, innovation into and development of new drugs would be stifled. This is not the place to debate whether that assertion was right or wrong. We will come back to the historical evolution of medical indication claims in a separate contribution in a subsequent issue of this Journal.¹⁹ For the moment, the reader should accept for the purpose of following the line of reasoning that those "prayers" were listened to.

It is also necessary to add at this point that according to the EPC, and prior to the coming into existence of the EPC also in some of its future Member States, methods of medical treatment were and are still excluded from patentability, i.e. the use of a medicament for the treatment of a medical condition is not a patentable claim.²⁰ The rationale for this exclusion was not a single one. It was believed that there were ethical, societal and public health reasons which should ensure that medical professionals would not be hindered in their daily activities.²¹ Accepting the exclusion, using medical treatment claims to protect further uses of an existing drug was a venue no longer open for pharmaceutical companies.²²

With a view to accommodate the concerns, the drafters of the EPC introduced what was then called the first medical use of a known substance. That was an exception to the standard principles of novelty. Not surprisingly, the exception was put into the provision dealing with novelty, i.e. art.54. According to art.54(5) EPC 1973,²³ it is possible to obtain purpose-limited product protection for the first medical use of an already existing drug. Such a patent claim would typically read as "product X for the use as a medicament". It will immediately be understood that this is a very wide claim indeed, covering *all* medical applications of a known substance.²⁴ As a matter of practice, in virtually all cases, the claim is part of the patent which claims the chemical entity as such.

What now if there was a situation where one invented yet another medical indication of an existing drug; for instance, assume that someone invents a use for that drug for the treatment of a certain condition? And what about the situation where another party (or for that matter the same party) invents yet another use of that same substance, for instance that the drug can be used for the treatment of yet another condition?²⁵ There was nothing in the statute about that eventuality. The pharmaceutical industry pushed very hard to gain patent protection for this kind of situation, arguing that research into developing these new applications of existing drugs was expensive and laborious and deserved to be

shielded from immediate copying by competitors if this type of research, which was claimed to be of much benefit to society, were to be continued. Case law eventually provided a solution and also allowed claims for what were then called second and further medical indications. Absent a statutory provision under the EPC 1973, case law had to be inventive, and came up with what was then called the "Swiss claim", according to which one could protect "the use of a substance X for the manufacture of a medicament for the treatment of disease Y". *157

The reason for this rather complicated claim formula was that there were some stumbling blocks within the EPC that prevented the courts coming to a more elegant solution. In view of the fact that art.54(5) EPC 1973 only allowed claiming the first medical indication as a product, a product claim was no longer possible. And according to art.52(4) EPC 1973, medical treatment methods could equally not be patented. That had as a consequence that a claim covering the "use of a substance X for the treatment of disease Y" was equally not possible. A claim for the use of a substance is nothing more than a method claim, and the above-mentioned claim would hence cover a medical treatment. Faced with these limitations, the Enlarged Board of Appeal (EBA) in the seminal G5/83 case²⁶ came first to the conclusion that the EPC had not envisaged the exclusion of second and further medical indication patents, and then devised a claim formulation that would fit within the confines of the then EPC 1973. As such a Swiss claim does not protect the product as such, it was allowable.

There is in the meantime quite a substantial body of case law covering such further medical indication patents. The most common types are those inventions relating to a novel group of subjects,²⁷ sub-populations (at least in some jurisdictions),²⁸ relating to a new route or mode of administration,²⁹ relating to a different technical effect and leading to a truly new application,³⁰ and those relating to a new dosage regime for an existing drug.³¹

On the occasion of the negotiation of a new EPC, it was considered useful to codify the patentability of second medical uses. A new provision was introduced to that effect. It was considered that the easiest way would be to allow also product claims for second and further medical uses, as that would be in line with what was already in existence for the first medical use, and it would also allegedly do away with the complications which were experienced with the Swiss claims. This new provision hence specifically allowed purpose-limited product claims for second and further medical indication claims, confusingly also in art.54(5) EPC 2000 (the first medical indication claim principle now laid down in art.54(4) EPC 2000).³² A typical claim under this new provision would read "product X for the use in the treatment of disease Y". This type of claim is what is called a purpose-limited product claim, i.e. it protects the product but the scope is limited to the specific purpose or function of the product as laid down in the patent. For the present type of claim, that would mean that product protection is not absolute in the sense that it protects all applications of the product, the standard rule in patent law,³³ but would only protect the product limited to the specific application, which is laid down in the "for the use in the treatment of ..." part of the claim.³⁴

For patents with a filing or priority date after 28 January 2011, patent claims may no longer be formulated in the "old" regime Swiss claim formulation.³⁵ The new art.54(5) EPC with the accompanying new product claim formulation will be applicable only to patents for which the date of the decision to grant the patent under consideration was taken on or after 13 December 2007, which is the date on which the new EPC 2000 entered into force. If the decision to grant was taken before that date, only "Swiss-type" claims are allowed for any second or further medical use (provided these claims meet with all the other requirements *158 of the Convention).³⁶ That implies that the new claim formulation will be admissible for patent applications filed before the entry into force of the EPC 2000, but for which no decision to grant has been taken at that moment. As the Technical Board of Appeal held in T1570/09, once a new claim formulation has been introduced in a patent application that falls within the new regime, there is no reason anymore to allow a Swiss claim formulation.³⁷

An interesting question is whether both types of claims, which are currently both widespread in still enforceable and valid patents, have a different scope of protection. The Swiss claim is a use or method claim, while the new claim formulation under the EPC 2000 is a product claim. That in itself already suggests a different scope.

A recent decision by a Technical Board of Appeal indeed confirms that there is a difference in scope between a Swiss claim now no longer allowed and a patent claim under art.54(5) EPC 2000. In T1780/12,³⁸ the TBA held that:

"It follows from the above analysis ... that the claims under consideration belong to different categories, i.e. purpose-limited process claim vs. purpose-limited product claim and differ in addition in at least one technical feature. It is generally accepted as a principle underlying the EPC that a claim to a particular physical activity (e.g. method, process, use) confers less protection than a claim to the physical entity per se ... It follows that a purpose-limited process claim also confers less protection than a purpose-limited product claim."³⁹

That difference in scope could be expected to have relevant consequences for infringement, an issue to which we will revert in the fourth section of this contribution. But as we will see, it is not certain that the scope of protection is in effect that much different between the two types of claims the Board refers to.

Irrespective of the legal regime applicable, both the "old" regime and the current regime allow the patentability of what is called second and further medical indications.

Medical indication claims and patent infringement

Introduction

One of the main issues that have arisen in respect of medical indication claims is the infringement issue. And as we know that medical indication claims will play a crucial role in a world of personalised medicine, scrutinising enforcement issues is of the utmost relevance. In what follows, a very critical overview is given of the most likely medical indication patent infringement scenarios. As we will see, there are some surprising and at the same time worrying conclusions to be drawn here.

Medical indication patents, skinny labelling and off-label use in Europe

As we have seen above, it is perfectly possible to obtain a patent for an already existing medicinal product for the treatment of a new condition, for a new mode of administration, for a sub-population (at least in some jurisdictions), for a new dosage regime, etc.

One of the issues that arise in this connection is so-called off-label or cross-label use, which refers to the practice whereby physicians prescribe generic versions of drugs for the treatment of conditions which are still under patent protection (and whereby the generic version has not received a market authorisation *159 for such patented medical indication).⁴⁰ Off-label use is a very common practice in Europe, and occurs very frequent in, for instance, neonatology and for paediatric use.⁴¹ It is claimed that at least 21 per cent of all drug prescriptions may be off-label use.⁴² In some areas of medicine it is much higher, such as for instance new biological drugs for the treatment of cancer where it has been said to be around 75 per cent.⁴³ Off-label use is in most countries not specifically regulated in the statute, even though it is regulated by various other forms of regulatory instruments.⁴⁴ In some countries there is statutory regulation for off-label use for specific types of patients.⁴⁵ France has a more generic system in place which is called "recommandation temporaire d'utilisation" or RTU. According to the ANSM (Agence nationale de sécurité du médicament et des produits de santé), an RTU is elaborated by the ANSM when the two following conditions are fulfilled: (1) There is an unmet therapeutic

need, i.e. there is no appropriate alternative medicine with an MA or a cohort "temporary authorisation for use" (ATU) in the indication in question; and (2) the benefit/risk ratio of the medicine is assumed to be favourable based on the available scientific efficacy and safety data. Hence, an RTU aims to fulfil two objectives: (1) to render the use of off-label prescribed medicines safer by looking objectively at their therapeutic benefit with respect to the risks to which they expose patients; and (2) to ensure that the pharmaceutical company in question implements monitoring for patients treated in the context of this waiver of MA specifications. An RTU therefore helps improve knowledge about a medicine for a given use and encourages the pharmaceutical company to submit an extension of indication request. RTUs are temporary measures that may not exceed three years.⁴⁶ Recently some changes have been made to the system.⁴⁷ An RTU can now be issued to authorise the off-label use of a medicinal product if there is no medicinal product with the same active substance, the same dosage and the same pharmaceutical form that is already approved or under an ATU in the considered indication or in the considered conditions of use. Thus, the French Medicines Agency (ANSM) can now issue an RTU even if a therapeutic alternative is available, provided that this alternative does not have the same active substance, dosage and pharmaceutical form.⁴⁸

Even though, in most cases, EU Member States are careful not to state too openly that the off-label policies which are allowed have a cost-saving rationale for the healthcare system, there is some evidence that, at least in some of the cases, the recent change in France as set out above being only one of them, cost is a factor for allowing or condoning off-label use.⁴⁹ A good example of cost effects is the case of ***160** Avastin and Lucentis. Avastin (or Bevacizumab) is an off-patent drug that is authorised for the systemic treatment of metastatic colorectal and breast cancer by intravenous infusion. Ophthalmologists are using intra-ocular (intravitreal) injections of Avastin off-label to treat neovascular age-related macular degeneration (AMD), a chronic disease of the elderly. Lucentis has been specifically authorised for that latter condition, is protected by a patent, but has a cost of approximately 50 times the cost of the off-label use Avastin product.⁵⁰

Those government policies of cost-saving off-label use may sit uncomfortably with the judgment of the CJEU in the *Commission v Poland* case, where it was held that financial considerations cannot, in themselves, lead to recognition of the existence of special needs justifying derogation from the rule that only drugs which have been approved can be brought on the market.⁵¹

The generic manufacturer will as a rule not have sought to obtain market authorisation for the patented medical indication, but will have obtained market authorisation for the drug as such and for any other medical indications which are no longer under patent protection. That practice is also referred to as "skinny labelling", which refers to the system whereby a generic pharmaceutical company that wants to obtain a market authorisation for a medicinal product which is as such off-patent, but for which there is a patent for a further medical indication, e.g. for a dosage regime or for the use in the treatment of a different disease, can "carve out" in the market authorisation the medical indication(s) which is/are still under patent protection. To that effect, a market authorisation is obtained which is limited to the medical indications which are no longer under patent protection, a so-called "skinny label".

Since 2004, this has been recognised in the European medicines legislation, which expressly allows for so-called "skinny labelling" of generic drugs (the carving-out from the product information (e.g. the summary of product characteristics (SmPC) and patient information leaflet (PIL)) of indications or dosage forms that are patent protected). [Article 11 of Directive 2001/83](#)⁵² provides in that connection that

"for authorisations under [Article 10](#) [the abridged procedure], those parts of the summary of product characteristics of the reference medicinal product referring to indications or dosage forms which were still covered by patent law at the time when a generic medicine was marketed need not be included".

Article 3 of Regulation 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency contains a similar provision.

Skinny labelling serves in fact a double purpose. It allows generic manufacturers to bring the drug on to the market for indications that are no longer under patent protection. The corollary to this is that it also enables pharmaceutical companies which have patent protection for other medical indications to prevent generic players entering the market with a drug for such patented medical indications. Even though skinny labelling allows patent holders to be protected against the use of generic drugs for patented uses (and should at the same time protect generic manufacturers against patent infringement for those patented medical indications), this will not prevent that in practice off-label use will still take place. *161

Medical indication patents and infringement—general principles

Principles to determine who is liable under which type of infringement

Turning now to patent infringement for medical indication patents, there are in fact a number of scenarios that can be envisaged. There is the relatively straightforward situation where the generic drug manufacturer has obtained a market authorisation for a patented use and plans to bring the drugs on to the market for, among others, the patented medical indication. That would constitute a rather straightforward infringement situation. There is a second scenario where the generic drug manufacturer has not obtained a market authorisation for a patented medical indication but only for those indications which are no longer patent-protected, and brings nevertheless the product on to the market for use in a patented medical indication, by for instance marketing it for that use (which scenario is not very likely as in the absence of a market authorisation for a specific patented use there would be a liability risk in tort by marketing it for an unauthorised use). That would also constitute a rather straightforward infringement situation. The more complex scenarios are those where there is no market authorisation for a patented medical indication (hence a skinny label), and the drug is not actively promoted for use in a patented medical indication. However, there could be off-label use by the physician and the pharmacist. The question then arises whether there would be infringement even in a situation where the drug is as such not marketed for the patented medical indication, but happens to be so used in practice.

If it concerns such off-label use in general, such as for instance the administration of a different dosage to a patient sub-population, or the treatment of a disease which is still under patent protection, there are fundamentally two questions which deserve our attention. The first one is the question of whether that off-label prescription use can constitute an infringement. The second issue or question is, if such off-label use could constitute infringement, who can be held liable for such infringement?

In effect, even though the first question is very important as it sets the threshold for the second question, it is the latter question which will show to be most relevant. The question whether off-label use can constitute infringement is a relatively easy one, as the answer is affirmative, it being the use of a product for the use in the treatment of a patented medical indication. More complicated is the answer to the question as to who can be held liable for that infringement. At first glance, one would think that, as it is the physician who performs the off-label use, the latter would be liable. That is correct in itself, but it paints only a very partial picture. In order to obtain a complete overview of the infringement question, one has to analyse also the role of the other players in the "chain" to see whether these other players could also be held liable, as they could potentially present a more appealing target for patent holders. The main players in the chain are the generic drug manufacturer supplying the drug, the wholesaler supplying the drug further to the pharmacists, the said pharmacists dispensing the drugs to the patients,⁵³ and obviously also the physician prescribing the drug for a patented use. The final player in the chain is the patient taking the drug. We can already exclude the patient from being liable for any infringement, as the taking of the drug for a patented indication by the patient will always be considered to be a private use, and such use is exempted from infringement liability in the patent statute. *162⁵⁴

It is difficult to overestimate the relevance of the above questions. If one were to take the position that the generic drug manufacturer would be liable for infringement because of the off-label use by physicians and pharmacists for a patented medical indication, even in the case of a skinny-label product, then it would be very difficult for the generic manufacturers to continue doing their business. There will always be a credible risk for infringement, and there would be no way for the generic manufacturer to avoid such liability, even in a situation of a skinny-label use. Even though the manufacturing and the supply of the generic drug which is as such no longer patented cannot constitute an infringement in itself at first glance, the fact that that very drug can be prescribed and dispensed for a patented medical indication can trigger an infringement risk for the generic manufacturer, making it very difficult if at all possible to supply the generic drug at all. We will evaluate whether that risk is credible or not.

Additionally, apart from knowing which party can be held liable, it is also crucial to understand under which regime any of these parties could be held liable, and whether indeed all criteria have been fulfilled to hold them so liable. In fact, those questions are intrinsically linked. Even if one may have identified a potential party who can be held accountable, there can only be infringement if all requirements for infringement have been met, and that is not necessarily the case for all players in the chain under all circumstances.

To determine infringement, we have to distinguish between direct and indirect or contributory infringement. Direct infringement of a product patent is the situation where the generic drug manufacturer directly commits any of the exclusive acts of making, disposing of, offering to dispose of, using or importing the patented product or keeping it whether for disposal or otherwise supplying.⁵⁵ For the use of patented processes, that would imply using the patented process or offering it for use. Finally, but not less importantly, for the process of making a product, there will be infringement if the generic drug manufacturer disposes of, offers to dispose of, uses or imports the product directly obtained by the patented process. If the alleged infringer can prove that the product so directly obtained was made by means of a different process, there will be no infringement.⁵⁶ The latter defence is likely to be of very little or no use at all in the present situation. The novelty and inventive step of the manufacturing process does not reside in the process parameters, but in the medical indication of the product made by the manufacturing process. A potential infringer will have exactly that medical indication available for the product manufactured, as that is the only inventive contribution to the state of the art and hence the only subject-matter worth using.

Indirect or contributory infringement is the other type of infringement. In the UK, and for that matter in any other European country as the provision relating to indirect infringement is based on art.26 of the Community Patent Convention (which never entered into force), indirect infringement takes place when the alleged infringer supplies or offers to supply in the UK a person other than a licensee or other person entitled to work the invention with any of the means, relating to an essential element of the invention, for putting the invention into effect when he knows, or it is obvious to a reasonable person in the circumstances, that those means are suitable for putting, and are intended to put, the invention into effect in the UK.⁵⁷ Only manufacturing is not covered by indirect infringement. Applied to the subject-matter of this contribution, this would cover the situation where the generic drug manufacturer has supplied the drugs (which are the means relating to an essential element of the invention) for use by a third party to potentially ***163** directly infringe the patent, i.e. the other players in the chain, including the physician and the pharmacist. We will dwell further upon some of the specificities once we reach that point.

An additional layer of complexity is that, in the case of Europe, we have to make a distinction between two regimes. As we have seen earlier, under the "old" regime, patent protection for a further medical indication is claimed under the Swiss claim formula, which claims the use of a substance X for the manufacture of a medicament for the treatment of disease Y. Such a claim is in fact a manufacturing claim. Under the EPC 2000 system, a second medical indication claim would be a purpose-limited product claim, protecting the "product for the use in the treatment of medical indication Y".

Divergence between countries and the special case of Germany

Yet a further layer of complication is that the standards for determining infringement in this particular area do seem to vary between countries. The standard used in the UK will perhaps to a large extent not differ very much from the standard used in many other European countries (even though this is yet to be tested), but it seems to be quite different from the one applied in Germany. German case law has over the years developed a specific concept for determining whether there is infringement for medical indication claims, which is admittedly a rather complex one.⁵⁸

Under German case law, there can (or maybe we have to say "could" in view of recent case law, about which more further below) only be an issue of direct infringement for Swiss claims if there is something which is called "sinnfällige Herrichtung" or "manifest making-up".⁵⁹ Manifest making-up may lie in the particular configuration of the substance or article, or in the addition of a package leaflet. The addition of a package leaflet may be treated as a notional part of "manufacture". The article has to be "set up as such for the patented use". This means that there must be a direct and purposive connection between the measure of manifest making-up on the one hand and the production and sale of the product on the other hand, this connection holding the user unambiguously to the patent-protected use.⁶⁰ Under this rationale, a use claim to the use of a product for the treatment of a certain condition will only receive patent protection if already in the preparation of the product the patented use or treatment is conceived or aimed at.⁶¹ Preparation of a product without aiming at the treatment would hence not carry out the inventive idea, and it can consequently be argued that it would not constitute an infringement. The criterion of "manifest" in "manifest making-up" is only fulfilled when it is possible to determine on the basis of objective parameters that the protected purpose was aimed at, at the time of producing the drugs.⁶² Those objective parameters could be packaging, mentioning certain indications in the Summary of Product Characteristics or patient leaflet, and other objective parameters which allow one to conclude that the product has been brought on the market to treat a certain condition. *164⁶³

German case law does hence seem to look for

"some outward manifestation in the manufacture itself (which may include the packaging, but not advertising) which can be specifically attributed to the new use".⁶⁴

But it requires looking into the intentions of the manufacturer or user of the infringing product. Advertising for a certain use would, in the view of German case law, not constitute a "manifest making-up", however, which seems to be a rather narrow interpretation indeed.⁶⁵ That also shows some of the limitations of the concept. Under the case law, advertising the product for an infringing use would *not* constitute an infringement act, because it allegedly does not fall within the concept of the "manifest making-up". There is no making-up of the product as such by advertising. Arguably, this is likely to be different in other jurisdictions when it comes to determining knowledge of the generic manufacturer of intended use by the user, as we will see further on. It seems to show a rather narrow or restricted view of what is "manifestly making-up" under German case law, which is not likely to be found in other jurisdictions. It further seems that the concept of "manifest making-up" assumes some kind of intentional element in the mind of the manufacturer of the allegedly infringing product, something which also seems to be absent under UK law, as we will see later.

However, the idea that there could be direct infringement under German case law has come under pressure recently in the light of a very interesting case. Under German case law and the literature, for determining scope of protection and infringement a "use claim" ("Verwendungsanspruch"), as is also a Swiss claim, is put on an equal level with a product claim.⁶⁶ That means that, as a Swiss claim is considered to be a product claim, the supplying of the product which has been "manifestly made-up" would then constitute an infringing act. However, according to this recent case, there can only be direct infringement if the purpose or use of the claim has been effectuated by the party committing the alleged

infringement.⁶⁷ That would not be done by the supplier of the drugs (i.e. the generic manufacturer), as he is merely producing the drug and not using it for the patented medical indication; hence there would be no direct infringement, but it could be indirect infringement if all requirements to that effect have been fulfilled. We will discuss this further once we analyse the position of the various players in the chain.

Taking all of the above knowledge into account, we will now pursue a detailed analysis of the consequences of both statutory and case law made law regarding infringement for further medical indication claims.

Infringement liabilities—an overview

The reader will find Table 1 (below) a useful summary overview of the infringement risks for each player in the chain. As the table shows, this is an area of the law suffering from a major degree of legal uncertainty. The subsequent subsections of this part will analyse in detail those infringement risks.

YES/NO means that there is likely to be liability, but a defence could be invoked. *165

Table 1

Liability—Swiss infringement	Direct	Indirect—Swiss	Indirect
	—	—	—
	EPC 2000		EPC 2000
Physician	YES	NO	NO
	NO		
Pharmacist	YES	YES	YES
		NO	
Generic manufacturer	YES	YES	YES
	YES/NO	YES/NO	
	NO		
	NO		

Direct infringement

Direct infringement under the Swiss claim

As we have seen earlier, the Swiss claim is a process claim, and the relevant provisions under UK law would be [s.60\(1\)\(b\) and \(c\) of the UK Patents Act 1977](#). Of particular relevance here is [s.60\(1\)\(c\) of the Patents Act 1977](#) and other national equivalent provisions, which protects for a process claim also the product directly obtained by the patented process. In other words, with a process claim, those parties using the process would be directly infringing, but so would those who supply the product directly obtained by the patented process. For a Swiss claim, the product directly obtained by a claim for the use of a substance for the manufacture of a medicament for the use in the treatment of a certain medical indication, e.g. a certain type of pain, would be the drug so manufactured. In other words, for a Swiss claim that would imply that those who dispense the drug for that specific indication would be directly liable.

But that raises a crucial question, and that is when is there dispensing of the product so directly obtained in the case of s.60(1)(c), or for that matter when is there use of the patented process under s.60(1)(b) "for the use" in the specific claimed medical indication.

The reason for asking this question is that the process is not just any ordinary process for making a product. It is a process for making a product with a specific purpose. With the Court of Appeal in the [Warner Lambert v Actavis](#) case, it can be said that the part of the claim referring to "for use in the treatment of ..." must entail some kind of limitation, otherwise this claim would not be distinguishable from any other claim or for that matter from the prior art.

"For use"

The limitation "for use" requires at least some form of purpose or intention. The drug is not just produced; it is produced for a certain use, which exactly distinguishes the claimed process from the prior art products and processes. How can we interpret this limitation then?

As for the nature of the "for use" limitation, useful guidance can be taken from the UK [Warner-Lambert](#) case, where the Court of Appeal held that:

113. "I start with the claim of direct infringement under [section 60\(1\)\(c\) of the Act](#). The issue under this subsection is a question of construction of the claim. Like any such question, the task for the court is to determine what the skilled reader of the patent would understand the patentee to be using the language of the claim to mean. In this connection there is a certain amount of common ground in that both sides accept that the claim must involve some form of mental element. It is thus not sufficient to construe 'for' in the conventional, objective sense of 'suitable for'. The reason is that the skilled person would understand that the claim so construed could not possibly distinguish over known uses of the known drug, Pregabalin *166 as used for the known use would be 'suitable' in this sense for the new use. To construe the claim as covering the manufacture of a drug merely because it was suitable for pain treatment would be to give it a scope which was far broader than the patentee's contribution to the art.

114. The next point to note is that both parties have retreated to a degree from the common ground before the judge that 'for' means 'suitable and intended for'. Thus Mr Turner, in his written submissions, whilst continuing to accept that the claim requires an element of 'intention-like *mens rea*', submits that it is wrong to start with the word 'intention' and embark on an exercise of deciding what that means, and to go on to hold that that form of intention must be attributed to the manufacturer. The word in the claim is 'for', which denotes purpose. Mr Speck, for his part submits that it is not appropriate to fix on the word intention and then embark 'on a wide ranging review of how the word intention' or "intended" is used in different areas of the law' when the real issue is what the mental element in the claim is. I agree that a search for the appropriate meaning of 'intention' which does not appear in the claim, is likely to throw one off the scent. ...

122. *Against that background the skilled person would understand the word 'for' in the claim to be providing a link between the act of manufacture using pregabalin and the ultimate intentional use of the drug by the end user to treat pain.* The critical issue for me to decide is what is sufficient to constitute that link. An extreme view might be that if the drug is in fact used for the patented indication then it has been made 'for' that indication, whatever the manufacturer's intention might be. Mr Turner did not contend for that construction. I think he was right not to do so. It would mean that a manufacturer could not tell whether he had made use of the subject matter until after, and perhaps a long time after, he had disposed of the product. The realistic candidates are therefore (a) foreseeability that the drug will intentionally be used for the patented indication and (b) a subjective intention to that effect. ...

126. The test which I have proposed has structural similarities to that under [section 60\(2\)](#), where the question is also what a person (in that case the seller) knows or could reasonably foresee about the end use of a product. That, of course, is not a reason for adopting it when construing the claim in this patent. It does, however, provide confirmation that the test I have proposed is a workable one. On the other hand, I can see real difficulties with the application of an 'aiming or targeting' test in the present circumstances if it means more than the test I have proposed. It means in effect that the

patentee must prove that it is Actavis' wish or desire that they sell some Lecaent for pain. How does the patentee go about establishing this wish or desire if it is not enough to show that it is known or foreseeable that some of their product is being intentionally used for pain? It seems to me that there is substance in Mr Turner's complaint that to adopt such a strict requirement of intention will rob Swiss claims of much of their enforceability.

127. *I can therefore see no reason why the skilled person would conclude that the word 'for' implied subjective intent. He would understand that the manufacturer who knows (and for this purpose constructive knowledge is enough) or could reasonably foresee that some of his drug will intentionally be used for pain is making use of the patentee's inventive contribution, in the same way as a manufacturer who actively desires that result. In my judgment, therefore, the skilled person would understand that the patentee was using the word 'for' in the claim to require that the manufacturer knows (in the above sense) or can reasonably foresee the ultimate intentional use for pain, not that he have that specific intention or desire himself.* *167 ...

129. Turning to the second question, section 60(1)(b) makes it an infringement to use the process. Unlike 'offering a process for use' and indirect infringement under section 60(2), liability under this part of section 60(1)(b) has no mental requirement: liability is strict. How does one tell whether a manufacturer is using the manufacturing process of the claim, and therefore rendering himself liable for patent infringement? *The answer must be when he manufactures pregabalin when he knows or foresees that users will intentionally administer it for pain.*" ⁶⁸

If we can believe the UK court, the standard for interpreting the word "for use" in a purpose-limited Swiss claim would in any event not mean subjective intent, but would mean that if the manufacturer knows or could reasonably foresee that some of his drug will intentionally be used for pain is making use of the patentee's inventive contribution, there could be an issue of direct infringement. That is a very low standard indeed, and it can in fact be assumed that every generic manufacturer can reasonably foresee that some of his drugs will be intentionally used for a patented use, as every generic manufacturer is aware of off-label use by physicians. The UK court also concluded that no subjective intent was required on the side of the infringer.

The above standard and the manner we can interpret it would lead to the situation that a generic manufacturer would always be liable for infringement, as soon as there was knowledge on the side of the manufacturer that the drugs so produced would be intentionally used in a patented medical indication. It would in that connection not matter how small the proportion was of the drugs that would be intentionally used for a patented medical indication.

And it is exactly for that consequence that its reasoning has come under fire by the recent judgment of Arnold J in the same case. Actavis argued that:

"Floyd LJ's construction apparently had the consequence that, if it was foreseeable to an unlicensed manufacturer of pregabalin that 'some of his drug' (as Floyd LJ put it at [127], emphasis added) would be intentionally administered for the treatment of pain, then all of that manufacturer's acts of manufacture of pregabalin would be infringing acts even though it was foreseeable that the remainder of its pregabalin would be administered for the treatment of non-patented indications ... Furthermore, this would be so even if it was foreseeable that the majority (possibly even the vast majority, depending on what was meant by 'some') of the pregabalin made by that manufacturer would be administered for the treatment of the non-patented indications and even if the majority (possibly the vast majority) was in fact administered for the treatment of those indications. Still further, all of the pregabalin would be infringing product, and thus anyone who subsequently dealt in it would also infringe on a strict liability basis." ⁶⁹

Arnold J held that:

"I think it is reasonably clear from Floyd LJ's judgment that he did not intend his interpretation to have this consequence. The only indication I can see as to how he thought it was to be avoided, however, comes when he discusses the question of remedies. As noted above, he suggested that any 'potential unfairness' of his interpretation in the first of the two 'hard cases' he considered could be mitigated by restricting the scope of the injunction so that it did not prevent the sale of the product. This suggests that he considered that the injunction might somehow be tailored so as only to prohibit

manufacture of pregabalin which it was foreseeable would be intentionally administered to treat pain, and not pregabalin which it was foreseeable would be administered for non-patented indications, although his statement that it might be unjust to grant an injunction at all indicates that he appreciated *168 that this could be very difficult. Similarly, it appears that he envisaged that the financial remedy would only apply to pregabalin which it was foreseeable would be intentionally administered to treat pain, presumably on a statistical basis." 70

I think it is clear from the above that tailoring injunctive relief with a view to avoiding the generic manufacturer in fact being harmed in his legitimate business of selling generic drugs for non-patented indications is a very difficult task indeed, with which the courts even admit themselves that they struggle. The generic manufacturer cannot predict which pack of the generic drugs it produces will in effect be used for a patented medical indication, and it can be questioned how this can be determined in real life. Where Floyd LJ suggests that no injunctive relief should be granted at all, it must be said that even though this sounds to some extent equitable, it poses serious questions as to how second medical indication claims could then usefully be enforced in this context, if one assumes this would be a desirable avenue.

The intentional element

A subsequent question is then, once one accepts that the wording "for" included an intentional element, how that intentional element is to be interpreted. The recent judgment in the [Actavis v Warner Lambert](#) case discussed this issue:

634. "... Floyd LJ made it clear at [121] that intentional administration was at the heart of the invention, at [122] that the word 'for' provided the link between the manufacture of pregabalin and the intentional use of the drug, at [127] that the word 'for' required knowledge or foresight of the ultimate intentional use, at [128] that there were two mental states involved and at [129] that a manufacturer infringes when he knows or foresees that users will intentionally administer pregabalin for the treatment of pain. Thus the requirement of intention is central to his interpretation. It is plainly not a pure test of foreseeability ...

635. Secondly, if intention is required, counsel for Pfizer advanced three alternative cases as to how that requirement could be fulfilled. The first alternative is predicated on the assumption that the relevant intention is that of the prescribing doctor. On that basis, counsel for Pfizer submitted that it was sufficient if the doctor intends pregabalin from any source to be administered to the patient for the treatment of pain. The second alternative is predicated on the assumption that the relevant intention is that of the dispensing pharmacist, if necessary in combination with the doctor. On that assumption, counsel for Pfizer submitted it was sufficient that the pharmacist knows that the doctor has prescribed pregabalin for pain and dispenses the generic manufacturer's product. The third alternative is predicated on the assumption that the relevant intention was that of the patient, if necessary in combination with the doctor and pharmacist. On that assumption, counsel for Pfizer submitted it was sufficient that the patient knows that the doctor has prescribed pregabalin for pain and that the pharmacist has dispensed the generic manufacturer's product.

636. Counsel for Actavis submitted that the relevant intention was that of the prescribing doctor. *I agree that the intention of the doctor is highly relevant, if not exclusively so. Floyd LJ expressly referred to 'the doctor' at [119], and at [121] he made the point that the novelty of the claim derives from 'the intention of producing the new therapeutic effect'. It is the prescribing doctor who intends to produce the new therapeutic effect (here treating pain) because it is the doctor who has the requisite medical knowledge (derived from the SmPC for Lyrica, and hence from the clinical trials carried out by Pfizer to substantiate the claim made in the Patent of efficacy for neuropathic pain, or from the doctor's appreciation that *169 pregabalin may also be effective for treating other kinds of pain if prescribed off-label, as is also claimed in the Patent).*

637. Counsel for Actavis also submitted that it was not sufficient that the prescribing doctor intended pregabalin from any source to be administered for the treatment of pain. I agree with this. Floyd LJ expressly referred at [127] to the manufacturer foreseeing that 'some of his drug will intentionally be used for pain [emphasis added]'. Furthermore, it would make no sense for it to be sufficient that the doctor intended pregabalin from any source to be administered for pain. Infringement must depend on what the manufacturer can foresee happening with the pregabalin it manufactures, not pregabalin made by others. Moreover, statistically, it would be probable that pregabalin from any source would be made by Pfizer and hence non-infringing on any view.

638. What about the pharmacist? Floyd LJ does not expressly refer to the pharmacist in his analysis, but as counsel for Pfizer pointed out, his language in [122]–[129] is quite general, referring, for example, to ‘intentional use for pain’. After considerable hesitation, I have concluded that, on Floyd LJ’s reasoning, the intention of the pharmacist is also relevant. *In general, of course, the pharmacist will simply intend to dispense the drug which the doctor has prescribed for the purpose of treating whatever indication the doctor has prescribed that drug for. Moreover, in general, the pharmacist will not know what that indication is. In those circumstances the pharmacist’s intention adds nothing to that of the doctor. Even if the doctor prescribes generic pregabalin for treating pain and the pharmacist dispenses the generic manufacturer’s product, neither the doctor nor the pharmacist nor the two in combination will have intended that that product be administered for the treatment of pain.* But what if the pharmacist knows that the doctor has prescribed generic pregabalin for treating pain and the pharmacist dispenses the generic manufacturer’s product? In those circumstances it seems to me that it can be said that the result is intentional administration of the generic manufacturer’s product to treat pain.

639. As for the patient, notwithstanding Floyd LJ’s reference in [128] to ‘the end user’, I cannot see that the patient’s intention is relevant. The patient is the one who is being treated. In general the patient intends to take whatever drug the doctor has prescribed for whatever condition the doctor has prescribed it for. Usually the patient will not have any medical knowledge about the efficacy of that drug for that condition. Moreover, the patient will rely on the pharmacist to dispense the correct drug, and in general the patient will not have any choice as to the source of that drug. Indeed, many patients will be oblivious to the source of the drug.”⁷¹

I think this is a very semantic approach to the requirement of intention. If I understand the judgment correctly, the intentional element would only be proven and hence there could only be infringement if the physician had prescribed a specific generic drug from a specific manufacturer and/or the pharmacist had dispensed as a consequence of that prescription also a generic drug from that specific manufacturer. As that is unlikely to ever happen, I think it shuts the door quite firmly on infringement. This can or cannot be an equitable solution, but I think it is questionable on legal grounds. I will come back to this in the subsection “Concluding comments” and in the section “Policy considerations and proposed solutions” below. *170

Application to the various players in the chain

Let us now try to apply the above principles to the various players in the chain. What about the physician prescribing the medicament and the pharmacist dispensing the medicament under such a Swiss claim? The claim is a manufacturing claim, i.e. the use of a substance for the production of a drug for a certain medical indication. For the physician and the pharmacist, there does not seem to be an issue under s.60(1)(b), as those players are not using the substance for any manufacturing. But what about s.60(1)(c), which protects also the product so directly obtained and hence penalises any use or dispensing of the substance obtained by the patented process? As we have seen, one has to assume that the purpose limitation is relevant and to be taken into account.

The physician will “use” the product so obtained for the patented medical indication, and will do so intentionally in the meaning we have explained above. There could hence be an infringement issue here.⁷² In the view of the UK High Court in the [Warner Lambert](#) case (which has to that effect been overruled in appeal), even though it can be agreed that the product so obtained is the medicament, the doctor is still not affected by the claim. The reason for this is that the process is for the manufacture of a medicament for a specific use, and the intention in the “for use” or “for the treatment” limitations needs to be evaluated from the perspective of the party carrying out the process of manufacture, and not the prescribing physician or dispensing pharmacist.⁷³ Arnold J repeated that position recently in the [Warner Lambert](#) case when it came back to him as the trial judge:

“Although at one stage (see in particular the letter to the Department of Health dated 28 October 2014 quoted in paragraph 696 below) Pfizer asserted that doctors would infringe the Patent if they prescribed generic pregabalin for pain, counsel for Pfizer accepted in her closing submissions at trial that doctors did not infringe. In any event, it is very difficult to see how a doctor could be liable for infringement of the Patent merely by writing a generic prescription

for pregabalin for pain, since for all the doctor would know the prescription could well be fulfilled by the pharmacist dispensing Lyrica." ⁷⁴

I would not agree with that analysis, and nor did the Court of Appeal. The liability under s.60(1)(c) is for the product directly obtained by the patented process, and as a manufacturing claim is a process of making a product, the product directly obtained is the drug so manufactured. A use of a substance for the manufacture is in fact nothing more than a method for making a product, and hence the product directly obtained is the drug so produced. One needs obviously take into account the element of "intention" laid down in the wording "for use" or "for the treatment", but that needs to be analysed from the perspective of the person using the product directly obtained by the patented process, as that is what the statute protects against. Arguing otherwise would take away the enforceability of the manufacturing claim against anyone who uses the product directly obtained apart from the manufacturer, and I am not sure that this is what the legislature has intended. The aim of the introduction of this provision was to strengthen process protection, ⁷⁵ and it would go against that purpose to provide such a limited scope as the one suggested by the High Court and some of the literature. It would otherwise allow having no infringer at all if for instance the manufacturing would have happened in a non-patent country, and the use of the product directly *171 obtained were to take place in a country where there is patent protection. Taking the position that only the manufacturer is addressed would imply that no one would be liable.

If we applied the German approach, with the "sinnfällige Herrichtung", there would equally be a problem for the physician, as he/she would put the purpose of the claim, i.e. the use in the treatment of the patented medical indication, into effect, and under recent case law that may constitute a direct infringement.

The pharmacist would also dispense the product so directly obtained for the patented use, but is unlikely to know that he has dispensed it for that particular purpose, as the prescription does not contain any information as to the intended purpose. ⁷⁶ However, if one follows the reasoning developed by the Court of Appeal in the [Warner Lambert](#) case, the criterion should be that he knows (and for this purpose constructive knowledge is enough) or could reasonably foresee that some of the drug he dispenses will intentionally be used for pain. By doing and knowing that, he is making use of the patentee's inventive contribution, and there could hence be a direct infringement issue under s.60(1)(c). ⁷⁷ Following the German approach would not lead to a fundamentally different answer here. The reasoning would then be that the pharmacist dispenses the drug which has been "manifestly made up" for the patented use. ⁷⁸ The problem I have with this conclusion is that it assumes that the products which the pharmacist dispenses have indeed been so "manifestly made up". But that needs to be proven, I would assume, which would require that one first identifies the subjective intent of the producer of the drug.

The extemporaneous preparation by the pharmacist, which is exempted from patent infringement in a number of jurisdictions, ⁷⁹ is unlikely to be of any relevance here. As said earlier, no infringement issue arises under s.60(1)(b), as the pharmacist is not using the process.

What about the generic drug manufacturer? Once again, we have to distinguish between infringement of the process under s.60(1)(b), and infringement of the process by supplying the product directly obtained by the patented process under s.60(1)(c). As we have seen above when we discussed the parameters of what is meant to be understood by the limitation "for use", the generic manufacturer runs the risk of facing an infringement claim if he knows (and for this purpose constructive knowledge is enough) or could reasonably foresee that some of his drug will intentionally be used for pain because he would then be making use of the patentee's inventive contribution, in the same way as a manufacturer who actively desires that result. As we have said above, the threshold for the standard developed by the UK courts seems to be rather low. As far as s.60(1)(b) is concerned, if it can be proven that the generic manufacturer is using the manufacturing process for making a certain drug for the use in a claimed treatment, and he knows or foresees that the drug so produced will be used intentionally for the protected treatment, there seems to be a good case for infringement. ⁸⁰

As far as s.60(1)(c) is concerned, the situation is very similar to the ones for the physician and pharmacist, with the only difference that it is likely to be more easy to prove that the generic manufacturer who dispenses the product directly obtained by the manufacturing process, i.e. the drug, knows (and for this purpose constructive knowledge is enough) or could reasonably foresee that some of his drug will intentionally be used for pain is making use of the patentee's inventive contribution, and this would hence constitute a direct infringement. That would be the case, notwithstanding the hypothesis that the generic manufacturer would have performed so-called skinny labelling, i.e. has carved out the patented medical indication from the market authorisation, Summary of Product Characteristics and the leaflet coming with the package.

As we have said earlier, there could be a defence in the context of injunctive relief if the generic manufacturer could prove that he had taken all reasonable measures to prevent the drug he produced being *172 used intentionally for a patented medical indication.⁸¹ Furthermore, any injunction has to ensure that it does not pose a barrier to legitimate trade. As Arnold J said in the Warner Lambert case:

656. "I accept that, in general, a defendant is under a statutory duty not to infringe a patent. I also accept that, in general, it is up to the defendant to decide what to do to avoid infringement and to take the necessary steps to achieve that. I do not accept that that is the end of the matter, however. *For the reasons I discussed in HTC Corp v Nokia Corp [2013] EWHC 3778 (Pat), [2014] Bus LR 217 at [3–[32], I consider that the court is required to ensure that an injunction is proportionate and does not create barriers to legitimate trade.* I understood counsel for Pfizer to accept this. In an appropriate case that may require the form of the injunction to be more specific than the conventional general form: see e.g. *Oracle America Inc v M-Tech Data Ltd [2012] UKSC 27, [2012] 1 WLR 2026 at [10]* (Lord Sumption).

657. *In the present circumstances it is arguable that the grant of an injunction in general form would be disproportionate and/or create barriers to legitimate trade since it would be likely to force Actavis' withdrawal from the lawful market for the non-patented indications.* The same applies to the specific forms of injunction sought by Pfizer in the alternative. As Floyd LJ suggested, it might therefore not be appropriate to grant an injunction at all."⁸²

Additionally, we have to take into account the intentional element as well, as developed by Arnold J in the *Warner Lambert* cases. As we have seen above, the intention of both the physician and the pharmacist needs to be taken into account with a view to establish whether there is infringement. Even if the doctor prescribes a generic version of a drug for treating a patented medical indication and the pharmacist dispenses the generic manufacturer's product, "neither the doctor nor the pharmacist nor the two in combination, will have *intended* that *that* product be administered for the treatment of the patented medical indication".⁸³ As we have seen, this will in most cases firmly shut the door on a successful infringement claim.

Even though it may be an equitable solution, as we have seen earlier, we see no ground for agreeing with it from a legal point of view. It seems also to be in conflict with what was held by the Court of Appeal in the same case.

Under the German approach, the situation is somewhat complicated. Under the less than very recent case law of higher courts, there would be a direct infringement if the products so produced and disposed of have been "manifestly made-up" for the patented use. There is no need to refer to the concept of products directly obtained by the patented process, as under German case law a use claim for a medical use can for determining scope and infringement be equalised with a product claim. We have seen earlier that this "manifestly making-up" is not necessarily an easy concept to understand, and that it may presuppose that there is an element of subjective intent required in the mind of the party producing the drugs that those products are aimed at use in the patented medical indication. It would, under this approach, hence depend on the evidence as to whether that subjective intentional element can be proven.

Following the recent LG Hamburg case, there can only be direct infringement if the purpose or use of the claim has been effectuated by the party committing the alleged infringement.⁸⁴ That would not be done by the supplier of the drugs (i.e. the generic manufacturer), as he is merely producing the drug and not using it for the patented medical indication,

hence there would be no direct infringement, but it could be indirect infringement if all requirements to that effect have been fulfilled. Following that case law, there would be *no* direct infringement for the generic drug manufacturer. *173

Equally, under German case law, it has been decided that subscribing to repayment contracts for providing drugs under the national health insurance system would in any event be considered to be such a making-up, if such commitment would not exclude the patented use from the scope of application of such contracts.⁸⁵ The UK courts have not expressed themselves finally on this issue. In the Netherlands, it has been decided that if a generic manufacturer gains a tender contract with a health insurer for the supply of drugs, and knowing that the tender did not exclude any patented medical indications from the contract, then there is a question of (indirect) infringement.⁸⁶

Interestingly, in a recent Dutch case, the Court of Appeal held that in a second medical use claim relating to ribavirin covering a sub-population, there could be no direct infringement of the Swiss claim by the generic manufacturer. The Summary of Product Characteristics (SmPC) for the generic drug explicitly excluded the patented medical indication, i.e. the specific sub-population.⁸⁷ The court reasoned that the fact that the present patent claim covers a sub-population implies that the active ingredient had already been used for the entire population prior to patenting the sub-group as a medical indication. There can only be infringement if the alleged infringer would benefit from the patented indication. That could only be the case if the generic manufacturer specifically indicates that the medicines so produced are destined for use in the sub-group. In the view of the court this was not the case, demonstrated by the SmPC limitations. There was consequently no direct infringement.⁸⁸

The patient taking the product with the patented medical indication (e.g. the patented dosage) is in principle also a direct infringer under this scheme, as he uses the product directly obtained by the patented process for the patented medical indication, but as this is a private use, this act is exempted from patent infringement under most patent acts.⁸⁹

Direct infringement under the EPC 2000 purpose limited product claim

An important subsequent scenario one has to evaluate is the new claim formulation which has been introduced by the EPC 2000. According to the new art. 54(5) EPC, a patent claim can now protect the "product for the use in the treatment of disease Y". In other words, a purpose limited product claim will now cover the product limited to the medical indication claimed. Under the rules of direct infringement, where the invention is a product, he who makes, disposes of, offers to dispose of, uses or imports the product or keeps it whether for disposal or otherwise commits a direct infringement (s.60(1)(a) UK Patents Act 1977).

As the new claim formula is a purpose limited product claim, the exclusive acts need to be carried out with the purpose limitation in mind. In other words, in our view all that has been said earlier about the knowledge or foreseeability that the product will be used intentionally for the use in the patented medical indication seems to be equally applicable here *mutatis mutandis*. It makes in our view no difference in interpreting the meaning of the words "for use" whether it concerns a Swiss-type process claim or whether it concerns a purpose limited product claim. In both instances, the relevant issue is to construe to meaning of the "for use" limitation, and that seems to be the same. As the new type of claim has only been introduced since 2007 (and knowing that it takes quite a few years to get a patent application to grant), it is too early to have case law in this regard.⁹⁰ What follows is based on our own analysis. *174

Equally so, the purpose limited product claim format would in our view also make no difference for the application of the German "manifest making-up" approach, further supported by the fact that German case law equalises a method claim for a medical treatment with a product claim.⁹¹

Application to the various players in the chain

When we want to apply the above principles to the various players, it deserves mentioning that it will probably be easier to prove infringement, as liability for infringement of a product claim is not dependent on the use of any specific process. Making, dispensing and using the patented product will be an infringement.

As far as the physician is concerned, it could be argued that he uses the patented product for the patented medical indication. If we consider that there is the additional element of knowledge of an intentional use for the patented medical indication, that does not seem to take away any of the liability, as the physician will have perfect knowledge of the intentional use, as he is the one who is performing the use. Arnold J in the [Warner Lambert](#) case, when it came back to him as the trial judge, was of the view that there was no infringement under a process Swiss claim, and looking at his reasoning, there is no reason to assume that it would be different for a product claim:

"Although at one stage (see in particular the letter to the Department of Health dated 28 October 2014 quoted in paragraph 696 below) Pfizer asserted that doctors would infringe the Patent if they prescribed generic pregabalin for pain, counsel for Pfizer accepted in her closing submissions at trial that doctors did not infringe. In any event, it is very difficult to see how a doctor could be liable for infringement of the Patent merely by writing a generic prescription for pregabalin for pain, since for all the doctor would know the prescription could well be fulfilled by the pharmacist dispensing Lyrica." ⁹²

We have said earlier that we think this reasoning is not correct. ⁹³

Following the German approach, as a use claim was already interpreted for purposes of determining scope and infringement as a product claim, the answers would be identical to the ones given for the Swiss claim. If we apply the German approach, with the "sinnfällige Herrichtung", there will equally be a problem for the physician, as he/she will put the purpose of the claim, i.e. the use in the treatment of the patented medical indication into effect, and under recent case law, that may constitute a direct infringement.

With regard to the pharmacist, even though it is unlikely to know that he has dispensed the patented product for the particular patented purpose, as the prescription does not contain any information as to the intended purpose, applying the UK [Warner Lambert](#) case, the criterion should be that it knows (and for this purpose constructive knowledge is enough) or could reasonably foresee that some of the drug it dispenses will intentionally be used for the patented medical indication. By doing so and knowing that, it is making use of the patentee's inventive contribution, and there could hence be a direct infringement issue under s.60(1)(a), as it dispenses a product that is patent protected for a specific use.

Following the German approach would not lead to a fundamentally different answer here. The reasoning would then be that the pharmacist dispenses the drug which has been "manifestly made-up" for the patented use. ⁹⁴ The problem I once again have here with this conclusion is that it assumes that the products which the pharmacist dispenses have indeed been so "manifestly made up". But that needs to be proven, I would assume, which would require that one first identifies the subjective intent of the producer of the drug. *175

The extemporaneous preparation by the pharmacist, which is exempted from patent infringement in a number of jurisdictions, is equally here unlikely to be of any relevance.

In respect of the generic manufacturer, the following needs to be mentioned. The generic manufacturer will make, dispense, etc., the patented product. There will be infringement if those acts are performed with the patented medical indication in mind. Once again, everything that has been said earlier in the context of Swiss claims regarding generic manufacturers seems to be applicable mutatis mutandis, with the additional comment that as this is a product claim, no

recourse must be had to constructs of products directly obtained by the patented process, which will make establishing infringement at least from that perspective easier.

In conclusion, skinny labelling and carving out of the patented medical indication from the market authorisation will as such not suffice to escape infringement, as even despite such carving out, the generic manufacturer will often have knowledge that the product he supplies will be used for use in the patented medical indication, and under the UK standard this would suffice to establish infringement.

As said earlier, there could be a defence in the context of injunctive relief if the generic manufacturer could prove that he has taken all reasonable measures to prevent that the drug he produces is to be used intentionally for a patented medical indication.⁹⁵ Furthermore, any injunction has to ensure that it does not pose a barrier to legitimate trade.⁹⁶

Also here, in line with what we have said when dealing with direct infringement for Swiss claims, we have to take into account the intentional element as well, as developed by Arnold J in the [Warner Lambert](#) cases. As we have seen above, the intention of both the physician and the pharmacist needs to be taken into account with a view to establish whether there is infringement. Even if the doctor prescribes a generic version of a drug for treating a patented medical indication and the pharmacist dispenses the generic manufacturer's product, "neither the doctor nor the pharmacist, nor the two in combination, will have *intended* that *that* product be administered for the treatment of the patented medical indication".⁹⁷ As we have seen, this will in most cases firmly shut the door on a successful infringement claim. I think his reasoning would equally be applicable to the situation of a product claim.

Also here, even though it may be an equitable solution, as we have seen earlier, we see no ground for agreeing with it from a legal point of view. It seems also to be in conflict with what was held by the Court of Appeal in the same case.

Under the German approach, the situation is as we know somewhat complicated. Similar as for Swiss claims, under the less than very recent case law of higher courts, there would be a direct infringement if the products so produced and disposed of have been "manifestly made-up" for the patented use. There is no need to refer to the concept of products directly obtained by the patented process, as under German case law a use claim for a medical use can for determining scope and infringement be equalised with a product claim. We have seen earlier that this "manifestly making-up" is not necessarily an easy concept to understand. In our view, that criterion would still be fulfilled despite a carving out, for instance because the drug has been available under a health insurance tender contract for all medical indications.

As already explained when discussing Swiss claims, following the recent LG Hamburg case, there can only be direct infringement if the purpose or use of the claim has been effectuated by the party committing the alleged infringement.⁹⁸ That would not be done by the supplier of the drugs (i.e. the generic manufacturer), as he is merely producing the drug and not using it for the patented medical indication, hence there would be no direct infringement, but it could be indirect infringement if all requirements to that effect have been fulfilled. Following that case law, there would be *no* direct infringement for the generic drug manufacturer. *176

The already discussed recent Dutch case relating to sub-populations would in our view not be decided differently if it concerned a product claim.⁹⁹ There will consequently be no direct infringement under a product claim.

Equally in line with what was said under the analysis of direct infringement for Swiss claims, the patient taking the product for the patented medical indication (e.g. the patented dosage) is in principle also direct infringer under this scheme, as he uses the product for the patented medical indication, but as this is a private use, this act is as already seen exempted from patent infringement under most patent acts.

Concluding comments

The UK approach uses a requirement of knowledge in the mind of the alleged infringer that the product will be intentionally used for a patented use. There is some merit in the approach followed by the UK court. A purpose limited Swiss claim (but for that matter also a purpose limited product claim) aims to protect the use of a product for a specific new and inventive use. It is that new use that is the centre of the invention. The contribution lies in the new use. Protection is given for the use of the product for that new use (or for the product for that use in a purpose-limited product claim). The scope of protection will at least also cover any product for the patented use (as the product directly obtained by the patented process in a Swiss claim, or as the product for that use in a product claim). As the invention aims to protect a specific new and inventive use, it is not illogical to argue that in order to conclude whether there is infringement, the purpose of the claim must be put into effect, i.e. use for the patented medical indication. It is equally not illogical to say that if a party knows that the products it manufactures will be used for the patented use, that party would be liable for infringement, even though it is admittedly a rather low standard. We then also assume that the wording "intentional use" should be understood as meaning that the party using the product has the intention to use it in a way protected by the patent, e.g. for the treatment of certain pain protected by the patent. Such an interpretation would indeed make sense.

An additional layer of the analysis will require that it should be established how the intentional element is fulfilled and by which party. Here the reasoning of Arnold J is at best difficult to follow, and it can be questioned whether it is indeed a proper interpretation of the intentional element. He concedes that the intention of the doctor in prescribing the generic drug for a patented medical indication is highly relevant in establishing the intentional element, which is definitely an acceptable premise. But he then continues by holding that, even if the doctor prescribes the generic drug for a patented medical indication and the pharmacist dispenses the generic manufacturer's product, "neither the doctor nor the pharmacist nor the two in combination will have *intended* that *that* product be administered" for use in the patentee medical indication, *in casu* the treatment of pain.¹⁰⁰

In my view, the above is an extreme semantic interpretation of the intentional element. If I understand the judgement correctly, the intentional element would only be proven and hence there could only be infringement if the physician had prescribed a specific generic drug from a specific manufacturer and/or the pharmacist would as a consequence of that prescription have also dispensed a generic drug from that specific manufacturer. The reader should be informed that I do not say that the pharmacist would have dispensed a drug from a specific generic manufacturer, as that is what he will always do. The argument is that the pharmacist, as a result of a specific prescription from a physician prescribing a specific generic drug from a specific manufacturer for a patented medical indication, will dispense that very specific generic drug from that specific generic manufacturer for the treatment of the specific patented medical indication. It is clear that such a threshold will almost never be met. Even though the threshold that there could be infringement if the alleged infringer (generic manufacturer) knows that his drugs are intentionally going *177 to be used for the treatment of a patented medical indication is quite low indeed, as we have seen above, the consequences of this low threshold seem to be entirely reversed by the extreme semantic approach explained above.

The probable consequence of this semantic approach by Arnold J is that there will never be infringement. That casts serious doubts over the enforceability of further medical indication claims in a context of off-label use. I also doubt whether his interpretation is in conformity with what Floyd LJ held. Evidence for that doubt is that Floyd LJ was actually quite concerned that there would be a serious case of infringement for the generic manufacturer which might also have an effect on the non-infringing part of that manufacturer's business (some of the drugs produced and supplied will be used for non-infringing applications, some for patented medical indications), but his view was that such infringement should be remedied in the injunctive relief stage, as discussed earlier. Floyd LJ said in this context:

132. "Another hard case is that in which a defendant has taken all the steps open to him to avoid his medicine being prescribed for the new use, yet those steps are, due to the structure of the marketplace, insufficient to stop it happening. Actavis' test would provide a defence in those circumstances, because the defendant could credibly say that he did not

target those sales which he was striving manfully to prevent. The hard case arises because of the peculiarities of the UK's market place for drugs. Normally a vendor of a product can control by contract the uses to which his product is put and require any intermediary to include similar terms. I do not think we should allow the regulatory environment to dictate the scope of the claim in this way." ¹⁰¹

The above suggests that a generic manufacturer who is taking all reasonable steps to prevent the generic drug he supplied being used for an infringing use, but is not capable of doing so, and hence has knowledge that the drug is going to be intentionally used for a patented use, would have a defence in an infringement case.

It is submitted that the discussion is a very difficult one indeed. On the one hand there is a legitimate interest on the part of generic manufacturers, but also on the part of society as a whole, that generic drugs can be sold for non-patented medical indications. On the other hand there are also the interests of patent holders to be able to enforce their patent rights. The issue of off-label use puts pressure on reconciling these interests. We could collectively decide that we prefer that generic drugs should be available at all times, in which case a very narrow interpretation of infringement concepts would be required. One must ask oneself the question, however, whether reverting to an extreme semantic interpretation of the statute to achieve that effect, while at the same time largely denying enforceability of second medical indication claims, is the approach to follow. Off-label use does have the real effect of harming the interests of the patent holder who will lose revenue to generic manufacturers: the case law is clear on this. The solution provided by Floyd LJ that a generic manufacturer would have a defence in an infringement claim if he can credibly say that he did not target those sales which he was striving manfully to prevent ¹⁰² seems to be a fairer and more reasonable solution. We could of course also decide that the most effective solution could be to ignore or even abolish second medical indication patents, but it can be questioned whether that is not throwing away the baby with the bathwater. We will discuss this further in the section below dealing with policy suggestions.

It must also be said that the approach followed in the UK is not necessarily followed in all other European countries and in the literature. It has been argued in the literature that, with a view to bringing a case of direct infringement, the party committing the allegedly infringing acts must have committed those acts with the aim of putting into effect the purpose of the claim, i.e. the use for medical treatment. An implicit, *178 non-desired use or a use for the patented purpose that was not intended by the party committing the acts would not constitute a direct patent infringement, as even though the product which is patented is used (or any other exclusive act is performed), it is not done so with a view to carry out the patented purpose. ¹⁰³ That would imply that a subjective element of intent is required, i.e. the party manufacturing the products must have the intention that those products will be used for the patented use. It is not surprising that the literature expressing this view is German, as this approach is very akin if not entirely based on the case law based concept of "manifest making-up" or "sinnfällige Herrichtung", which we have explained earlier. ¹⁰⁴ It has been held that there can be no direct patent infringement in situation of off-label or cross-label use if there is no "sinnfällige Herrichtung" to use the drugs so produced for the patented medical indication by the generic manufacturer. ¹⁰⁵ Such a standard would be stricter.

The UK approach would accept that there is infringement if the party who supplies the products knows that the user of those products intends to use them for a patented medical indication. But it does not require that the party who supplies the products must have put them on the market with the intention that the parties who use them put the invention into effect. The German approach requiring the "manifest making-up" seems to require a more subjective element of intent in the mind of the manufacturer of the drugs, i.e. he must have prepared the products in one way or the other so that they can be used for an infringing use. The fact that the products so made are suitable for the intended use is not sufficient. ¹⁰⁶

Even though such a test sounds more equitable at first glance, it could present evidentiary issues. How does one show the element of intent? Take for instance the example where a drug manufacturer may have produced the drug, offers it for sale for non-patented uses, but finds itself suddenly confronted with the situation that there is an off-label use. Under the German approach, if there is no evidence that the drugs produced have been "made-up" for the patented use, there

would be no infringement, even though he might very well have knowledge that there will be off-label use for a patented medical indication. As knowledge is not enough, there is only infringement if an element of intent can be proven.

The UK Court in the [Warner Lambert v Actavis](#) case already alluded to this issue as well for not adopting such a strict standard:

"On the other hand, I can see real difficulties with the application of an 'aiming or targeting' test in the present circumstances if it means more than the test I have proposed. It means in effect that the patentee must prove that it is Actavis' wish or desire that they sell some Lecaent for pain. How does the patentee go about establishing this wish or desire if it is not enough to show that it is known or foreseeable that some of their product is being intentionally used for pain? It seems to me that there is substance in Mr Turner's complaint that to adopt such a strict requirement of intention will rob Swiss claims of much of their enforceability." ¹⁰⁷

We will come back to this thorny issue in the section "Policy considerations and proposed solutions" below. *179

Depending on the interpretation followed, it emerges that off-label use for patented medical indications is likely to present real infringement risks for all players in the chain. Depending on the stance taken, a generic manufacturer who is lawfully entitled to supply generic versions of drugs for non-patented medical indications faces infringement liability if his generic drugs are prescribed and dispensed for patented medical indications, even though the generic manufacturer may not have wanted this to happen by adopting a skinny label. Every generic manufacturer knows that the products so delivered can and will be used in off-label use. And it will not always be possible to avoid infringement because of specificities of the national healthcare system, which may not only not allow limiting supply contracts to non-patented medical indications, but may even have an active policy of promoting the prescription of generic drugs for budgetary purposes, and hence indirectly promote off-label use. That would bring all of the above players, but in practice most likely the generic manufacturer as the most relevant one, into the position that infringement is unavoidable.

Indirect infringement

Indirect or contributory infringement is the other type of infringement. In the UK, but for that matter in any other EU country as the provisions relating to indirect infringement are based on art.26 of the Agreement Relating to Community Patents which never entered into force, ¹⁰⁸ indirect infringement takes place when the alleged infringer

"supplies or offers to supply in the United Kingdom a person other than a licensee or other person entitled to work the invention with any of the means, relating to an essential element of the invention, for putting the invention into effect when he knows, or it is obvious to a reasonable person in the circumstances, that those means are suitable for putting, and are intended to put, the invention into effect in the United Kingdom". ¹⁰⁹

Applied to the subject-matter of this contribution, this would cover for instance the situation where the generic drug manufacturer has supplied the drugs (which are the means relating to an essential element of the invention) for use by a third party, i.e. the other players in the chain among whom are the physician and the pharmacist, to potentially directly infringe the patent, i.e. to prescribe and dispense the generic drug for a patented medical indication. Whether those other players in the chain equally run a liability risk for indirect infringement will be discussed later.

Before we can discuss the infringement issues under respectively the Swiss claim and EPC 2000 claims, we need to elaborate on some key concepts of indirect infringement to the extent that they are relevant for this contribution.

The requirements for indirect infringement

There are four key requirements to be fulfilled with a view to demonstrate indirect or contributory infringement. These do not constitute the entirety of the requirements, but they are the most relevant for our purposes.

Must there be a direct infringer if one wants to establish indirect infringement?

It does not seem to be necessary to establish direct infringement in order to be successful in establishing indirect infringement. It has been held in the literature that the concept of indirect infringement has been *180 established as an independent form of infringement which is not dependent on the finding of a direct infringement.¹¹⁰ Furthermore, according to German case law, there is no need to be able to point to a direct infringer with a view to prove indirect infringement.¹¹¹ What is required is that the means are capable of being used by a third party to practise the invention. It is not required that the means are supplied to someone who must effectively put the invention into effect.¹¹² But it must be theoretically possible.¹¹³ That is also the reason why the High Court in the [Warner Lambert](#) case held that there could be no indirect infringement, as its view was that the Swiss claim was only aiming at the manufacturer and as none of the other players were manufacturing the product, it was not theoretically possible to have direct infringement in that way, as in actual fact the generic manufacturer had already manufactured the drug.¹¹⁴ That view has now at least been questioned by the Court of Appeal, also in view of the fact that in other jurisdictions, indirect infringement by the generic manufacturer has been accepted despite very similar if not identical factual circumstances. We will come back to this later.

Means relating to an essential element of the invention

There can only be a case of contributory infringement if the situation concerns the supply of means relating to an essential element of the invention. Even though this concept is in most cases a difficult one to determine, for the issues that are the subject of the present contribution they are not problematic, as there is no doubt that the means supplied, i.e. the drugs, will relate to an essential element of the invention, the latter being the (use of) the drug for (the manufacture of a medicament for) use in the treatment of a certain medical indication.

Suitable for use in the patented invention

The means supplied to a third party must be suitable to put the invention into effect. For the present purposes, there is no doubt about the suitability of the means, those being the drugs so supplied; hence we will not dwell any further on this particular requirement.

Intended for use in the patented invention

The concept of "intended for use in the patented invention" is a crucial parameter in the law of contributory infringement, and of particular relevance for the subject-matter we discuss here.

The concept has been sufficiently clarified in case law. Under UK case law, the wording "intended for use" does not refer to the supplier, but to the person so supplied. The [Grimme](#) case is the leading case here. The court held:

107. "Returning to [s.60\(2\)](#) the following questions arise:

i) Whose intention is referred to? The possible candidates are the supplier himself, his direct customer or the ultimate user. Or perhaps no specific person at all—the *181 inquiry being whether the 'means' and the circumstances

surrounding it being offered or supplied are such that some ultimate users will intend to use or adapt the 'means' so as to infringe. We call this the 'inherently probable' view.

ii) How specific must the intention be? Must it be a present settled intention at the time of alleged infringement? Or will a contingent future intention do? ...

iii) When must the intention be formed? Must it exist at the time of the supply (or offer to supply) or can it be formed later?

108. First then the person who must have the intention. One can rule out the supplier himself. The required intention is to put the invention into effect. That the supplier himself does not intend to do. The question is what the supplier knows or ought to know about the intention of the person who is in a position to put the invention into effect—the person at the end of the supply chain. Arnold J put it pithily in [KCI Licensing v Smith & Nephew \[2010\] EWHC 1487 \(Pat\) \[2010\] FSR 740](#) at [200]: It is implicit in this reasoning [i.e. that of Lewison J in [Cranway v Playtech \[2009\] EWHC 1588 \(Pat\) \[2010\] FSR 3](#)] that the relevant intention is not that of the supplier. In my judgment this is correct. S.60(2) makes it clear that there can be infringement not merely if the supplier knows that the means are intended to put the invention into effect, but also if that would be obvious to a reasonable person in the circumstances. That is inconsistent with a requirement of intention on the part of the supplier. Thus the relevant intention must be that of the person supplied.

109. Next, must the required intention be that of the person directly supplied by the alleged infringer? ...

112. What then of the 'inherently probable' view? This was essentially that for which Mr Chacksfield argued. He submitted that it was enough if the supplier knew (or it was obvious in the circumstances) at the time of his offer to supply or supply that some (disregarding freak use) ultimate users would intend to use, adapt or alter the 'means essential' so as to infringe.

113. Against this view it can be said that Article 26 requires that the alleged infringer must know (or it must be obvious etc.) that the means are intended to put the invention into effect. The present tense is used. So it can be said that a future intention—even a probable future intention—is not enough.

114. Notwithstanding the force of that linguistic point, we conclude that the 'inherently probable' view is indeed the correct construction of the provision. We do so for a number of reasons. ...

131. ... *In short, the knowledge and intention requirements of Art. 26 and section 60(2) are satisfied if, at the time of supply or offer of supply, the supplier knows, or it is obvious in the circumstances, that ultimate users will intend to put the invention into effect.*" ¹¹⁵

This position is also in conformity with German case law. In *Deckenheizung* it was held:

"[22] ... According to established statute of the senate, the intention of using the protected invention is a circumstance that is within the sphere of the buyer (*Antriebsscheibenaufzug*). However, the condition of indirect patent infringement is not met only when the buyer had already actually decided to use the devices in a patent-infringing manner and the vendor or supplier knew it. *Rather, it is met when an intent to use the devices for patent-infringing uses is obvious to a third party based on the circumstances as a legal condition, in other words it must be obvious to the vendor or to suppliers *182 of the devices suitable for use according to the patent. This is meant to facilitate verification of indirect patent infringement. This allows one to consider the condition as being in place when, from the point of view of a third party [the supplier] objectively considering the circumstances, a sufficiently certain expectation exists that the buyer will intend to use the offered or delivered devices for patent-infringing purposes.*" ¹¹⁶

In other words, in respect of the standard for determining whether the means supplied are intended for use in the patented invention, the intention must stem from the person supplied. The criterion is further fulfilled if the person who supplies or offers to supply knows, or it is obvious in the circumstances, that ultimate users will intend to put the invention into effect. It further implies that the requirement is fulfilled if the supplier, considering objectively the circumstances, has a sufficiently certain expectation that the person supplied will intend to use the means so offered for patent infringing purposes.

Looking at those criteria, it can be concluded that there is evidently going to be some degree of uncertainty in determining whether the knowledge or expectation of intended use by the person supplied is present in the mind of the supplier or

not. As the case law held, if the supplier has suggested the use to the person supplied, that will in any event be a sign that knowledge of the intended use is proven.¹¹⁷

If we try to apply that knowledge to the subject-matter of this contribution, what would be the result? As off-label use is known to the generic manufacturer, will that be enough to fulfil the criterion that there is knowledge of the intended use?

Entering into an agreement for the supply of drugs with a health insurer without limitation as to the medical indications covered could probably be seen as a suggestion for that use. But what in circumstances where there is no such contract, or where there has been a limitation in the contract excluding supply for the patented medical indications? Despite these limitations, it is still very likely that off-label use will take place. Can we then still assume that there is sufficient knowledge of the intended use and hence contributory infringement?

In what follows, and in particular the analysis of the various hypothetical situations under both the Swiss claim and the EPC 2000 claim, we start from the assumption in the various scenarios that there would be no case for direct infringement against the various players in the chain. As we have seen, in our view there are direct infringement claims available against most of the players, but for the sake of argument, it is assumed that such would not be the case.

Indirect infringement under the Swiss claim

As we know, the Swiss claim is a claim covering the use of a substance for the manufacture of a medicament for the treatment of a specific medical indication. How does one evaluate contributory infringement for these types of claims? As we have seen, the key criterion seems to be the concept of "intended use". We know that it is fulfilled if the person who supplies or offers to supply knows, or it is obvious in the circumstances, that ultimate users will intend to put the invention into effect. It further implies that the requirement is fulfilled if the supplier, considering objectively the circumstances, has a sufficiently certain expectation that the person supplied will intend to use the means so offered for patent infringing purposes.

As the law states, indirect infringement presupposes that the means must be supplied to put the invention into effect. For a Swiss claim (covering the use of a substance for the manufacturing of a medicament for the use in the treatment of certain disease or condition), putting the invention into effect would normally be the manufacturing of the drug for the use in the patented medical indication. That is not going to be *183 done by the physician or the pharmacist, or for that matter by any party other than the manufacturer of the drugs who also supplied them as the "means".

How then could there be indirect infringement, as that is what has clearly been decided in several cases. There is case law in Germany accepting indirect infringement by generic manufacturers by supplying the drug to physicians and pharmacies.¹¹⁸ There is also a case in the Netherlands where indirect infringement was also accepted on that basis, even though admittedly without any proper reasoning.¹¹⁹ Those cases do not exactly divulge why they think that the party so supplied would put the invention into effect, and how that could happen in the first place.

The Court of Appeal in the [Warner Lambert](#) case also struggled with this question:

134. "It will be seen that courts of two member states have, at least in provisional proceedings, granted relief to prevent what they considered to be indirect infringement of Swiss claims without any express indication of how they considered that the invention would be put into effect.

135. I agree that there are difficulties with the indirect infringement claim for the reason which the judge gave, namely the absence of a downstream event which, as a whole, can be regarded as putting the invention into effect. However, for three reasons, each of which is in my judgment sufficient, I would allow the indirect infringement case to go to trial.

136. The first reason is that which I have already given, namely that the courts of two EPC member states considering this same question have held that, at face value, indirect infringement can arise in these circumstances.

137. The second reason is that, if, as I have held, there is a case of threatened or actual infringement of the process claim under [section 60\(1\)\(b\)](#), then it follows that dealings downstream in the direct product of the process are also infringements under [section 60\(1\)\(c\)](#). Although this may not add anything to the direct infringement case, it is wrong to strike it out as a viable additional cause of action.

138. The third reason is that I consider it is arguable to say that when [section 60\(2\)](#) speaks of 'putting the invention into effect', it may be legitimate to look not just at whether any one person is carrying out the invention in a sense which would give rise to liability of that person for an act of infringement. It may be that the invention is put into effect if pregabalin is manufactured by one person and supplied to another who intentionally uses it for the treatment of pain. In those circumstances, a person who supplies pregabalin with the requisite knowledge (i.e. that prescribed in [section 60\(2\)](#) itself) does provide means suitable and intended to put the invention into effect, albeit by the combination of manufacturer and user, rather than by any one person alone. It may be that this is the reasoning which underlies the decisions in the Dutch and German cases which I have referred to.

139. An analogous problem arises where one step of a two step process is carried out by A and the second step is carried out by B. Absent a claim of joint tortfeasance, could it not be said that by supplying the result of the first step to B, A is contributing to putting the invention into effect (by A and B together)?

140. It follows that I would allow the appeal against the striking out of the [section 60\(2\)](#) claim." Arnold J in the [Warner Lambert](#) case could not see in any possible way how a Swiss claim could lead to an indirect infringement for any party other than the generic manufacturer: *184

684. "The fundamental difficulty with Pfizer's claim under [section 60\(2\)](#) remains, as it has always done, that claims 1 and 3 of the Patent are claims to processes of manufacture, but there is no act of manufacture by any party downstream from Actavis, nor even the prospect of such an act. This is so even if manufacturing (or 'preparation', to use the word in the claims) for this purpose includes packaging with appropriate instructions. In particular, there is no act of manufacture by pharmacists, nor any prospect of such an act. It follows that, although there is no difficulty in concluding that Lecaent's active ingredient is 'means, relating to an essential element of the invention, for putting the invention into effect', Lecaent is not suitable for putting, or intended to put, the invention into effect: either the invention has already been put into effect by the time that Lecaent leaves Actavis' hands or it is not put into effect at all. Accordingly, I conclude that Actavis have not infringed claims 1 and 3 of the Patent pursuant to [section 60\(2\)](#)." ¹²⁰

A recent first instance decision in the Netherlands seems to confirm the view held by Arnold J that liability for indirect infringement is difficult to establish, if at all, but even extrapolates this view to *all* players including the generic manufacturer. The court reasoned that one can assume that the supply of the generic drug can be considered to be the "means relating to an essential element of the invention". Such supply must be for putting the patented invention into effect. Putting the invention into effect is nothing more than the preparation of the drug for the treatment of the patented medical indication. It was not contested that such preparation does not take place anywhere in the chain of players once the generic manufacturer has so prepared the generic drug. Additionally, a quest for finding indirect liability by invoking art.64(2) EPC (the product directly obtained by the patented process is protected by the patent for the process) was equally not accepted by the court, as that would depart from the concept of indirect infringement and would be an issue of direct infringement. ¹²¹

Is there then no case to be made for indirect infringement of a Swiss claim? I am not convinced that there is no such case to be made, contrary to what both Arnold J and a recent Dutch case claim. In my view, a case could be built invoking the fact that a patent for a process also protects the product directly obtained by the patented process. So, if one applies the principle of indirect infringement of supplying the means to a third party to put the invention into effect, and if the product so produced is also protected by the patent under the aforementioned principle, then the party so supplied could directly infringe the patent by dealing with the product directly obtained by the patented process. ¹²² That would then explain how the supply of the means could be seen as being suitable and intended to put the patented invention, i.e. the manufacturing of the product for the use in the treatment of a certain medical indication, and the product so directly obtained for the treatment of that medical indication, into effect by disposing of or using that product directly obtained.

For Germany, a finding of indirect infringement can reside in the fact that under German case law and the literature, for determining scope of protection and infringement a "use claim" ("Verwendungsanspruch"), which a Swiss claim also is, is put at equal level with a product claim.¹²³ That means that as a Swiss claim is considered to be a product claim, the supplying of the product which has been "manifestly made up" would then constitute an infringing act. The party who would then be so supplied would be capable of directly infringing by dealing with the product for the specific purpose claimed in the patent.

It must be admitted though that the supply of the drug which has been "manifestly made up" could in fact already constitute a direct infringement, hence it is not easy to see what a claim for indirect infringement could contribute. However, a recent German case holding that there was indirect infringement seems to ^{*185} disagree with that position, and does seem to hold that there can only be direct infringement if the purpose or use of the claim has been effectuated.¹²⁴ That would not be done by the supplier of the drugs (i.e. the generic manufacturer); hence there would be no direct infringement, but it could be indirect infringement if all requirements to that effect have been fulfilled. This seems to be the result of some of the particularities of German law relating to medical indication patents, and I am not sure a similar reasoning would be followed in other EU Member States not applying the "manifest making-up" concept.

Application to the various players in the chain

If we might assume for a second that we could indeed overcome the hurdle of understanding how there could be indirect infringement, who could be held liable for such infringement?

The physician? Is the clinician, by prescribing the drug for a patented medical indication, supplying means to a third party to put the invention into effect? As we have said, a Swiss claim will also protect the drug so produced, and the patient will hence use the drug for the patented medical indication. But it is doubtful whether a prescription can be seen as a supply of the drug, as prescribing is something different from supplying the means.¹²⁵ Under the German approach, the result would be the same.

The pharmacist? The pharmacist is dispensing the products directly obtained by the patented process to the patients. Taking into account what we have said above regarding determining when there could be indirect infringement for a Swiss claim, it could be argued that the pharmacist is supplying the means, i.e. the drugs, to the patients who will then put the invention into effect, because the patient will use the product obtained by the patented process for use in the patented medical indication. The key question here is whether the pharmacist knows, or it is obvious in the circumstances, that ultimate users will intend to put the invention into effect. The pharmacist will normally not know in any specific case, but it knows in general that certain patients will use it for the intended use. It could be argued that this is enough to conclude that there is a claim for indirect infringement against the pharmacist. The same answer could be given if one applies the German approach, where the pharmacist could be held to "manifestly make up" the drugs for the patient to put the purpose of the invention into effect, i.e. the use in the treatment of the patented medical indication. It must be emphasised that the conclusions we have drawn here are not in conformity with the view of Arnold J in the [Warner Lambert](#) case, where he concluded that there was no case for indirect infringement to be made, and did not allow an appeal against that part of his judgment. Our reasoning would, however, be in line with what Floyd LJ argued in the same case, even though he was having doubts. I have to admit that I am also in doubt about the actual position I would take in this. There is a lot to say for the reasoning of Arnold J, but I found a line of argumentation arguing that there could be indirect infringement quite credible indeed.

The generic drug manufacturer as the supplier of the drugs? Taking into account what we have said above regarding determining when there could be indirect infringement for a Swiss claim, it could be argued that the generic drug manufacturer is supplying the means, i.e. the drugs, to the patients who will then put the invention into effect, because the patient will use the product obtained by the patented process for use in the patented medical indication. The key

question of whether the generic manufacturer knows, or it is obvious in the circumstances, that ultimate users will intend to put the invention into effect seems to have a positive response, as the generic manufacturer will know that the drug so supplied will be used off-label. The answer would be the same under the German approach, and has in fact been confirmed in a recent case to constitute indirect infringement, provided the means so supplied are "manifestly made up".¹²⁶ We also emphasise in this connection that both Arnold J and at least one Dutch court decision are *186 of the view that there can be no successful indirect infringement claim here, while Floyd LJ was somewhat in doubt about this issue. I once again admit that I am also in doubt here.

Depending on the stance taken, the above overview could lead to a situation where both the pharmacist and the generic manufacturer incur a non-negligible infringement risk, which seems to be very difficult to avoid, if at all.

Indirect infringement under the EPC 2000 purpose-limited product claim

Under the EPC 2000 product claims, analysing the indirect infringement question is much more straightforward. As it concerns a product claim, the supply of the product to a third party so that such third party could commit a direct infringement is at least more intuitive, as that third party will use, dispense, etc. the protected product. In other words, the complications which we have discussed with Swiss claims are largely absent.

Applying the concept to the various players in the chain gives an identical result as the hypothetical answer we have been giving for the Swiss claims, i.e. assuming that Swiss claims can give rise to indirect infringement based on the constructs we have elaborated there. To the extent that those constructs would not be legally feasible, there would be no indirect infringement under the Swiss claims (but that would conflict with court decisions in at least two European jurisdictions), but there would still be infringement under the EPC 2000 product claims.

Indeed, those constructs do not need to be used for the EPC 2000 product claim. An indirect infringement claim would arise for each party who supplies or offers to supply means, i.e. drugs, for an intended use of the invention, which is the use of the drug for a protected medical indication. In what follows, the responses under the German approach are identical to those under the Swiss claim, as German case law interprets a "use claim" for determining scope and infringement as a product claim.

The physician? Is the clinician by prescribing the drug for a patented medical indication supplying means to a third party to put the invention into effect? As we have said in the context of the Swiss claim, and the current EPC 2000 is no different in this particular respect, it is doubtful whether a prescription can be seen as a supply of the drug, as prescribing is something different from supplying the means. There is hence equally likely to be no indirect infringement for the physician under an EPC2000 claim.

The pharmacist? The pharmacist is dispensing the products protected by the purpose limited product claim to patients. It could then be argued that, to the extent that such dispensing would not be considered to be a direct infringement (and we have seen that in our view it is a direct infringement), the pharmacist is supplying the means, i.e. the drugs, to the patients who will then put the invention into effect, because the patient will use the product for use in the patented medical indication. The key question here is whether the pharmacist knows, or it is obvious in the circumstances, that ultimate users will intend to put the invention into effect. The pharmacist will normally not know in any specific case, but it knows in general that certain patients will use it of the intended use. It could be argued that this is enough to conclude that there is a claim for indirect infringement against the pharmacist. We want to add in this connection that the objections that were raised by Arnold J in establishing indirect infringement in the context of a Swiss claim are in our view no longer valid in the context of an EPC 2000 product claim, and we think that a finding of indirect infringement could be concluded.

The generic drug manufacturer as the supplier of the drugs? It could be argued that the generic drug manufacturer is supplying the means, i.e. the drugs, to the patients who will then put the invention into effect, because the patient will use the product for use in the patented medical indication. The key question of whether the generic manufacturer knows, or it is obvious in the circumstances, that ultimate users will intend to put the invention into effect seems to have a positive response, as the generic manufacturer will know that the drug so supplied will be used off-label. *187

It seems that a finding of indirect infringement for both the pharmacist and the generic manufacturer is much easier to establish than under the Swiss claim, as an EPC 2000 claim is a product claim which does not require additional intellectual constructs such as use of the products directly obtained by the patented process. In our view, our conclusions are in conformity with the current case law in UK, the Netherlands and Germany, even though there is as such no case law dealing with EPC 2000 claims to date. It is once again clear that both the pharmacist and the generic manufacturer are unlikely to be able to deflect infringement.

Comparison between "intended use" in indirect infringement and "for use" in direct infringement

The reader will have noticed that for both the evaluation of direct infringement and indirect infringement of a purpose limited claim (and it does not matter whether it is a Swiss process claim or an EPC 2000 product claim), it will be necessary to establish some form of knowledge on the part of the supplier/user of the drug that end-users will intentionally use the drug for the patented medical indication.

For direct infringement, all that is required is to prove that the person who produces, dispenses or uses the product which is protected for a certain medical indication knows or it is foreseeable for him that the product so produced will be used intentionally for the patented purpose.

For a claim for indirect infringement, it must be proven that the means so supplied are suitable and intended to be used for putting the invention into effect, i.e. for use in the patented medical indication. The word "intended", according to UK and German case law, would in fact mean that it is fulfilled if the person who supplies or offers to supply knows, or it is obvious in the circumstances, that ultimate users will intend to put the invention into effect. It further implies that the requirement is fulfilled if the supplier, considering objectively the circumstances, has a sufficiently certain expectation that the person supplied will intend to use the means so offered for patent infringing purposes.

In both cases, there is an evaluation to be made of whether the producer/user/supplier has knowledge that the end-user will use the product intentionally for a patented use. There is hence not much, if any, difference to be found between the level of knowledge that is required and the intended use under both forms of infringement. If that is true, then the standard for evaluating whether there is knowledge of intended use for direct infringement of a process or product claim for a medical indication would be virtually identical to the one evaluating whether the means supplied are intended to be used for committing an infringement under the principle of indirect infringement. That would mean in turn that the meaning of the wording "for use" in a medical indication claim aims at the same intention as the intended use under indirect infringement.

Even though the above is likely to coincide with what the Court of Appeal thought in the [Warner Lambert](#) case, Arnold J held in the same case that this reasoning may be erroneous:

"It appears from Floyd LJ's judgment that he may have considered that there was no greater difficulty in such a case than may arise with a claim under [section 60\(2\)](#) in cases like [Actavis v Lilly](#). Counsel for Actavis submitted, however, that this was incorrect. As counsel pointed out, under [section 60\(2\)](#), it is only the act of supplying (or offering to supply) the 'means, relating to an essential element of an invention, for putting the invention into effect' that is an infringement, not the act of manufacturing the means. Furthermore, the 'means' do not become infringing articles any dealing in which will be a strict liability infringement. In those circumstances it is relatively straightforward to confine the effects of a finding

of infringement to the proportion of the 'means essential' which is foreseeably intended to put the invention into effect. The position here is different, because foreseeability on the part of the manufacturer does not provide a sufficient basis to distinguish between infringing and ***188** non-infringing acts of manufacture, particularly when it comes to parties downstream from the manufacturer." ¹²⁷

It seems that the law regarding the intentional element in medical indication claims is yet to be crystallised. I do think that there is a sound basis for arguing that the meaning should be similar if not identical across both types of infringement, and even though Arnold J seems to disagree, in the actual reasoning of his judgment relating to both types of infringement, it looks as if the interpretation is very similar indeed.

Conclusion

Where does this lengthy section on patent infringement leave us now? First of all, it is striking to see that further medical indication claims lead in fact to quite a substantial infringement risk for most players in the chain.

It is secondly also undeniable that physicians are affected at least in some way. As we have seen, the aim of the EPC was to ensure that medical treatment remained exempted from patent protection. As we have also seen, that has in effect not meant that physicians could not be touched by the patent system, as patents for certain products or instruments may in practice mean that they are not available to the physician. However, that is a different problem from the one we have pictured in the above scenarios. According to the above scenarios, there is a high likelihood that physicians and pharmacists alike will be liable for direct or indirect infringement of medical indication claims.

What this shows us is that under most circumstances, the generic drug manufacturer will not be able to avoid infringement, not even under a scenario of skinny labelling. What is even more, the generic manufacturer runs serious risks for infringement under both direct and indirect infringement. Every generic manufacturer knows that the products so supplied will be used in off-label use. As we have seen, the criteria of knowledge for direct infringement and intended use for indirect infringement are very similar if not identical, leading to very similar or even identical conclusions.

I am also not convinced that even if the generic manufacturer would be able to exclude the patented medical indication from a tender contract with a health insurer, which does not even seem to be readily possible in various jurisdictions, this would lead to an escape route from infringement. The generic manufacturer would still have knowledge of the fact that there would be off-label use by the physician and/or pharmacist, and under the current state of at least UK law, this could be sufficient to incur a liability claim for infringement. National healthcare policies will also have an effect on all players, especially for those which have a generic drug preferential system, stimulating physicians and pharmacists to prescribe generic versions wherever possible.

The current state of the law presents for all players in the chain an insurmountable infringement risk, which seems at least for the generic drug manufacturer to be even unavoidable whatever measures taken. That could easily lead to an "eviction" of the generic manufacturers from the market, leaving the playing field entirely to the proprietary companies. That is not a desirable development and in our view the present situation should be remedied in the interest of society and public health. That is the subject the subsequent section dealing with policy considerations and proposed solutions.

It must be added, however, that at least in the UK the courts seem to be willing to invoke equitable defences in terms of injunctions, such as establishing that in practical effect, if the off-label market only corresponds to a limited percentage of the total product market for the generic drug, no damages would be due. However, I have to admit that this leads often to quite complex calculations and arguments, and I am not convinced that the line is that easy to draw for all drugs and in all jurisdictions. I hence do not necessarily see this as a very comforting mitigation of the infringement risk. ***189**

Policy considerations and proposed solutions

Introduction

We have seen that the prime reason for making medical treatments non-patentable is that it was deemed for socio-ethical and public health reasons undesirable that the activities of physicians would be subject to patent protection. We have also seen that some medical indication patents sit very closely to what are in effect almost medical treatment methods. If we look at some of the further medical indication patents, in particular those which protect the treatment of further medical conditions or the ones protecting dosage regimes, it must be admitted that those patents come very close to the treatment performed by the physician. Admittedly, these patents do not cover the medical treatment as such, but they only cover the use of an existing drug for the manufacture of a medicament for the treatment of a new condition or of an existing condition in a new dosage (under the old Swiss claim formulation) or the existing drug for the use in the treatment of a new condition or in a different dosage (under the new EPC 2000 claim type). Adhering to a strict legal interpretation, one could argue that as there is no interference with the treatment as such, there is no problem. Taking a somewhat broader approach tells us a different story, however. It cannot be denied that those patents do have an effect on the physician.

We have equally seen in the previous section that all players in the pharmaceutical manufacturing and health chain are not only affected by medical indication claims, but run also considerable and credible infringement risks, which are even unavoidable for some players, e.g. generic manufacturers, irrespective of the measures they would take.

All of the above demonstrates that the current state of affairs is undesirable and not in the interest of society and public health. It is our view that this state of affairs is unsustainable and needs to be changed.

The question is how to do this. The present author is not advocating an abolition of the patent system. It is believed that, even though there are patent practices in the pharmaceutical industry which are questionable,¹²⁸ overall the patent system is likely to be beneficial to the development and advancement of health, in view of the huge investments which are needed to develop new drugs and treatments, which are at risk in the absence of patent protection. But it can equally not be seen as a social optimum that so many players in the healthcare provision chain could be held liable by doing what they are mandated to do by their profession, i.e. looking for the best treatment for patients, and/or trying to avoid infringement by not marketing drugs for patented medical indications. One of the foundations on which the patent system is based is that we have all agreed to introduce patents because at the end of the day it is deemed that the benefits of having such a system outweigh the negatives of providing exclusive rights and monopolistic like of protection. That social contract needs to be adhered to, and it can be questioned whether the current state of affairs meets the parameters of that social contract.

It is for that reason that it is believed that changes are necessary. In what follows, I will provide and analyse a number of proposals with a view to achieve a more socially desirable equilibrium between patent protection and the interest of society to a good provision of healthcare.

The therapeutic freedom exception

It is clear from the above analysis that there is a substantial risk, at least in theory, for infringement on the part of both the physicians and pharmacists. Even though admittedly both are rarely if ever sued for infringement, it is far from impossible that both players might become the subject of injunctions with a view to avoid future infringement. There are no statutory provisions in Europe which exempt both players from infringement. I would say that this is undesirable. Both physicians and pharmacists are crucial players *190 in the provision of healthcare and it would in my view be somewhat unacceptable if they would become subject to patent infringement injunctions, as that could have a negative effect on provision of the best healthcare and best value drug provision. One could argue against this that the statute has

never immunised the physician against infringement, and indeed there are possible situations where a physician might infringe patents out of the context of further medical indications (e.g. he/she could use a medical instrument (which has been patented) where such a medical instrument is in fact a patent infringing one. Most people would accept that to be a patent infringement).

Whatever one may think of the relationship between physicians, pharmacists and patent owners, I think it is desirable that this dark shadow of patent infringement risk should not hang over those players, so that they can concentrate on what society is expecting them to do, which is to provide the best possible healthcare for the population. That would imply the creation of another exemption, covering those specific players. In fact, in Switzerland, there is a proposal on the table to introduce an exemption to that effect. According to the Swiss Government, a second medical indication claim, definitely in the EPC 2000 product format, would not only protect the delivery and use of the product, but also the prescription of a known and no longer protected drug for a new and patented medical indication.¹²⁹

The aim of the proposal is to introduce a new art.9(1)(g) into the Swiss Patent Law, according to which the therapeutic freedom of physicians is guaranteed and the delivery, use and prescription of a drug for a patented medical indication for an individual patient will not be held to be a patent infringement.¹³⁰ If approved, this provision would be a pioneering one in Europe, as it casts in statute the concept of therapeutic freedom of the treating physician, a concept that is silently recognised in patent law of several EU Member States but not in any patent statute. It goes without saying that such a provision could potentially have far-reaching consequences for patenting personalised medicine.

It would be advisable to introduce such provision in the patent statutes of all other countries, as it frees medical professionals from the risk of patent infringement, which the exclusion from patent protection of medical treatment methods under the EPC has tried to achieve. I find it somewhat surprising to see that it has not been suggested before and in more countries, but that could be explained by the fact that pharmaceutical companies have never taken action against physicians and pharmacists for patent infringement. However, in an age of personalised medicine, where the importance of further medical indication patents will exponentially grow, it is not a given that it will not happen in the future.

As a side note, under US patent law there is no exclusion of medical treatment methods from patentability. That also implies that there is no need to revert to complex patenting strategies such as the ones applicable in Europe. Limiting ourselves to infringement here, US patent law is, rightly so, rather friendly towards the medical profession when it comes to the use of patented medical treatment methods. Under 35 USC §287(c), medical practitioners are not liable to damages for infringement of patented medical treatment methods.¹³¹

Quo vadis with the present situation?

As we have said earlier, therapeutic freedom for clinicians and pharmacists should definitely be a first step. The sooner a therapeutic freedom exception is incorporated into the patent systems of the EPC Member States, the better. It is only a first step, however, to come to a solution for the multiple problems *191 we are faced with regarding patent infringement for second and further medical indication patents. As we have seen, there seems to be in particular a problem for generic manufacturers. Off-label use is capable of triggering infringement claims irrespective of precautionary measures taken by generic manufacturers.

How can this problem be resolved? The easiest but not necessarily the best solution could be to do nothing, and say that this is how the patent system works. Leaving the situation as it is may have as a consequence that generic manufacturers will be evicted from the market because, even though they can supply drugs which are off-patent, as long as there is a further medical indication patent on the active ingredient, they run the risk of infringement as set out above. That is not likely to be a good solution for patients and society at large, as it would basically kill competition in drugs that are no

longer protected by IP rights. There is hence an urgent need for a more structural solution or solutions. In what follows, a variety of proposals are made, which are not all equally viable.

Abolish medical indication patents

A first option could be to abolish medical indication patents altogether. That is very unlikely to be a realistic avenue to take, as the pharmaceutical industry has striven for many years to obtain this form of protection, and it is unlikely that a legislature will have the courage to do away with it. This is even less likely in the context of current trends in personalised medicine, where the relevance and importance of medical indication research and patents seems to grow exponentially. In other words, the era of personalised medicine has made medical indication patents one of the most attractive forms of patent protection, which means that it is highly unlikely that the pharmaceutical industry (including the biotechnology industry) will not do whatever it can do to preserve this form of patent protection.

I am also not convinced that this would be an optimal solution. There are plenty of examples where further medical indication patents have proven to be quite important innovations which have come to the benefit of healthcare. One can think of patients who could previously not be effectively treated for their condition and who suddenly find themselves after many years of research in a situation where a drug which was not originally designed for treating their condition will now become available for treating it. Abolishing medical indication patents would then become a scenario of throwing away the baby with the bathwater.

There are also doubts as to whether such a solution would be compliant with TRIPS, which does not allow to discriminate on the basis of technology, and provides in art.27(1) that patents shall be granted for inventions in all fields of technology, and patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced. The Agreement does have some exceptions, and allows members to exclude medical treatment methods from being patentable (art.27(3) (a)). It furthermore allows members to exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including protecting human, animal or plant life or health. Excluding second medical indication inventions from patentability seems at first glance to discriminate against technology. Even though there are countries where second medical indication inventions are not patentable as such, there are in most cases alternative forms of patent protection in place for this type of invention. For instance, in the US, second medical indication patents as we know them in Europe do not exist, but a very similar effect is achieved there by allowing patents for methods of medical treatment, which would in the case of a second medical indication protect the treatment so prescribed and not the drug for the treatment so prescribed.

From a legalistic point of view, there does not seem to be much room for abolishing medical indication patents. That would leave the legislature with the evaluation of the opportunity cost of abolishing them anyway. Apart from the aforementioned legalistic objections, what would be the benefits and drawbacks of abolishing medical indication patents? The reason for having medical indication patents is often claimed ¹⁹² to be to stimulate investment and innovation in the search for new treatments. In the absence of patent protection, that innovation would be lacking. This argument is very difficult to verify, and it brings us back to the fundamental rationale of the patent system in the first place. It would lead us too far to go into the details of the various economic and other rationales of the patent system. ¹³² It suffices to say here that in a world of personalised medicine, where it is effectively the case that treatments quite often reside in further medical indications of various formats (a new medical condition which can be treated with an existing drug, a new group of patients that has been identified which would benefit from treatment with an existing drug, the development of a specific dosage or administration regime for specific patients who would otherwise not benefit from the treatment, etc.), it is not an easy decision for a legislature to stand firm and say that there will be no patent protection for those treatments, creating the risk that research into these further treatments will come to a standstill.

Abolish exclusion for medical treatment methods and abolish medical indication patents

A related option could be to abolish medical indication patents, and at the same time abolish the exclusion of medical treatment methods from patentability. That would have as an effect that product claims are no longer possible, and that inventions will be claimed in the form of a method claim for the treatment of a certain medical condition.

What would be the benefits of such a solution? It would first of all do away with the relatively difficult interpretation of further medical indication claims, and it would bring the invention down to what one tries to achieve in first instance. It would also make an end of the not always very clear distinction between the provision of drugs for a very specific medical treatment which is claimed and the medical treatment itself. It would in other words probably provide more legal certainty for society and all of its players. There is also no problem with the TRIPs Agreement in such a scenario. Provided that there was a therapeutic freedom exception, clinicians would also be free from liability claims.

What are the drawbacks? One of the main drawbacks is obviously the concern that medical professionals would be hindered by those patents. That does not necessarily need to be the case, provided that additional measures are introduced into the patent system. One of them would in any event need to be a therapeutic freedom exception, i.e. that clinicians would be allowed to use the patented invention without committing an infringement, or at least without being held liable for it. But that may not be enough. As has been suggested in the literature, the mere fact that there is a patent on a medical treatment method could as such have a negative effect, as it may already cause a lack of access to the invention owing to practices of patent holders.¹³³ Furthermore, it might be difficult to accept that medical treatment methods could be patentable for public (health) policy and socio-ethical reasons.¹³⁴ Finally, and quite importantly, even if one were to introduce medical treatment methods as being patentable, this would not necessarily make the situation for generic manufacturers more comfortable. Yes, they would no longer be directly infringing, as the production of a drug that can be used in a patented medical treatment does not constitute direct infringement of the patented method. But they would still run the risk of committing indirect infringement, as they provide the means which will be used by the clinician to commit a direct infringement. That in sequence will imply that the entire discussion as to "suitable and intended" needs to be had for such cases. *193

In effect, allowing medical treatment methods to be patentable would have some benefits, but in view of the multiple objections from a public (health) policy and socio-ethical point of view, added to the fact that it does not in effect create that much more legal certainty, means that it is not an ideal candidate for a good solution.

Abolish medical indication patents and replace by protection certificate of limited duration

Another related option could be to abolish medical indication patents and replace them by some type of protection certificates of limited duration of, for instance, a maximum of five years.¹³⁵ The protection certificates would need to fulfil all patentability requirements, as normal patents would do. Limiting protection for second medical indication inventions to a limited period of time which is much shorter than the one for ordinary patents would assist in making second medical indications available for competition much earlier, which would benefit patients in the long run. It can be readily assumed that the investment required to develop a second medical indication is much more limited than that for bringing on the market the molecule as a drug, and there is hence a rationale for saying that protection does not need to last that long, and that competition in the market should be guaranteed much earlier, so as to optimise the benefits for patients and society at large. This solution attempts to find a balance between the need to stimulate investment in this area of technology by offering a temporary exclusive right and the right for society to have access at the best healthcare at the best possible price. The limited period of protection offers that balance, as competition will be able to enter the market for a relatively short period of exclusivity, which returns to society at least some of the monopoly profits gained by patent protection lasting for the full 20 years.

There is, however, a slight catch with this solution, and that is that if pharmaceutical companies had the prospect of having only a limited period of exclusivity, two things could happen. Those companies could decide that the certificate of protection is not worth the investment, which could have as a consequence that innovation in the area of further medical indication could stall, and as we have seen, further medical indication research is bound to become more important in an era of personalised medicine, and hence will also benefit patients. I am not convinced that this negative evolution will happen, as quite a substantial number of further medical indication patents do not require the vast amounts of investments that are required to come on the market with the first drug based on the patented chemical entity. Hence the cost-benefit ratio might still convince pharmaceutical companies to use this scheme. A second consequence could be that pharmaceutical companies obtaining such protection certificates will market the drugs protected by a further medical indication at an extremely high price, knowing that the term of protection is limited and hence the term of gaining a return on their investment is accordingly limited. It is difficult to predict whether that will happen, but it can definitely not be excluded. An argument against thinking that it will happen is that those companies obviously have an interest in selling products, and charging extravagant amounts will not be conducive to sales. That can be true, but all will depend on the specific market for the drug, whether there are substitutes available, whether it is a drug for a common or less common condition, etc.

There are similar doubts as to whether such a solution would be compliant with the TRIPS Agreement as the option of abolishing second medical indication patents altogether. The TRIPS Agreement does not allow discrimination on the basis of technology, and by not granting normal patent protection for further medical indication inventions, it could be argued that there is such discrimination. It must be clear that ¹⁹⁴ such an alternative system, even if it were deemed to be compliant with TRIPS, which is doubtful, would not resolve all problems, as there is still the term of five years within which the problems we have analysed will occur. But in view of the fact that the term is so limited, there may be less inclination to rely on off-label use, in particular if such off-label use was at least indirectly inspired by cost saving considerations. A term of five years without access to cheaper alternatives is easier to "fund" than a fully fledged patent term. What the solution will obviously not resolve is off-label use that is prescribed for medical reasons in cases where there would be no alternative medication available, a practice not uncommon in healthcare, as we have seen (e.g. neonatology, paediatric use, certain cancers, etc.).

Prohibit off-label use

Another route which can be taken is to regulate strictly or even prohibit off-label use by medical professionals. That is unlikely to ever materialise for a number of reasons. First of all, off-label use is allowed in Europe, not necessarily because it is actively regulated to that effect, but in most instances it is a matter of condoning those practices.¹³⁶ Off-label use is also crucial to a proper functioning of the healthcare system. In paediatric use there is an abundance of off-label use, in the absence of specific drugs for paediatric use. Prohibiting off-label use would have very negative effects on those areas where it is widespread. Secondly, budget constraints on healthcare systems also imply that those systems are happy to see off-label use, as the prescription of a generic drug will cost less to the system. In some countries, those practices are actively stimulated by healthcare systems in what is sometimes called a preferential system of prescription, generic prescription or generic substitution.¹³⁷ Thirdly, any such arrangement would have to be taken at European level, which promises to make matters even more complicated. Fourthly, if we were to prohibit off-label use, many patients would be likely to suffer, as it is a fact that there are in specific circumstances and for specific groups of patients no "label" drugs available. Neonatology and paediatrics are good examples. In other words, we have to avoid once again throwing away the baby with the bathwater. Fifthly and finally, even if there were more regulated prohibition of off-label use, I would be of the view that this might still lead to effective off-label use in the individual circumstances in a clinical setting. Even some of the proponents of prohibiting organised off-label use profess that a formal prohibition of off-label use, i.e. a use that is no longer allowed under regulatory provisions, would not hinder the therapeutic freedom of the clinician, who would still be allowed to prescribe off-label use in individual circumstances where such off-label use would be the best

therapeutic option for the patient.¹³⁸ It would be ethically indefensible to claim that there could be no off-label use in certain circumstances. This is not the place to have a full debate on whether off-label use should be prohibited or not, but it is clear that if the proponents of prohibition admit themselves that off-label use in individual cases by clinicians should still be possible, this would not be very helpful in a patent infringement context. There would in such a case still be a threat of infringement, and it could be argued that even in those circumstances the generic manufacturer would have knowledge of the intentional off-label use. We must not forget that the present infringement case law is not necessarily based on state-organised off-label use; hence I am not convinced that even a qualified prohibition as is suggested would do away with the problems of patent infringement. *195

Restrict liability to require all measures which are reasonably within control of alleged infringer

A route which at first instance does not sound very appealing, but which could be a feasible alternative if implemented in the way shown below, is to leave it to case law and be confident that the courts will come up with a solution which sustains the generic pharmaceutical industry while at the same time respecting patents obtained for medical indications. As we see from the recent case law and from the analysis we have made above, this is quite an adventurous route and the outcome is quite uncertain, as it will then all boil down to how the concept of "intent" and the constructive knowledge of the generic drug manufacturer of that intent are interpreted. Even though certain factual constellations that we have seen in the recent case law could justify certain conclusions of non-infringement by courts, it remains unclear how far the law can be stretched. If the criterion is that there will be infringement if the generic manufacturer knows that his product is going to be used in the treatment of patented medical indications, then this could, following a certain interpretation, imply that generic manufacturers will always be liable as they all know that there is off-label use in the medical world. The specifics of the regulatory framework around the organisation of the healthcare system will also play a role. As we have seen, in many countries there is definitely a system of preferential prescription of the generic drug, and in some countries there is a system of generic substitution where the pharmacist is under an obligation to dispense the generic. Those arrangements are all factors in how the generic manufacturer could be held liable for the use of his drugs in the treatment of patented medical indications.

With a view to avoid any of the uncertainties laid out above, recourse would have to be taken to a narrower interpretation of the concept of knowledge of intentional use. In this line of reasoning, generic companies would only be liable for infringement if they had not taken all reasonable measures within their control to ensure that the drugs they manufacture and supply were not used for a patented medical indication. As the case law stands now, the burden on generic companies seems to be particularly heavy, as the criterion is that they would incur liability if they knew, or it was reasonable to assume from the circumstances that they could have known, that their drugs were going to be intentionally used by medical professionals for treating patented medical indications. The proposed interpretation would narrow the grounds for liability in the sense that the generic manufacturer, even if he knows that the drugs he manufactures and puts on the market will be used for the treatment of a patented medical indication, will not be liable if he has taken all reasonable measures within his control to prevent an infringing use. The question is then obviously what is to be understood by "all reasonable measures within his control". It would in any event include measures such as expressly indicating in the leaflet that the drug is not authorised for patented medical indications,¹³⁹ not marketing it in any shape or form for the patented indication directly or indirectly, etc. But it would not include having to take responsibility for the off-label use by clinicians and pharmacists which the generic manufacturer has not induced or influenced himself. That may also imply that there would be no liability if a generic manufacturer were not able to exclude the use for a patented medical indication under a health insurance supply and/or reimbursement tender contract because the contract and/or regulatory provisions do not allow so. And it would also imply that generic manufacturers cannot take liability for healthcare systems' regulatory regimes such as preferential generic drug use or generic substitution regimes.

There is some support for this suggestion in the judgment of Floyd LJ in the [Warner Lambert](#) case, where he said that:

132. "Another hard case is that in which a defendant has taken all the steps open to him to avoid his medicine being prescribed for the new use, yet those steps are, due to the structure of *196 the marketplace, insufficient to stop it happening. Actavis' test would provide a defence in those circumstances, because the defendant could credibly say that he did not target those sales which he was striving manfully to prevent." ¹⁴⁰

I think it is a feasible standard, but I think it might require some tinkering with the regulatory system as well. It will probably exclude a certain amount of potentially infringing use, which will be to the benefit of bona fide generic manufacturers. The corollary to that is that the brand name manufacturer will see some infringing use not penalised, but that is part of the balancing act we have referred to earlier. The major drawback of this solution is that it remains pretty much a decision-taking process by the courts on an ad hoc basis, and not a system that can be mechanically and automatically applied and implemented, which provides more legal certainty.

Statutory change excluding liability if the product made/supplied has substantial non-infringing use

An alternative solution could be to create a statutory change, mimicking what is available in the US. Under US law:

"Whoever offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or *commodity of commerce suitable for substantial noninfringing use*, shall be liable as a contributory infringer." ¹⁴¹

In other words, if it can be proven that there is a substantial non-infringing use of the components so supplied, there will be no infringement. ¹⁴² Applied to the subject of our present discussion, if the drugs so supplied by the generic manufacturer had a substantial non-infringing use, which would be the case if they were available for other non-patented medical indications, there would be no infringement.

This provision is only applicable, however, to indirect infringement, which shows immediately that transplanting this provision into European patent law would only be of limited use, as we have seen that there is a serious risk of direct infringement for most players. Expanding it to provisions of direct infringement cannot be performed as such, as the basic rule under patent law is that a patent for a product provides absolute product protection, protecting against *all* uses of the patented product. If one wanted to incorporate a new provision into the patent statute governing direct infringement and substantial non-infringing uses, this would need to be limited to all cases where the patent claim is a purpose-limited product claim. But even in that eventuality, it would still unduly limit the rights of the patent holder, as there would suddenly no longer be a claim for infringement for an infringing use, by virtue of the fact that the provision aims at immunising producers of products which have a substantial non-infringing use.

The conclusion should be that such a transplant does not seem to be viable under any circumstances. The only way that it could be made viable is to incorporate an element of knowledge of intent into the provision, as it must still be possible to claim for infringement of the infringing uses. The knowledge or intent would then relate to the infringing or non-infringing use respectively. That then brings us back to the starting point of our discussion, and hence does not provide any improvement over the status quo. *197

Apply the German approach of "manifest making-up"

A further option to narrow the scope of infringement risk for generic manufacturers could be to introduce an element of intention in the mind of the alleged infringer as a requirement for infringement. If the alleged infringer had not prepared or produced the drugs with a view to make them available for use in the patented medical indication, there would be

no infringement. That is a stricter approach than the one currently taken by the UK courts, which seems to require an element of knowledge in the mind of the alleged infringer that the products will be intentionally used for the patented medical indication. Hence, it shifts the element of intention from the end-user or other player in the chain to the generic producer.

That would come close to the German concept of "manifest making-up" or "sinnfällige Herrichtung". As we have seen, manifest making-up may lie in the particular configuration of the substance or article, or in the addition of a package leaflet. The addition of a package leaflet may be treated as a notional part of "manufacture". The article has to be "set up as such for the patented use". This means that there must be a direct and purposive connection between the measure of manifest making-up on the one hand and the production and sale of the product on the other hand, this connection holding the user unambiguously to the patent-protected use. The criterion of "manifest" in "manifest making-up" is only fulfilled when it is possible to determine on the basis of objective parameters that the protected purpose was aimed at, at the time of producing the drugs. Those objective parameters could be packaging, mentioning certain indications in the Summary of Product Characteristics or patient leaflet, and other objective parameters that allow one to conclude that the product has been brought on to the market to treat a certain condition. German case law does therefore seem to look for "some outward manifestation in the manufacture itself which can be specifically attributed to the new use".¹⁴³ But it requires looking into the intentions of the manufacturer or user of the infringing product. In fact, Arnold J in the [Warner Lambert](#) case took the position that infringement could only be established if there was an intentional element in the mind of the manufacturer, on the basis of which there would then be no infringement if that manufacturer who operates under a skinny label had never intended the drug so manufactured to be used in a patented medical indication.¹⁴⁴

This approach has the advantage that it looks at first glance fair and equitable. It would only involve liability on the part of the generic manufacturer if it had intended to supply the drugs for a patented medical indication. Whether that is in fact a better option is yet to be seen. As we have seen, the German approach has also its limitations. Advertising the drugs for the patented use does not seem to fulfil the requirement of "manifest making-up", which is a rather (too) strict approach.

Furthermore, there will always be evidentiary issues. How does one show the element of intent? Under the German approach, if there is no evidence that the drugs produced had been "made up" for the patented use, there would be no infringement, even though the generic manufacturer might very well have the knowledge that there would be off-label use for a patented medical indication. As knowledge is not enough, there is only infringement if an element of intent can be proven. The UK court in the [Warner Lambert v Actavis](#) case already alluded to this issue as well for not adopting such a strict standard:

"On the other hand, I can see real difficulties with the application of an 'aiming or targeting' test in the present circumstances if it means more than the test I have proposed. It means in effect that the patentee must prove that it is Actavis' wish or desire that they sell some Lecaent for pain. How does the patentee go about establishing this wish or desire if it is not enough to show that it is known or foreseeable that some of their product is being intentionally used for pain? It seems to me that there *198 is substance in Mr Turner's complaint that to adopt such a strict requirement of intention will rob Swiss claims of much of their enforceability."¹⁴⁵

Can it be seen as fair that a party who knows that the products it so makes are going to be used intentionally for a patented use is not committing an infringement if it has no intention at the time of production that these products should be used for the patented use? On the other hand, can it be seen as fair that a party who knows but does not have any intention of seeing its products used in a patented medical indication would be liable for infringement under the UK approach as it stands now? While the UK approach seems to have chosen, on the balance of probabilities and taking into account evidentiary issues, to set a standard that favours the patent holder, the German approach seems to have set a standard which may favour the alleged infringer. In that sense, as we try to find a solution that provides a more

balanced approach towards the liability of generic manufacturers for patent infringement, the German approach could be an option, even though it has been criticised in the German literature as being overly complicated and artificial. Additionally, there are evidentiary issues to deal with.

Devise a system where the regulatory system and the patent system co-operate

A solution that at first glance is very appealing would be to organise a system where the regulatory system, which includes the organisation of the healthcare system, would assist in avoiding any patent infringement. That would require both systems to be linked to some extent, which is not only a formidable task, but without doubt also a controversial one. I am quite confident that the liability issues that such a solution might raise for the regulatory system are very likely to present a huge obstacle. The system would require ensuring that patented products and medical uses could be clearly distinguished from non-patented products and medical uses. In effect, that would mean that the players in the healthcare system, among whom are physicians and pharmacists, would prescribe and dispense the generic version of the drug for non-patented uses and the brand name for patented uses. This looks at first instance a relatively easy task, but it is clear that those active in the healthcare system have obviously very little or no knowledge of the patent system and of the scope of patent claims, and it would be quite unreasonable to expect that from them. Putting such a system into place would require patent holders and generic manufacturers to co-operate with putting such a system into effect.

Arnold J in the [Warner Lambert](#) case already alluded to the need for such a system:

722. "I have now lived with this case for nine months. During that time, I have heard and determined the applications which led to the [Warner-Lambert I](#), [II](#), [III](#) and [IV](#) judgments, I have heard and determined a number of other case management applications, I have heard the trial and I have written this judgment. During that time, I have reflected repeatedly and at length on the issues raised by this litigation. At the end of that period of reflection, I remain more convinced than ever that the best solution to the problem of protecting the monopoly conferred by a second medical use patent while allowing lawful generic competition for non-patented indications of the substance in question is to separate the patented market for the substance from the non-patented market 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 reference to the generic name of the substance (the INN).

723. Prescribers cannot be expected to know when this is required, nor should they be required to take steps to find out. What is needed is for centralised and authoritative guidance to be given to prescribers as to when this practice should be adopted. Such guidance also needs to be conveyed to other relevant stakeholders, and in particular to the software providers. *199 The question is who is to issue such centralised and authoritative guidance. This is a particular challenge for the decentralised (some might say fragmented) English healthcare system since the 2012 Act. As I understand it, the Secretary of State considers that he lacks the power to issue such guidance (see [Warner-Lambert I](#) at [75]). That being so, the only body in England which appears to have the necessary power and authority is NHS England. In Wales, Scotland and Northern Ireland, the devolved governments appear to have the necessary power and authority.

724. In the present case, NHS England issued guidance as a result of an order made by this Court on an application by Pfizer. Regardless of the legal soundness of that procedure, it had two practical advantages. The first was that it provided a convenient forum to enable the interested parties to negotiate what was to be done, when and by whom. In the end, this was all agreed. The second was that the procedure included the protection for the NHS and for the generic companies of a cross-undertaking in damages. This is particularly important because of the risk that the second medical use patent may prove to be invalid if challenged, as has transpired in the case of claims 1 and 3 of the Patent if I am right.

725. Looking to the future, however, it does not seem to me to be in anyone's interests for these problems to be dealt with in the ad hoc manner in which they were addressed in this case. It is not as if the situation which arose in this case could not have been predicted. On the contrary, as soon as it was known that the SPC had lapsed, the resulting scenario was entirely predictable. (And if I am right that Pfizer planned to allow the SPC to lapse, for whatever reason, then Pfizer was in a position to predict it even before then.) In general, information as to patent expiry dates and loss of data exclusivity dates is in the public domain and can be ascertained in advance. I nevertheless recognise that it is probably too much to expect NHS England to keep track of such dates and to plan for the resulting situations. I consider that it

behoves patentees who want their second medical use patents enforced to provide NHS England with all the information and assistance it requires to enable it to issue appropriate guidance as and when required. I also consider that it behoves generic companies who want their interests in obtaining untroubled access to lawful markets protected to cooperate with NHS England as well. I recognise that generic companies are always understandably reluctant to disclose their future commercial plans to anyone, but the potential interest of generic companies in a skinny label launch (whether or not pending a challenge to the validity of the patent) to avoid a second medical use patent will usually be obvious. In short, what is needed is a system for dealing with these situations." ¹⁴⁶

Putting such a system in place would present multiple problems. There might be doubt over the exact scope of the patent, and it is not certain who would provide the authoritative view on this, apart from the courts, which brings us back to square one. There are also issues of commercial strategy, and it can be expected that brand name pharmaceutical companies will feel quite reluctant to co-operate in a system that aims at organising competition for them and losing market share, while generic manufacturers will be very reluctant to divulge strategic information such as product launch dates well in advance of the actual launch.

I am also not convinced that it is a solution that would effectively work in all healthcare systems. It is without a doubt easier to put into effect in centralised state healthcare systems, but seems to be much more complicated in the case of decentralised public-private or private healthcare systems. *200

But, however attractive this solution might look for certain healthcare systems, it still does not solve the problem of off-label use, unless one concludes that organising such a system would require the abolition of off-label use, which we have argued not to be a feasible solution.

Conclusion

This contribution has touched upon a very topical problem, the patentability of further medical indication claims in Europe and how they can be infringed in the context of a personalised medicine era. It demonstrates that in an age of personalised medicine, the importance of medical indication claims is bound to grow exponentially. It is therefore crucial to have a very good understanding under which conditions such patents can be granted and under which circumstances they can be infringed.

This article has demonstrated that there is a growing trend of filing for medical indication claims that sit very close to the therapeutic activities of the physician. That is as such not desirable, as medical treatment methods have been deemed not patentable for several decades on the basis of socio-ethical and public health grounds. It could be perceived that a growing number of medical indication patents attempt to capture the therapeutic activities of the physician. The case law also struggles with this problem. One remedy could be to abolish the exclusion of medical treatment methods from patentability, but we have shown that this is not only unlikely to happen, but will also not solve the current problems.

We have subsequently analysed in considerable detail the various patent infringement scenarios of the various players in the pharmaceutical product chain, i.e. the generic manufacturer, the prescribing physician and the pharmacist dispensing the drugs to the patient. This detailed analysis has never been done before in the English literature and shows very interesting if not always very enjoyable results. It shows that virtually all players run a considerable liability risk for patent infringement, also in the case of an off-label use, and equally also so by virtue of regulatory requirements such as preferential generic drug prescription schemes and generic substitution requirements within healthcare systems. That is as such pretty alarming, and calls for a number of interventions so as to avoid public health being harmed.

To that effect, as a primary measure, a therapeutic freedom exception needs to be introduced for both the physician and the pharmacist, so as to avoid these players feeling in any way inhibited in keeping the health of patients as the primary focus of attention.

We have also demonstrated that further measures are required. Generic manufacturers seem to be particularly targeted, even in circumstances which are beyond their control, such as off-label use or for that matter generic substitution requirement policies within national healthcare systems. Even though this article does not claim that generic manufacturers should not be held accountable for patent infringements they commit, and hence we do not advance the suggestion that generic companies should be immunised against patent infringement claims, it is submitted that they should not be so held liable for activities beyond their control. We have demonstrated that the current approach in the case law of at least some countries to hold generic manufacturers liable for patent infringement if they know that the products they manufacture will be intentionally used by the other players in the treatment of a patented medical indication is a standard which is not sustainable. It would effectively evict generic companies from the drug market, and that is not in the interest of public health and public healthcare costs.

To that effect, we have made a number of proposals that could be considered to change the current situation. We have made it clear that some of those proposals are likely to be non-viable as they could conflict with international treaty obligations. We have, however, provided a number of solutions which could be readily implemented by the courts. These solutions fundamentally aim at narrowing the currently very wide scope of what is considered to be "intent" or "knowledge". Some of those solutions also suggest introducing the concept of "intent" in the mind of the alleged infringer instead of the current approach where intent in the mind of the end-user seems to be used as a standard. *201

It is believed that some of the proposals we have made are not only sustainable, but also balance the interests of the patent holders with the interest of society to provide the best healthcare at affordable prices and the interests of generic manufacturers to be able to market freely their products for non-patented uses, the latter being seriously jeopardised under the current state of the case law. The case law in the UK seems to suggest that it would not prefer a case law based solution, but would prefer a system where the patent system and the healthcare/regulatory system co-operate with a view to arrive at a separation between patented and non-patented uses, which should be strictly adhered to by physicians and pharmacists in their prescription and dispensing behaviour. That seems to be a fair solution, but apart from the fact that it is very difficult to put into practice, it does not seem to cover all eventualities, which leads us to the conclusion that a combination of one or more of the interpretative solution presented here may seem preferable. This contribution has not provided the definitive answer to the challenges we are faced with in an age of personalised medicine, but it is hoped that it will at least contribute usefully to the debate about future legal development in this area.

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Footnotes

- 1 Senior Lecturer in Intellectual Property Law, University of Liverpool, Law School: email: S.Bostyn@liverpool.ac.uk.
- 1 G5/83 [EISAI/Second medical indication \[1985\] OJ EPO 60](#).
- 2 See [2016] I.P.Q, Issue 3 (forthcoming).
- 3 *European Commission, "Pharmaceutical Sector Inquiry: Final Report" (8 July 2009)*, http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf [Accessed 15 March 2016].
- 4 Those strategies encompassed patent filing strategies, patent related exchanges and litigation, settlements and reverse payments, life-cycle strategies and use of secondary patents, among which medical indication patents, other interventions to delay generic entry, whether at the level of data exclusivity or at the regulatory level. For details, see *European Commission, "Pharmaceutical Sector Inquiry: Final Report (8 July 2009)*, pp.181–378, http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf [Accessed 15 March 2016].

For more reading on this inquiry, see, e.g., Nicoleta Tuominen, "An IP perspective on defensive patenting strategies of the EU pharmaceutical industry" [2012] E.I.P.R. 541; Matthew Cole,

- "Pharmaceuticals and competition: first strike to the Commission?" [2013] E.C.L.R. 227; Sean-Paul Brankin, 'Patent settlements and competition law: where is the European Commission going?' (2010) 5(1) *Journal of Intellectual Property Law & Practice* 23; Hanns Ullrich, "Strategic patenting by the pharmaceutical industry: towards a concept of abusive practices of protection" in, Josef Drexl and Nari Lee (eds), *Pharmaceutical Innovation, Competition and Patent Law: A Trilateral Perspective* (Cheltenham: Edward Elgar Publishing, 2013), pp.241–272; Josef Drexl, "AstraZeneca and the EU sector inquiry: when do patent filings violate competition law?" in *Pharmaceutical Innovation, Competition and Patent Law* (2013), pp.290–322.
- 5 Commission, "Executive Summary of the Pharmaceutical Sector Inquiry Report", p.14, point 3.2.6, http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication_en.pdf [Accessed 15 March 2016].
- 6 *European Alliance for Personalised Medicine, Innovation and Patient Access to Personalised Medicine* (2013), p.8.
- 7 This will be covered in a subsequent issue of this journal, dealing with the historical evolution and current practice into patenting medical indications and the non-patentability of medical treatment methods in Europe.
- 8 Where reference is made in this article to "pharmaceutical products", "medicaments" or "drugs", this is meant to include both medicines based on traditional chemical and pharmaceutical research and medicines stemming from biotechnological research, such as, for instance, antibodies, which according to at least one study seem to be particularly suitable for off-label use, and are equally one of the most important weapons in the personalised medicine era. See I. Danés et al., "Outcomes of off-label drug uses in hospitals: a multicentric prospective study" (2014) 70 *Eur. J. Clin. Pharmacol.* 1385.
- 9 *European Alliance for Personalised Medicine, Innovation and Patient Access to Personalised Medicine* (2013), p.8.
- 10 *European Science Foundation (ESF), "Personalised Medicine for the European Citizen: Towards more precise medicine for the diagnosis, treatment and prevention of disease (iPM)"* (Strasbourg, 2012), p.13.
- 11 H. Salter and R. Holland, "Biomarkers: refining diagnosis and expediting drug development—reality, aspiration and the role of open innovation" (2014) 276 *Journal of Internal Medicine* 215, 215.
- 12 K.K. Jain, *Textbook of Personalized Medicine* (New York: Springer, 2009), p.59.
- 13 Jain, *Textbook of Personalized Medicine* (2009), p.106.
- 14 Jain, *Textbook of Personalized Medicine* (2009), p.69.
- 15 "Interferon induced transmembrane protein 3": the protein encoded by this gene is an interferon-induced membrane protein that helps confer immunity to influenza A H1N1 virus, West Nile virus, and dengue virus. A variant to that gene affects that immunity. See <http://www.ncbi.nlm.nih.gov/gene/10410> [Accessed 15 March 2016].
- 16 I. Sample, "Genetic testing could pinpoint people most at risk from flu", *Guardian*, 8 September 2015.
- 17 For more details, see E. Ventose, *Medical Patent Law: The Challenges of Medical Treatment* (Cheltenham: Edward Elgar Publishing, 2011); F.-E. Hufnagel, "Der Schutzbereich von Second Medical Use Patenten" [2014] G.R.U.R. 123; P. Meier-Beck, "Patentschutz für die zweite medizinische Indikation und ärztliche Therapiefreiheit" [2009] G.R.U.R. 300; D. Thums, 'Patent Protection for Medical Treatment—A Distinction Between Patent and Medical Law' (1996) 27 *I.I.C.* 423; H. Schacht, *Therapiefreiheit und Patentschutz für die weitere medizinische Indikation* (Baden-Baden: Nomos Verlagsgesellschaft, 2014); Eva-Maria Müller, *Die Patentfähigkeit von Arzneimitteln: Der gewerbliche Rechtsschutz für pharmazeutische, medizinische und biotechnologische Erfindungen* (Berlin, Heidelberg: Springer-Verlag, 2003).
- 18 *Bristol-Myers Squibb Co v Baker Norton Pharmaceuticals Inc* [1999] R.P.C. 253 Ch D at [43].
- 19 See [2016] I.P.Q., (forthcoming).
- 20 See EPC 2000 art.53(c): "European patents shall not be granted in respect of: ... (c) methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body; this provision shall not apply to products, in particular substances or compositions, for use in any of these methods."
- 21 See G2/08 ABBOTT RESPIRATORY/Dosage regime [2010] OJ EPO 456, reasons 5.3. We will come back to medical treatment methods in a subsequent issue of this Journal.
- 22 In the US, medical treatment methods are perfectly patentable.
- 23 EPC 1973 art.54(5) reads: "The provisions of paragraphs 1 to 4 shall not exclude the patentability of any substance or composition, comprised in the state of the art, for use in a method referred to

in Article 52, paragraph 4, provided that its use for any method referred to in that paragraph is not comprised in the state of the art." Under the EPC 2000, the almost identical provision is now in art.54(4).

- 24 Schacht has, probably rightly, thus criticised the very broad scope of those first medical indication claims: see *Schacht, Therapiefreiheit und Patentschutz für die weitere medizinische Indikation (2014)*, pp.260–267.
- 25 For example, a drug that is used for the treatment of epilepsy, and it is later discovered and patented that that same substance can also be used for the treatment of pain.
- 26 G5/83 EISAI/Second medical indication [1985] OJ EPO 60.
- 27 T19/86 [1989] OJ EPO 24; T893/90 of 22 July 1993; T233/96 of 4 May 2000.
- 28 T1399/04 SCHERING/Combination therapy HCV, decision of 25 October 2006; T734/12 GENENTECH, INC/Arthritis patients with an inadequate response to a TNF-alpha inhibitor, decision of 17 May 2013.
- 29 T51/93 of 8 June 1994; T138/95 of 12 October 1999.
- 30 T290/86 [1992] OJ EPO 414; T254/93 [1998] OJ EPO 285; T1020/03 [2007] OJ EPO 204.
- 31 G2/08 ABBOTT RESPIRATORY/ Dosage regime [2010] OJ EPO 456.
- 32 EPC art.54(5): "Paragraphs 2 and 3 shall also not exclude the patentability of any substance or composition referred to in paragraph 4 for any specific use in a method referred to in Article 53(c), provided that such use is not comprised in the state of the art."
- 33 See G2/88 MOBIL OIL III/Friction reducing additive [1990] OJ EPO 93.
- 34 For more details on the distinction between absolute and purpose limited product protection, see *S.J.R. BOSTYN, Patenting DNA Sequences (Polynucleotides) and Scope of Protection in the European Union: An Evaluation (Luxembourg: European Communities, 2004)*, pp.56–66.
- 35 See G2/08 ABBOTT RESPIRATORY/Dosage regime [2010] OJ EPO 456, reasons 7.1.4; and Notice from the European Patent Office dated 20 September 2010 concerning the non-acceptance of Swiss-type claims for second or further medical use following decision G2/08 of the Enlarged Board of Appeal, [2010] OJ EPO 514.
- 36 Decision of the Administrative Council of 28 June 2001 on the transitional provisions under [Article 7 of the Act](#) revising the European Patent Convention of 29 November 2000.
- 37 T1570/09 PROTISTA/Alpha-ketoglutaric acid and pharmaceutically acceptable salts thereof for use in increasing HDL plasma levels, decision 16 May 2014, reasons 4.8.
- 38 T1780/12 BOARD OF REGENTS, UNIVERSITY OF TEXAS SYSTEM/Cancer treatment, decision 30 January 2014.
- 39 T1780/12 BOARD OF REGENTS, UNIVERSITY OF TEXAS SYSTEM/Cancer treatment, decision 30 January 2014, reasons 22.
- 40 See, e.g., the European Medicines Agency's (EMA) definition of off-label use from the guideline on good pharmacovigilance practices: European Medicines Agency (EMA) 2014: Guideline on good pharmacovigilance practices (GVP) Annex I—Definitions (Rev 3), EMA/876333/2011 Rev 3*: "Situations where a medicinal product is intentionally used for a medical purpose not in accordance with the authorised product information. Off-label use includes use in non-authorised paediatric age categories. Unless specifically requested, it does not include use outside the EU in an indication authorised in that territory which is not authorised in the EU." See also the definition of off-label use in [art.1\(16\) of the EU veterinary medicines directive \(Directive 2001/82 on the Community code relating to veterinary medicinal products \(\[2001\] OJ L311/1\), as amended](#)): "The use of a veterinary medicinal product that is not in accordance with the summary of the product characteristics, including the misuse and serious abuse of the product."
- 41 C. Lenk and G. Duttge, "Ethical and legal framework and regulation for off-label use: European perspective" (2014) 10 *Therapeutics and Clinical Risk Management* 537, 538.
- 42 I. Vrancken, "Off-label Prescription of Medication" (2015) 22 *European Journal of Health Law* 165, 168.
- 43 António Vaz Carneiro and João Costa, "Off-label prescription: Practice and problems" (2013) 32(9) *Rev. Port. Cardiol.* 681, 683.
- 44 For the UK, see *General Medical Council, "Good Medical Practice 2013: Good practice in prescribing and managing medicines and devices" (2013)*, paras 67–70, which allows for what is called there unlicensed drugs.
- 45 For an overview, see Lenk and Duttge, "Ethical and legal framework and regulation for off-label use" (2014) 10 *Therapeutics and Clinical Risk Management* 537, 538–539 and 542.

- 46 ANSM, "Temporary Recommendation for Use (RTUs). Principles and information on the methods used by the ANSM for establishment and implementation" (October 2012), <http://ansm.sante.fr/Mediatheque/Publications/Information-in-English> [Accessed 15 March 2016].
- 47 Décret n°2014-1703 du 30 décembre 2014, amending art.R5121-76-1 Code de la santé publique.
- 48 Cynthia Burton, "New French Rules on Off-Label Use" (21 January 2015), <https://www.insideeulifesciences.com/2015/01/21/new-french-rules-on-off-label-use/> [Accessed 15 March 2016].
- 49 One must make a distinction between government policies governing off-label use and government policies regarding generic use. The latter is clearly openly regulated. In the UK, physicians are actively encouraged to prescribe the generic version; as witness thereof, in 2008, there were more than 83% generic prescriptions. Some countries have additionally a generic substitution policy, which forces pharmacies to dispense the generic version of a drug even if the prescription is for the brand name. See Department of Health, "The proposals to implement 'generic substitution' in primary care, further to the pharmaceutical price regulation scheme (PPRS)" (5 January 2010), http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_110511.pdf [Accessed 15 March 2016]. Generic substitution is not allowed in the UK, but is compulsory in Finland and Sweden, for instance.
- 50 For more details, see, Rita-Marié Jansen, "The Off-Label Use of Medication: The Latest on the Avastin -Lucentis Debacle" (2013) 32 Med. Law 65.
- 51 Poland v European Commission (C-185/10) EU:C:2012:181 at [38].
- 52 Directive 2001/83 on the Community code relating to medicinal products for human use [2004] OJ L311/67–128, as amended by Directives 2004/24 and 2004/27.
- 53 The pharmacist's infringement risk can be based on a number of different actions. He can dispense the generic drug as he finds it on the prescription. He can alternatively also dispense a generic drug in the context of a generic substitution obligation in the regulatory framework. In some countries, pharmacists are under an obligation to provide always a cheaper generic substitution even if the prescription mentions the brand name. The latter is the case for, e.g., Finland and Sweden. Generic substitution is not allowed under the UK regulatory system. If the physician prescribes the brand name, the pharmacist must dispense accordingly. The prohibition on generic substitution in the UK is partly neutralised by the fact that in 2008, 83% of prescriptions were already for the generic drug. For details, see Mohamed Azmi Hassali et al., "The experiences of implementing generic medicine policy in eight countries: A review and recommendations for a successful promotion of generic medicine use" (2014) 22 Saudi Pharmaceutical Journal 491; Martin G. Duerden and Dyfrig A. Hughes, "Generic and therapeutic substitutions in the UK: are they a good thing?" (2010) 70(3) Br. J. Clin. Pharmacol. 335; Joan Costa-Font, Caroline Rudisill and Stefanie Tan, "Brand loyalty, patients and limited generic medicines uptake" (2014) 116 Health Policy 224.
- 54 e.g. the UK: see UK Patents Act 1977 s.60(5)(a).
- 55 See, e.g., for the UK: Patents Act 1977 s.60(1): "(1) Subject to the provisions of this section, a person infringes a patent for an invention if, but only if, while the patent is in force, he does any of the following things in the United Kingdom in relation to the invention without the consent of the proprietor of the patent, that is to say—
- (a) where the invention is a product, he makes, disposes of, offers to dispose of, uses or imports the product or keeps it whether for disposal or otherwise;
- (b) where the invention is a process, he uses the process or he offers it for use in the United Kingdom when he knows, or it is obvious to a reasonable person in the circumstances, that its use there without the consent of the proprietor would be an infringement of the patent;
- (c) where the invention is a process, he disposes of, offers to dispose of, uses or imports any product obtained directly by means of that process or keeps any such product whether for disposal or otherwise.
- 56 UK Patents Act 1977 s.60(1)(c).
- 57 See UK Patents Act s.60(2).
- 58 Schacht, *Therapiefreiheit und Patentschutz für die weitere medizinische Indikation* (2014), p.301.
- 59 Assendorf and Schmidt in Benkard, *Patentgesetz, 10th edn* (München: Verlag C.H. Beck, 2006), §5, Rdnr. 56: "Der Schutz des Verwendungspatents setzt erst in dem Augenblick ein, in dem die Herrichtung des betreffenden Stoffes (oder Stoffgemisches) für die geschützte Anwendung augenfällig (besser: sinnfällig) wird, also durch die Formulierung des Stoffes mit anderen inerten Bestandteilen für den betreffenden Zweck, die Konfektionierung, Dosierung oder die gebrauchsfertige Verpackung für den betreffenden Zweck, was letztlich auch durch

- einen Beipackzettel geschehen kann, sinnfälligen Ausdruck findet (BGHZ 68, 156, 161 —Benzolsulfonylharnstoff; 88, 209, 217—Hydropyridin). Der Schutz knüpft somit an objektiv feststellbare Kriterien an. Er erfasst dann aber auch nicht allein das Formulieren, Konfektionieren, Dosieren oder das gebrauchsfertige Verpacken, sondern unmittelbar auch das Anbieten, Inverkehrbringen (auch Export), Gebrauchen, Einführen und Besitzen des hergerichteten Stoffes oder Stoffgemisches (BGHZ 88, 209, 217—Hydropyridin). Auf diese Weise wird der Inhaber des Verwendungspatents auch gegen Importe der im patentfreien Ausland augenfällig für den betreffenden Zweck hergerichteten Stoffe (oder Stoffgemische) und gegen Exporte der so hergerichteten Stoffe geschützt. Mit dem Inverkehrbringen des so hergerichteten Stoffes genehmigt dessen Hersteller die Benutzung des hergerichteten Stoffes bei der geschützten Anwendung."
- 60 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [77], quoting 4A O 145/12 Chronic Hepatitis C Treatment, LG Dusseldorf, 14 March 2013.
- 61 Meier-Beck, "Patentschutz für die zweite medizinische Indikation und ärztliche Therapiefreiheit" [2009] G.R.U.R. 300, 303.
- 62 *Schacht, Therapiefreiheit und Patentschutz für die weitere medizinische Indikation (2014)*, p.297.
- 63 If the patented medical indication is long-term treatment of a specific condition, the fact that the packaging contains a multitude of pills and the fact that there is no information that the drug so produced by the generic manufacturer cannot be used as a long term treatment of that specific condition can be objective indications that there is a manifest making-up. See *Schacht, Therapiefreiheit und Patentschutz für die weitere medizinische Indikation (2014)*, pp.298–299.
- 64 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [81].
- 65 OLG Düsseldorf, Urteil vom 31.01.2013—I-2 U 54/11 (*Cystus*), BeckRS 2013, 11782.
- 66 See BGHZ 101, 159—Antivirumittel [1987] G.R.U.R. 794, 797: "Die vorstehenden Ausführungen gelten im Ergebnis unabhängig davon, ob man den Klagepatentanspruch als 'zweckgebundenen Stoffanspruch' oder als einen Verwendungsanspruch im Sinne der neueren Rechtsprechung des erkennenden Senats ('Benzolsulfonylharnstoff' und 'Sitosterylglykoside', a.a.O.) auffaßt."
- 67 LG Hamburg, Urteil vom 02.04.2015, 327 O 143/15, BeckRS 2015, 08691, at II.1.(cc)(2): "Vorliegend ist das Arzneimittel jedenfalls bereits durch seine Herstellung als sinnfälliger für die Anwendung im Sinne des vorliegenden Herstellungsverwendungspatents hergerichtet anzusehen, als dass es ohne Weiteres zur Behandlung von (neuropathischen) Schmerzen verwendet werden kann. Es bedarf keiner weiteren körperlichen Schritte oder Hinzufügung körperlicher Mittel, sondern lediglich einer Zweckbestimmung. Diese Zweck oder Verwendungsbestimmung trifft vorliegend der substituierende Apotheker, § 129 Abs. 1 S. 2 SGB V."
- 68 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [113]–[129] (emphasis added).
- 69 [Generics \(UK\) Ltd \(t/a Mylan\) v Warner-Lambert Co LLC \[2015\] EWHC 2548 \(Pat\)](#) at [627].
- 70 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [628].
- 71 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [634]–[639] (emphasis added).
- 72 See Meier-Beck, "Patentschutz für die zweite medizinische Indikation und ärztliche Therapiefreiheit" [2009] G.R.U.R. 300, 304.
- 73 [Warner-Lambert Co LLC v Actavis Group PTC EHF \[2015\] EWHC 72 \(Pat\)](#) at [99].
- Hufnagel also concludes that there would be no infringement but for very different reasons. He thinks that fundamentally the physician is caught by the claim, but there would be no infringement because it would fail to link the prescription for the protected medical use and the specific product prescribed. See Hufnagel, "Der Schutzbereich von Second Medical Use Patent" [2014] G.R.U.R. 123, 125.
- 74 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [686].
- 75 See *A. Benyamini, Patent infringement in the European Community, IIC studies: Studies in Industrial Property and Copyright Law 13 (Weinheim: VCH, 1993)*, pp.155–156.
- 76 That would be the approach followed by Arnold J in the [Warner Lambert](#) case discussed earlier.
- 77 Also of this view, but without rationale, see *Schacht, Therapiefreiheit und Patentschutz für die weitere medizinische Indikation (2014)*, p.311.
- 78 *Schacht, Therapiefreiheit und Patentschutz für die weitere medizinische Indikation (2014)*, p.311.
- 79 In the UK, [s.60\(5\)\(c\) UK Patents Act 1977](#): "An act which, apart from this subsection, would constitute an infringement of a patent for an invention shall not do so if— ... (c) it consists of the extemporaneous preparation in a pharmacy of a medicine for an individual in accordance with a prescription given by a registered medical or dental practitioner or consists of dealing with a medicine so prepared."

- 80 See also [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [129].
- 81 See in that context, [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [132].
- 82 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [656]–[657] (emphasis added).
- 83 See [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [638] (emphasis added).
- 84 LG Hamburg, Urteil vom 02.04.2015, 327 O 143/15, BeckRS 2015, 08691, at II.1.(cc)(2), discussed earlier.
- 85 See, LG Hamburg, Urteil vom 02.04.2015—327 O 140/15 (Warner-Lambert Co LLC v Aliud Pharma GmbH), BeckRS 2015, 08822.
- 86 Novartis AG v Sun Pharmaceutical Industries, Court of Appeal of The Hague, 27 January 2015, docket number C/09/460540 / KG ZA 14-185, case number 200.1 50.713/01.
- 87 Antiviral treatment for naive patients and patients having a HCV genotype type 1 infection were expressly "carved-out" from the market authorisation, as these were patent-protected.
- 88 Court of Appeal The Hague, 14 July 2015, Schering Corp (Merck Sharp & Dohme Corp) v Teva Pharma BV, docket number 358401/HA ZA 10-437, points 5.2 to 5.5 of the reasons.
- 89 e.g. under UK law, [UK Patents Act 1977 s.60\(5\)\(a\)](#).
- 90 This is at least partly also due to the fact that pharmaceutical companies will not focus too heavily on the enforcement of second medical use claims if they still have a live product claim on the chemical entity.
- 91 See BGHZ 101, 159—Antivirusmittel [1987] G.R.U.R. 794 at 797.
- 92 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [686].
- 93 See subsection "Application to the various players in the chain" above; and see further subsection "Concluding comments" below.
- 94 *Schacht, Therapiefreiheit und Patentschutz für die weitere medizinische Indikation (2014)*, p.311.
- 95 See in that context, [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [132].
- 96 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [656]–[657] (emphasis added).
- 97 See [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [638] (emphasis added).
- 98 LG Hamburg, Urteil vom 02.04.2015, 327 O 143/15, BeckRS 2015, 08691, at II.1.(cc)(2), already discussed earlier.
- 99 Court of Appeal The Hague, 14 July 2015, Schering Corp (Merck Sharp & Dohme Corp) V Teva Pharma BV, docket number 358401/HA ZA 10-437, points 5.2 to 5.5 of the reasons.
- 100 See [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [638] (emphasis added).
- 101 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [132].
- 102 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [132].
- 103 See, e.g., Andreas Schrell, "Zur Anspruchsformulierung bei zweckgebundenem Patentschutz" [2010] G.R.U.R. Int. 363, 365.
- 104 See subsection "Medical indication patents and infringement—general principles" above.
- 105 Hufnagel, "Der Schutzbereich von Second Medical Use Patenten" [2014] G.R.U.R. 123, 124.
- 106 See, e.g., 4A O 145/12 Chronic Hepatitis C Treatment, LG Dusseldorf, 14 March 2013, <http://www.duesseldorfer-archiv.de/?q=node/5064> [Accessed 16 March 2016], where it was held: "Inherent in the 'purpose-limited product protection' is a final element, namely a particular purpose actualisation. This forms a key constituent of the protected invention, which is only realised through the actualisation of the inherent purpose. If this purpose is neither aimed for nor attained in a purposive way, but instead a purpose other than that identified in the patent claim is actualised, then there is no utilisation of the patent ...
- For answering the question whether the purpose pursued is that identified in the patent or a different purpose, a practically reasonable yardstick must be applied that leaves no room for sophistry. The fact that a product is suitable, inter alia, for the purpose stated in the patent in suit does not mean that it also actualises that purpose. Instead, for utilisation of the teaching protected in the 'purpose-limited claim', it is also necessary that the purpose inherent in the patent in suit is achieved (actualised) to a practically considerable extent in the sense of the specific objective of the patented teaching." English translation from [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [75].
- 107 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [126].
- 108 Agreement Relating to Community Patents (Luxembourg, 15 December 1989) [1989] OJ L401/1. In the very first so-called Community Patent Convention of 1975, the provision was in art.30: see Convention on the European Patent for the Common Market (Community Patent Convention) (Luxembourg, 15 December 1975) [1976] OJ L17/1.

- 109 UK Patents Act 1977 s.60(2).
- 110 *Schacht, Therapiefreiheit und Patentschutz für die weitere medizinische Indikation (2014)*, pp.288–289; *Benyamini, Patent infringement in the European Community (1993)*, p.181.
- 111 Deckenheizung, BGH X ZR 153/03, published in German in [2006] G.R.U.R. 839 at [23].
- 112 M. Nieder, "Die mittelbare Patentverletzung—eine Bestandsaufnahme" [2006] G.R.U.R. 977, 978; BGH Luftheizegerät [2001] G.R.U.R. 228, 231; Deckenheizung, BGH X ZR 153/03, published in German in [2006] G.R.U.R. 839 at [24]. The English translation stems from [Grimme Landmaschinenfabrik GmbH & Co KG v Scott \(t/a Scotts Potato Machinery\) \[2010\] EWCA Civ 1110](#); [2011] F.S.R. 7: "Accordingly, the senate came to the decision more than once that it is not necessary for direct infringement of the patent by the buyer—either attempted or successful—to occur for an indirect patent infringement to occur, but rather it is sufficient merely for an offer or delivery of suitable devices to have occurred provided that the subjective prerequisites of its intention for use according to the patent are met."
- 113 *Hans-Rainer Jaenichen, Jürgen Meier and Niels Hölder, "Medical Use Claims: EPC 2000 and its Impact on Prosecution and Enforcement" in Prinz zu Waldeck und Pyrmont et al. (eds), Patents and Technological Progress in a Globalized World: Liber Amicorum Joseph Straus (Berlin, Heidelberg: Springer-Verlag, 2009)*, p.255 at p.268.
- 114 [Warner-Lambert v Actavis Group \[2015\] EWHC 72 \(Pat\)](#) at [113].
- 115 [Grimme Maschinenfabrik v Scott \[2010\] EWCA Civ 1110](#); [2011] F.S.R. 7.
- 116 Deckenheizung, BGH X ZR 153/03, published in German in [2006] G.R.U.R. 839 at [22]. (English translation from [Grimme Maschinenfabrik v Scott \[2010\] EWCA Civ 1110](#); [2011] F.S.R. 7).
- 117 Deckenheizung, BGH X ZR 153/03, published in German in [2006] G.R.U.R. 839 at [24].
- 118 LG Hamburg, Urteil vom 02.04.2015, 327 O 143/15, BeckRS 2015, 08691.
- 119 *Novartis AG v Sun Pharmaceutical Industries*, Court of Appeal The Hague, 27 January 2015, docket number C/09/460540 / KG ZA 14-185, case number 200.1 50.713/01. It must be added, however, that in a later decision as to the merits, it was held that there could be no such indirect infringement. See Court of The Hague, 25 November 2015, *Sun Pharmaceutical Industries (Europe) BV v Novartis AG*, docket number C/09/469148 / HA ZA 14-770, points 4.54 to 4.56 of the reasons.
- 120 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [684].
- 121 Court of The Hague, 25 November 2015, *Sun Pharmaceutical Industries v Novartis*, docket number C/09/469148 / HA ZA 14-770, points 4.54 to 4.56 of the reasons.
- 122 That has also been literally held in LG Hamburg, Urteil vom 02.04.2015, 327 O 143/15, BeckRS 2015, 08691.
- 123 See, BGHZ 101, 159—Antivirusmittel [1987] G.R.U.R. 794 at 797, discussed earlier.
- 124 LG Hamburg, Urteil vom 02.04.2015, 327 O 143/15, BeckRS 2015, 08691, at II.1.(cc)(2), already discussed earlier.
- 125 In that sense see also Hufnagel, "Der Schutzbereich von Second Medical Use Patentent" [2014] G.R.U.R. 123, 127.
- 126 LG Hamburg, Urteil vom 02.04.2015, 327 O 143/15, BeckRS 2015, 08691, at II.1.(cc)(2).
- 127 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [630].
- 128 The *European Commission's Pharmaceutical Inquiry Report* provides interesting reading in this regard.
- 129 See *Felix Addor and Christine Vetter, "Der Schutz der medizinischen Behandlungsfreiheit vor patentrechtlichen Verletzungsklagen", sic! (Zeitschrift für Immaterialgüter-, Informations- und Wettbewerbsrecht) 2014, Sondernummer 4/125 IGE, p.3*, https://www.sic-online.ch/fileadmin/user_upload/Sic-Online/2014/documents/245.pdf [Accessed 16 March 2016].
- 130 PatG art.9(1): "Die Wirkung des Patents erstreckt sich nicht auf: g. Handlungen im Rahmen einer medizinischen Tätigkeit, die sich auf eine einzelne Person oder ein einzelnes Tier bezieht und Arzneimittel betrifft, insbesondere die Verschreibung, Abgabe oder Anwendung von Arzneimitteln durch gesetzlich dazu berechnigte Personen."
- 131 35 USC §287(c): "With respect to a medical practitioner's performance of a medical activity that constitutes an infringement under section 271 (a) or (b), the provisions of sections 281, 283, 284, and 285 shall not apply against the medical practitioner or against a related healthcare entity with respect to such medical activity"
- 132 For a detailed overview of the various rationales and theories of patent protection with multiple references, see *S.J.R. Bostyn, Enabling Biotechnological Inventions in Europe and the United States: A study of the patentability of proteins and DNA sequences with special emphasis on the disclosure requirement, Eposcript Series No.4 (München: EPO, 2001)*, pp.23–64.

- 133 See *Ventose, Medical Patent Law (2011)*, p.70. Compulsory licensing could be a remedy in the case of refusal to provide access, but that is a very burdensome procedure which is fraught with problems and uncertainties. I therefore do not think this can reasonably be seen as an efficient solution.
- 134 As we have seen, in Europe, the non-patentability of medical treatment methods has been defended for many years on the basis of socio-ethical concerns. It would be somewhat illogical if those same legislatures were suddenly to decide that those concerns are no longer present.
- 135 The period of five years is inspired by the maximum term of protection provided by the Supplementary Protection Certificate system in Europe, which allows patent holders to extend the term of patent protection for the authorised pharmaceutical product for the stated maximum period as a compensation for the loss of effective patent protection due to regulatory approval requirements, as patents for pharmaceuticals cannot be enforced as long as there is no market authorisation granted for the pharmaceutical product. See [Regulation 469/2009 concerning the supplementary protection certificate for medicinal products \(codified version\) \[2009\] OJ L152](#).
- 136 As we have seen earlier, in most European countries, there are no statutory provisions regulating off-label use, but there are in many countries other forms of regulatory arrangements allowing off-label use.
- 137 As we have seen earlier, generic prescription is in many EU countries widespread, while generic substitution is not always allowed; for instance it is not allowed in the UK. For details, see Azmi Hassali et al., "The experiences of implementing generic medicine policy in eight countries" (2014) 22 Saudi Pharmaceutical Journal 491; in the Netherlands, there is also a system in place of generic prescription, based on a tender system, where the manufacturer winning the tender is allowed to supply the drug for all indications. See *Novartis v Sun*, Court of Appeal of The Hague, 27 January 2015, referred to earlier.
- 138 James Killick and Pascal Berghe, "Should Cost Prevail Over Safety? The Risks of Promoting Unauthorised Pharmaceuticals and Off-Label Use for Budgetary Consideration" (2014) 13(5) B.S.L.R. 172, 176.
- 139 Which is obviously problematic, as that changes over the lifespan of a drug, and it is impossible to constantly update leaflets, also because packages in stock with pharmacies might already contain outdated information by the time they get actually dispensed of.
- 140 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [132].
- 141 35 USC §271(c)—Infringement of patent (emphasis added).
- 142 Recent US case law has been clamping down on the scope of the provision though, and has held that if a generic manufacturer brings a drug on to the market which is mainly aiming at the patented use, and for which there are not many non-patented uses available, or for which it has not obtained a market authorisation, there is a case of at least contributory infringement. The fact that there is a substantial off-label use for non-patented indications is not a defence. See *Depomed Inc v Actavis Elizabeth LLC*, Civil Action No.12-1358 (JAP) (D.N.J. 2014).
- 143 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [81].
- 144 "If, as I held in *Warner-Lambert I*, the word 'for' in a Swiss form claim should be interpreted as requiring an intention on the part of the manufacturer that the medicament or pharmaceutical composition should be used for the new therapeutic use, then it is clear that Actavis have not infringed claims 1 or 3 of the Patent, since Actavis have never intended Lecaent to be used to treat pain": [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [661].
- 145 [Warner Lambert v Actavis \[2015\] EWCA Civ 556; \[2015\] R.P.C. 25](#) at [126].
- 146 [Generics v Warner-Lambert \[2015\] EWHC 2548 \(Pat\)](#) at [722]–[725].

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I.P.Q. 2016, 2, 151-201