ISSN 2003-2382

The patentability of Dosage Regimes:

How to receive and enforce Dosage Regimes patents in Europe

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ABSTRACT

Despite the therapeutical benefits of dosage regimes, being granted and securing patent protection for these types of inventions has always been difficult. Historically dosage regimes have generally been excluded from patent law as these were held to either lack industrial application or were caught by the medical methods exclusions arguing that these inventions unjustifiably limited the medical profession's choice of clinical practices. In 2010, the Enlarged Board of Appeal of the European Patent Office however held that dosage regimes are no longer excluded as such under the European Patent Convention 2000. In the post-EPC 2000 era the challenge is instead for dosage regimes to fulfill the requirements of novelty and inventive step. In seeking to bring greater clarity to the field of dosage regimes, this article aims at establishing what is required in order to be granted and enforce dosage regimes patents in Europe. In order to offer strategies to practitioners and potential patentees in regards to litigation as well as Research & Development tailoring, this article additionally contributes to the existing literature by providing for the first time, an empirical study of dosage regime patent decisions of the European Patent Office.

1. INTRODUCTION

Once a new active ingredient has been discovered, much information of its properties and pharmacokinetics[1] are unknown, even after all three clinical trial phases. Knowing more about the different parameters of its pharmacokinetics (drug absorption, drug distribution, drug metabolism and drug excretion) allows dosage regimes to be altered or developed. These adjusted regimes can then increase the efficacy of the drug as well as reduce its toxicity and side effects[2], making the drug effective and suitable for a larger proportion of the population. Whilst generic imitation has remained inexpensive and fast, drug discovery and development has become a longer and costlier process[3], enhancing the increasing need for providing incentives for the latter. For dosage regimes, the market and data exclusivity granted through the Marketing Authorisation Directive[4] does not provide an adequate incentive. This directive covers only active ingredients and offers an only 1-year extension of the existing exclusivity of the active ingredient by 1 year for second medical uses. This means that where more than one second medical uses exist, only the first will be rewarded through the directive.[5]. Solutions must be found elsewhere, such as in patent law.

Only in 2010, the Enlarged Board of Appeal (hereafter EBA) of the European Patent Office (hereafter EPO) attempted in Dosage regime/ABBOTT RESPIRATORY[6] to clarify the legal position of dosage regimes within the framework of the European Patent Convention 2000 (hereafter EPC). Whilst theoretically, it was decided that dosage regimes are patentable as long as these meet the requirements of inventive step and novelty, the position in practice remains nevertheless highly uncertain and unclear. This is enhanced further due to the uncertainty related to the ability and chances of succeeding in enforcing these types of patents through infringement proceedings in the unharmonized, post-grant landscape of the EPC. The EBA has not contributed with a definition of the term "dosage regimes.[7] This becomes even less straight forward because both in literature and different jurisdictions around Europe, different definitions of dosage regimes can be distinguished. For the purpose of consistent analysis, this article will, therefore, adopt the following widely used definition:

> *"Dosage regimes are decisions of drug administration regarding the formulation, route of administration, drug dose, dosing intervals and treatment duration".*[8]

Unfortunately, dosage regimes patents have never attracted much attention from scholars[9], other than with regards to their potential relationship to the controversial concept of "ever-greening". In seeking to bring greater clarity to the patentability of dosage regimes for practitioners, this article seeks to answer the desired question: "How can one receive, protect and enforce a dosage regime patent in Europe?" It, therefore, contributes to the existing literature by offering an in-depth analysis of EPC dosage regimes patents pre- and post-grant. Furthermore, this article offers for the first time an empirical study of EPO granted and refused dosage regime patents analysing the current position of these in practice.

2. THE PATENTABILITY OF DOSAGE REGIMES

2.1. Historical development of dosage regimes as a further medical use patent

At first, due to the adopted literal reading of the EPC, the EPO was reluctant to grant patents for any further medical uses. Whilst the Technical Board of Appeal (hereafter TBA) reiterated in Hoffman-la Roche/Pyrrolidine derivatives[10] that, only the first medical use was protected through the EPC 1973. In practice further medical uses were protected, however, their protection and accompa-

nying monopoly was granted to the patent owner of the first medical indication patent.[11] A patentee of a new known substance therefore in practice, also had a monopoly for future discoveries of new therapeutic effects. An approach that could negatively impact research on second medical uses of an existing drug. Hence, the EPO's approach could be seen as only considering the new discovery of an active ingredient as valuable pharmaceutical research ignoring the basic principle that molecules may have new medicinal properties.[12] As argued by Barry, "molecules should not be viewed as discrete objects but rather as constituted in their relations to complex informational and material environments".[13]

This interpretation of a wide scope of protection was however, diminished through the EISAI/second medical indication[14] to only cover the actual findings at the time of the patent filing. This was done whilst simultaneously concluding, for the first time, that second and further medical indications are capable of being patented on their own. The EBA, in this case, was concerned with the interpretation and interaction between article 54(5), regarding an exception to the general rule of novelty, and 52(4), regarding methods of treatment of the human body of the EPC 1973.

Even though in regards to the latter the issue was only concerned with "therapeutic methods" due to the EBA's reference to "medical indication" in its interpretation of article 54(5), it could be seen that it was referring not only to therapeutic methods but also other all other medical treatment found in article 52(4). Hence, the judgement had a much wider impact, affecting all types of methods including surgical, diagnostic and therapeutical.[15] Drawing a distinction between first and second medical indications, the EBA concluded that it could not "deduce from the special provision of Article 54(5) that there was any intention to exclude second (and further) medical indications from patent protection other than by purpose-limited product claims."[16] The inclusion of further medical use patents hence, originated out of the EBA's interpretation of the EPC's silence. Firstly, the EBA referred only in its decision to the fact that an intention could be deduced from the legislative history of the articles. However, this is inconsistent with the Munich Diplomatic Conference of 1973. Both the Dutch delegation and the Chairman[17], in response to the delegate of Yugoslavia, had expressly stated that Article 54(5) would apply only at first medical indication uses. With closer examination of the "travaux préparatoires", whilst opinions on second medical indications were divided, the majority was not in favour of their inclusion.[18]

1 Pharmacokinetics Can Be Defined As "The Study Of The Properties Of Drugs And Their Interaction With Living Organisms, Including Viruses" (Eckhard Beubler, Kompendium Der Pharmakologie (Springer Berlin Heidelberg 2018)).

2 Ibid.

3 S Basavaraj And Guru V. Betageri, 'Can Formulation And Drug Delivery Reduce Attrition During Drug Discovery And Development—Review Of Feasibility, Benefits And Challenges' (2014) 4 Acta Pharmaceutica Sinica B.

4 Directive 2001/83/EC On The Community Code Relating To Medicinal Products For Human Use (2001).

5 Justine Pila And Paul L. C Torremans, European Intellectual Property Law (Oxford University Press 2016).

6 G 0002/08 (Dosage Regime/Abbott Respiratory), 19.2.2010.

7 Ibid.

8 Roger L. Williams, 'Dosage Regimen Design: Pharmacodynamic Considerations' (1992) 32 The Journal Of Clinical Pharmacology.

9 S.J.R. Bostyn, 'Personalised Medicine, Medical Indication Patents And Patent Infringement: Emergency Treatment Required' (2016) Intellectual Property Quarterly.

10 T 0128/82, Hoffmann-La Roche (Ep0003602), Board Of Appeal Decision Of Epo, 12.01.1984.

11 "An Inventor Who For The First Time Makes A Known Compound (..) Should Be Rewarded To Cover The Whole Field Of Therapy." T 0128/82, Hoffmann-La Roche (Ep0003602), Board Of Appeal Of Epo, 12.01.1984; Accepted In T 0043/82, Roussel-Uclaf (Ep0003200) Board Of Appeal 16.4.1984.

12 Andrew Barry, Political Machines (Lightning Source 2014).

13 Andrew Barry, 'Pharmaceutical Matters' (2005) 22 Theory, Culture & Society.

14 G 0005/83, Eisai/Second Medical Indication, 05.12.1984; Ecli:Ba:1984:G000583.19841205.

15 Eddy D Ventose, Medical Patent Law (Edward Elgar 2011).

16 Op. Cit, Fn.14 (Para. 22).

17 " (..) A Further Patent Could Not Be Granted If A Second Possible Use Were Found For The Same Substance, Irrespective Of Whether The Human Or Animal Body Was To Be Treated With It." Minutes Of The Munich Diplomatic For The Setting Up Of A European System For The Grant Of Patents, Munich 10 September To 6 October 1973, At Para 54.

18 'Patent Protection For Second And Further Medical Uses Under The European Patent Convention' (2009) 6 Scripted.

Secondly, the EBA itself later referred to this ruling as a "praetorian approach" which was "a special approach to the derivation of novelty".[19] Even though the EBA did not give a definition as to what it meant by "praetorian", this term can be understood in the context of its origin in ancient Roman law.[20] Praetorian law according to Aemilius Papinianus is defined as "... that which in the public interest the praetors (judges) have introduced in aid or supplementation of correction of the ius civile (civil law)".[21] Seen in this light therefore, the EBA can be understood as indicating that EISAI went beyond what was agreed by the EPC 1973.[22] Thirdly, from a theoretical perspective, interpretation of silence is a risky and at times unclear matter. Eskridge, based on US law, illustrated the problems and difficulty of making any inferences from the legislator's silence[23]. Eskridge held that, it is very hard to aggregate preferences in a large group of people as well as to establish the meaning of their votes. From accounts of the diplomatic conference proceedings, it becomes evident that this problem is clearly present with regards to the EPC where reaching a clear voting outcome was often not possible due to different judicial backgrounds, interests and opinions.[24] Where, therefore, an amendment to the text of the Convention was not possible because of very close voting outcomes, this cannot accurately indicate a clear "intention of the legislator" as there may be multiple reasons for the legislator's passivity.[25] Fourthly, other than holding that further medical use patents in principle were patentable, the EBA also held that, "it seems justifiable by an analogy to derive the novelty for the process which forms the subject matter of the type of use claim now being considered from the new therapeutic use of the medicament".[26] However as, when one looks at Swiss-type claims, this means that in regards to novelty, the claim is directed to a process for preparation a product. This would mean that, the invention claimed is a process, however, the purpose limitation is not on this process, which as established formulates the subject matter of the claim but in fact on the product itself. This inconsistency in reasoning, therefore, means that the analogy is neither so clear nor direct as stated by the EBA.[27]

It can, therefore, be concluded that, the act of "creating" second medical use patents was done through an unauthorized extension of the EPC and, therefore should be seen as judicial law making. Even though this perhaps could have been done to meet the demands of the pharmaceutical market or the advances of research, which at the time of the drafting of the EPC was not so obvious (most advances and recognition of the importance of pharmacokinetics only took place in the 1980s and onwards)[28], it does not undermine the fact that the decision has been and still can be criticised for being invalid.[29]

In order to by-pass the problems created through this creative interpretation, the EBA established the so-called "Swiss-claims", which would secure patent protection for further medical use patents. Swiss claims had to fulfil two requirements: (a) the manufacture of a medicament and (b) a new application.[30] These essential requirements set out had the function of defining the patent's scope and novelty. Which types of claims satisfied these requirements, became a burdensome debate that resulted in the ever-extending reach of the EISAI principle.[31]

Dosage regimes have specifically fallen within this group of second medical uses types, where patentability was highly uncertain. In Gastrointenstinal compositions[32], concerning a route of administration[33] and in Liposome compositions/SEQUUS[34], the board held that dosage regimes were not patentable. In the latter it was reasoned, taking a narrow reading of EISAI/second medical indication that, the claims at issue concerning the time and dose of administration were not a method of treatment or therapeutic application with the meaning of article 52(4) of the EPC 1973 but claims related to a process. In "Thiazide diuretics"/EURO-CELTIQUE[35], the TBA held that specifically personalised dosage regimes are not patentable, reasoning that this falls within the sphere of competences of medical practitioners.[36] These decisions ignore however, the substantial input of intellectual and financial resources necessary to produce such regimes, which reach far-beyond what is within the routine of a medical practitioner.[37]

In contrast, the TBA took a completely different approach in Sereno/HCG. Drawing on DUPHAR/pig II[39] and ICI/cleaning plague[40] it concluded that the mode of administration might be a critical factor in a medical treatment, thereby seeing no reason why it should be held that there is no patentability per se without proceeding the

[19] Op. Cit, Fn.6 Para. 491.

[20] 'Is The Enlarged Board Of Appeal Of The European Patent Office Authorised To Extend The Bounds Of Patentability? (The G3/85 Second Medical Indication/Eisai And G2/08 Dosage Regimes/Abbott Respiratory Cases)' [2011] International Review Of Intellectual Property And Competition Law.

[21] Randall Lesaffer And Jan ArriëNs, European Legal History: A Cultural And Political Perspective: The Civil Law Tradition In Context (Cambridge University Press 2014) P.85.

[22] Op. Cit, Fn.20.

[23] William N. Eskridge, 'Interpreting Legislative Inaction' (1988) 87 Michigan Law Review.

[24] For Example, Para 167: Conference Of The Contracting States To Revise The 1973 European Patent Convention (Conference Proceedings) Munich, 20 To 29 November 2000 (Mr/24/00).

[25] E. Llewellyn Overholt, 'Statutes: Construction: The Legislative Silence Doctrine' (1955) 43 California Law Review.

[26] G 0005/83, Eisai/Second Medical Indication, 05.12.1984; Ecli:Ep:-Ba:1984:G000583.19841205.

[27] Op.Cit,Fn.20.

[28] Guenther Hochhaus, Jeffrey S. Barrett And Hartmut Derendorf, 'Evolution Of Pharmacokinetics And Pharmacokinetic/Dynamic Correlations During The 20th Century' (2000) 40 The Journal Of Clinical Pharmacology.

[29] Op.Cit,Fn.20.

[30] T 0787/00 Kirin-Amgen, Inc. V Gruppo Lepetit S.P.A. (Ep0428267) Board Of Appeal Decision Of The Epo, 26.6.2003

[31] Eddy Ventose, 'Patent Protection For Dosage Regimes In Europe: A Dissenting View' (2011) 6 Journal Of Intellectual Property Law & Practice.

[32] T 0317/95, Gastrointestinal Compositions (Ep0282132) Board Of Appeal Decision Of The Epo, 26.2.1999.

[33] It Must Be Noted That Comments In Regards To The Patentability Where Made In Obiter.

[34] T 0004/98 Sequus Pharmaceuticals, Inc. V Inex Pharmaceuticals Corporation (Ep0496813) Decision Of The Board Of Appeal Of The Epo, 9.8.2001.

assessment of novelty and inventive step. In regards to dosage regimes it could therefore be seen that the EPO was relatively divided and unclear as to their position and their importance as well as to the intellectual input required of dosage regimes. In contrast to second medical indications, the legal landscape of dosage regimes was shaped by great legal uncertainty, disadvantageous for both the patent offices and applicants.[41]

Matters were made even more unclear when it became apparent that multiple interpretations of the EISAI[42] judgement and its relationship to dosage regimes co-existed within the different TBAs. In T1020/03[43] the TBA had held that dosage regimes are patentable inline with Article 52(4). Relying on the statements made in obiter dicta in EISAI[44], according to which new formulations, dosages or synergistic combinations would in principle face no difficulty regarding the question of novelty. Furthermore, it claimed that the expressed views in T317/95[45], T0056/97[46], T0584/97[47], T0485/99[48], rejecting the patentability of dosage regimes, conflicted with the EISAI decision and had no real legal basis in the EPC. Whilst this decision was followed in some cases for example T0515/06[49] and T0708/02[50] in Smithkline Beecham Corporation/Treatment of ovarian cancer[51] the TBA concluded that EISAI was not concerned with the novelty of dosage regimes and its comments could only be taken as obiter dicta. Contradictions amongst the TBAs led to great uncertainty. With the introduction of the EPC 2000, it was beyond doubt that further medical use patents were patentable. However the question of dosage regime specifically was not answered until the TBA in Kos Life Science Inc./dosage regimes[52] referred the question of patentability to the EBA. In contrast to the general approach before, the TBA noted that considerations concerning public health and medical profession confidentiality should not be a primary consideration when interpreting the current law.

In dosage regime/ABBOTT RESPIRATORY[53] the EBA firstly clarified that the change from 52(c) EPC 1973 to article 53(c) EPC 2000 was an editorial and not a substantive change. Furthermore, the EBA was of the opinion that the intention of the legislator in regard to the changes brought to Article 52(4) of EPC 2000 was to enshrine the intentions set out in EISAI/second medical indication[54] and its subsequent case law. It appears contradictory as firstly, the intention and situation was not clear as outlined above and secondly, prior case-law prior to this case actually held that dosage regimes were in fact not patentable.[55] A potential clarification opportunity was therefore in part wasted.

Nevertheless, the EBA in G2/08 clarified that the term "any specific use" should neither be interpreted in a limiting way nor substantially different to 54(5) of the EPC. The EBA, therefore, adopted a wide reading of the provisions 54(4) and 54(5). It however also held that in regard to dosage regimes the freedom of medical practitioners should be protected at a national level, if found necessary. This means that a claim approved by the EPO may, in fact, be in conflict with the laws and restrictions at national level. Through this and the lack of uniform definition of dosage regimes, no clear harmonised position in regard to dosage regimes could be achieved.

Lastly, the EBA abolished Swiss type claims as the need for these had ceased to exist in the post-EPC 2000 era. The case G2/08[56] clarifies that any further improvement in therapeutic treatments can form the basis for a patent under the EPC as long as the patentability requirements are met. Whilst the development of the further medical use patents has developed in such a way that at least on a theoretical level this is true, it remains to be seen whether this will work in practice. The answer to this depends greatly on the interpretation of G2/08 and the application of the patentability requirements to different dosage regime patents.

35 T 0056/97 Euro-Celtique S. A. V Takeda Chemical Industries, Ltd, Board Of Appeal Decision Of The Epo, 30.8.2001.

36 Ibid.

37 Ulrich Storz, 'Extending The Market Exclusivity Of Therapeutic Antibodies Through Dosage Patents' (2016) 8 Mabs.

38 T 0051/93,Serono Pharmazeutische Präparate Gmbh (Ep0290644) Board Of Appeal Decision Of The Epo, 8.6.1994.

39 T 0019/86,Duphar (Ep0069407) Decision Of The Board Of Appeal Of The Epo 15.10.1987 (Where A Patent Was Granted For A New Subgroup Of Patients).

40 T 0290/86 Ici Plc V Blendax (Ep0000256) Board Of Appeal Of 13.11.1990.

41 Joshua S. Gans, David H. Hsu And Scott Stern, 'The Impact Of Uncertain Intellectual Property Rights On The Market For Ideas: Evidence From Patent Grant Delays' (2008) 54 Management Science.

42 Op. Cit, Fn.14.

43 T 1020/03, Genentech, Inc, Board Of Appeal Decision Of The Epo, 29.10.2004.

44 Op. Cit, Fn.14.

45 T 0317/95, Gastrointestinal Compositions (Ep0282132) Board Of Appeal Decision Of The Epo, 26.2.1999

46 T 0056/97 Euro-Celtique S. A. V Takeda Chemical Industries, Ltd, Board Of Appeal Decision Of The Epo, 30.8.2001.

47 T 0584/97, Elan Corporation, Plc V Forschungsgesellschaft Rauchen Und Gesundheit Mbh 5.12.2001.

48 T 0485/99 Novartis Nutrition Ag, Board Of Appeal Decision Of The Epo, 29.4.2004.

49 T 0515/06 Nestec S.A., Decision Of The Epo Board Of Appeal, 18.1.2007.

50 T 0708/02 Vericore V Alpharma As And Akzo Nobel N.V., Decision Of The Epo Board Of Appeal, 4.4.2006.

51 T 1001/01 Smithkline Beecham Corporation, Board Of Appeal Decision Of The Epo, 11.10.2007.

52 T 1319/04 Kos Life Sciences, Inc., Enlarged Board Of Appeal Decision Of The Epo, 22.4.2008.

53 Op. Cit, Fn.6.

54 Op. Cit, Fn.14.

55 Op. Cit, Fn.15.

56 Op. Cit, Fn.6.

2.2. Qualitative and Quantitative Study of the patentability of Dosage Regimes at EPO level

In accordance with article 52(1) of the EPC 2000 inventions are patentable if these are "new, involve an inventive step and are susceptible of industrial application." Whether or not an invention is new is assessed based on whether or not it fulfils the requirements of Article 54 of EPC 2000. Where an invention is novel, it must then also meet the inventive step requirements outlined in Article 56. Since G2/08[57] dosage regimes are theoretically patentable, in practice, it can be seen that many dosage regimes are not patented or fail an appeal/opposition. In regard to this, it appears that the problem does not lie with the ability to prove novelty but rather in the assessment of inventive step.

This has according to this article, two main reasons. Firstly, novelty is a requirement as established above, that is much easier to meet and secondly, the EBA made the assessment and the position of the EPO much clearer in regard to the assessment of novelty rather than that of the inventive step. TBAs were therefore granted much more freedom in their assessment of the inventive step requirement, creating greater legal uncertainty. And secondly, the EBA in G2/08[58] stated, in obiter, that dosages regimes run the risk of being used abusively. This unclear and vague statement resembling the pre-G2/08 attitude of the EPO could have additionally caused more confusion and discrepancies in TBA's interpretations to this date.

For the assessment of the inventive step requirement the EPO generally applies the problem and solution approach, which is subdivided into three steps: (1) Establishing the closest prior art. (2) Establishing the "objective technical problem" to be solved. (3) Considering whether or not the claimed invention, starting from the closest prior art and the objective technical problem, would have been obvious to the skilled person.

In order to apply the assessment of this requirement to the unclear areas of dosage regimes this empirical study aids in analysing potential features that lead to a higher chance of passing the inventive step requirement and therefore being patentable. Each step of the inventive step requirement is assessed by comparing common features in all sample cases. Features, of course, may not be viewed purely in an isolated context as they are analysed here. However, being aware of a potential factor could result in better identification of which dosage regimes have chances of being patented. This has the practical benefit that dosage regime patents applications and R&D of pharmaceuticals can be tailored towards those dosage regimes that are most likely to be successful in their application stage.

2.2.1 Method and Data Sample:

The sample Data consisted of 45 Dosage regimes cases of the EPO. The sample cases were collected with the help of the "Darts-ip" database of the private company Darts-ip, which specializes in IP case law. This database was selected as firstly, all EPO cases on Darts are obtained from the EPO itself and not through private entities[59] and secondly, Darts-ip collects decisions from all cases manually, allowing cases to be filtered through keyword searches.[60]

EPO dosage regime cases were collected based on free text keyword searches of "dosage regimes" and "dosage regime". Cases were then selected chronologically based on their decision date; most recent cases were given priority in selection. In order for the sample cases to qualify for this study, they had to meet two requirements: (1) the cases had to enter into a discussion on the requirement of inventive step (2) the core subject of the patent had to be at least one dosage regime in accordance with the definition.

This study was found to have an estimated margin of

[57] Ibid.
[58] Ibid.
[59] This Information was supplied to me by Darts-Ip.
[60] Katrin Cremers And Others, 'Patent Litigation In Europe' (2016) 44 European Journal Of Law And Economics.
[61] Op. Cit, Fn.6.
[62] Epo Guidelines, Chapter Vii, Section 5.
[63] T 116/90 Beecham-Wuelfing Gmbh V Hoechst Ag, Board of Appeal Decision of The Epo, 03.12.199.
[64] Ibid.
[65] Brigham And Women's Hospital, Inc. V Hoffmann, Matthias Maikowski Ninnemann (Ep2397189) Decision Of The Opposition Division Of The Epo, 11.07.2017.
[66] Hexal Vs.Panion & Bf Biotech (Ep1931689), Epo, 27.07.2017.
[67] Smithkline Beecham Plc V Oragotti & Associati (Ep0839039), Opposition Division Epo, 17.11.2006.
[68] T 0355/97, Noramco, Inc V Mallinckrodt Speciality Chemicals Company (Ep289297), Board Of Appeal Decision Of The Epo, 05.07.2000.
[69] T0611/07 Evonik Stockhausen Gmbh V The Procter & Gamble Company, Nippon Shokubai Company Limited And Basf Se, (Ep1105168) Board Of Appeal Decision Of The Epo, 18.09.2009.
[70] Bengt Domeij, Pharmaceutical Patents In Europe (Kluwer Law International 2000).
[71] Hexal Vs.Panion & Bf Biotech (Ep1931689), Epo, 27.07.2017.
[72] Genzyme Corporation V Generics [Uk] Limited (Ep2664334) Opposition Division Decision Of The Epo, 26.07.2017
[73] Decision For Refusal Of Application By The Epo (Ep1931354), 30.01.2014.
[74] T964/95, The Trustees Of Columbia University/New York V Ueno Seiyaku K.K.(Ep0286903) 05.05.1999.
[75] (T 0446/13 - Bayer Consumer Care Ag V Takeda Nycomed As (28.02.2017) .
[76] (T 1374/11 Laboratorios Del Dr.Esteve S.A V Labiana Life Sciences, S.A.U (11.03.2015);, Forward Pharma V Pentafarma, Sociedade Técnico-Medicinal, Strawman And Keltie (Ep1799196) Preliminary Decision Of The BoA Of Epo, 05.02.2018) .
[77] Bardehle Pagenberg, 'Assessment Of Inventive Step Under The Epc'. (2010) .
[78] Bengt Domeij, Pharmaceutical Patents In Europe (Kluwer Law International 2000).
[79] T 0142/94 Euroceltique S.A. V Basf Aktiengesellschaft, Decision Of The Board Of Appeal Of The Epo Of 16.1.1997.

errors equal to or smaller than +/- 12.7% and the confidence level equal to or greater than 90%. Currently, it is not possible to retrieve the actual population size of this study through the EPO, specifically PATSAT. The reason for this is that the EBA of the EPO did not provide a definition of dosage regime in its' recent decision.[61] As a result, no clear categorization of dosage regimes is currently available upon which clear statistics of the total number of decided dosage regimes cases could be obtained. It was however possible to obtain the total number, 6031, of decisions of "second medical use" patents from PATSAT. Even though this number included second medical indication cases which are not dosage regimes, this number nevertheless served as the closest possible estimation of the population size.

2.2.2. Results

2.2.2.1. The assessment of the selection of the closest prior art

Whilst defining the closest prior art is the very first step of the inventive step requirement, it continues to be highly influential and important throughout the entire assessment. Not only does it serve as a form of benchmark of comparison against which the invention is evaluated, it also defines the formulation and therefore the scope of the technical problem.[62] Out of the 45 cases in 37 cases the closest prior was related to the same active ingredient, a feature that clearly stems from the nature of dosage regimes patents. One exception to this is where the new dosage regimes are accompanied by new medical indication. In T116/90[63], the Board of Appeal held that only prior documents with the same medical indication could constitute the closest prior art document. Hence, where a dosage regime is accompanied by a new medical indication, far fewer documents will form part of the prior art and therefore, the chance of the closest prior art being "more distant" is increased.

Dosage regime patents also face the problem and risk of the closest prior art disclosing further considerations or thoughts. This is where the prior art discloses something, which has not been tested or verified (e.g. a further research opportunity/possibility). Even though this is not a problem that most dosage regime patents face, as only 6/45 studied cases directly discussed "further considerations" of the closest prior art, where it is discussed it can be detrimental to the outcome (75% of these cases were held to not being inventive). When these 6 cases are examined closer it becomes clear that, 5/6[64] of them were found to be non-inventive on the basis of them being a "routine optimization". Where the further consideration, however, is not found in the closest prior art but in alternative prior art, EP2397189[65] indicates that this would be far less likely to lead to the finding of non-inventiveness and therefore is less threatening to the overall assessment of patentability. Furthermore, 5 out of these 6 cases concerned a new dosage rather than another type of dosage regime. It, therefore, appears that this threat of "further considerations" is largely faced by applications concerning new dosages. An applicant hoping to later receive a new dosage patent or invest in new dosage research should, therefore, be careful with the formulation of publications to ensure that vague wording of hypotheses or potential further research ideas do not hinder a later patent application for a new dosage. However, this difficulty raised by further consideration of the closest prior art could be overcome through the demonstration of obstacles to following the consideration, as was successfully done in proceedings of EP1526871[66] or by submitting evidence/prior art that could indicate that the skilled person would have not necessarily followed the closest prior art suggestion, as was successfully done in proceedings concerning the patent, EP0839039.[67]

2.2.2.2 Technical problem

When it comes to the formulation of the technical problem, formulations in the form of "an improved..." resulted in a much higher chance of being found non obvious (5/7 cases) than formulations in the form of "an alternative..."(7/14 cases). Therefore, whilst the reformulation in the form of "alternative method" does not directly mean that a patent will be held to lack an inventive step, its chances are diminished. This finding is coherent with the general position of pharmaceutical patents in general, where reformulations of problems into the "an alternative ..." resulted in cases such as T0355/97[68] and T0611/07[69] in a finding of non-inventiveness. The EPO has given the term "improvement" a wide and extensive interpretation from the applicant's point of view, resulting in the fact that any, regardless of the type or size, improvement is considered.[70] Furthermore, a wide range of factors including therapeutic properties[71], reduction of side effects[72], patient compliance[73] and duration of effect[74] are excepted.

Whilst for showing an increase in patient compliance no additional evidence is required to be submitted and therefore is therapeutic to prove. In regards to any ground other than patient compliance, the technical effect was mainly rejected because of either the fact that no evidence was submitted (42.86%)[75] or that too many variations within the comparative study exist thereby not allowing it as evidence (42,86%).[76] Hence it is essential that much care and attention should be dedicated towards submitted evidence, especially in regards to comparative studies. These should also attempt as much as possible, to establish an improved effect.

2.2.2.3 Obviousness:

In order to establish obviousness, the EPO essentially asks whether, the skilled person starting from the closest prior art, solving the problem at hand, would have arrived at the solution taking into consideration the body of prior art and the "mental furniture" of the skilled person.[77] Whilst generally, the skilled person is not permitted to "fill in" gaps of the prior art with either theoretical knowledge or his own knowledge,[78] the same is not true for dosage regime cases. In regard to new formulations, the TBA has held that the skilled person would take account of parameters relating to controlled release formulation known from the prior art and theoretical calculations known in the field of pharmacokinetics for the design of drug formulations.[79] This means that in regard to dosage regimes, the person in the skilled art has a much more active role than e.g. first medical use patents.

The biggest threat to the 45 cases in regard to the assessment of obviousness was routine optimization (47% of all cases that were found to not have an inventive step were held to be obvious on this ground).[80] Those cases that were not found to be obvious on the ground of routine optimization, were generally rejected because of their close proximity to the closest prior art or other prior arts used in combination. In these cases, the EPO found that either applying known pharmacokinetic knowledge to the prior art results directly in the claimed invention[81], differences between the patent and the closest prior art were small[82] or prior art documents would have led the skilled person straight to the dosage regime in question.[83] On the other hand, reasons for finding of non-obviousness included that the prior art did not provide any hint or guidance,[84] or did not outline an improved solution[85]/efficacy[86] of the new dosage regime. The scope of what can be included in routine optimization appears to be relatively broad in regard to dosage regimes cases. Cases have for example cited molar ratio[87], most effective dose[88] specific dissolution profile[89], the combination therapy from 24 to 48 weeks[90], and daily dose[91] as acts which are considered to fall within the term routine optimization. Routine optimization is of course not a new principle however its application to dosage regimes is extremely wide.[92]

New doses appear to be the form of the dosage regime that is most likely/commonly rejected due to routine optimization. More than half of all 45 studied cases that were held to be a routine optimisation were applications concerning a new dose. Dosages, therefore, appear to be at the greatest risk of being rejected on this ground rather than other types of dosage regimes such as new formulations. One reason for this is that in multiple cases, the EPO has stressed that the act of deriving a dosage is merely a routine optimization.[93] In T1409/06, for example, the TBA concluded that "the board is of the opinion that mere determination of the dosage which yields the best effect does not involve an inventive step. The skilled person is aware that the intensity of a pharmacological effect depends inter alia on the concentration of the active ingredient. This is, therefore, a matter of mere routine optimization."[94]

Statements like these appear to be, however, at least somewhat contradictory to the G02/08[95] judgment. By generalized statements dosage regimes containing only a new dose are held to not be patentable because they are outright labelled as routine optimization cases (which are not generally patentable). Most dosage regimes containing only a new dose are therefore unlikely to be granted a patent. In practice little has changed, post G2/08[96] other than the ground upon which new doses are being refused a patent on. This is also reflected in the findings of the 45 studied cases where only 6/13 dosage regimes that concerned a new dose were considered to have an inventive step. Additionally, out of these 6, 4 were with a new and another dosage regime. It, therefore, is concluded that a dosage regime, which contains only a new dose, is only patentable in exceptional cases.

2.2.2.4 Discussion and strategies for potential patentees

From a closer analysis of the application of the patentability requirements of the EPC to dosage regimes through the studied 45 cases, a number of generalized strategies can be identified. Firstly, where a patentee of a first medical indication wishes to keep the option open to later research into the field of dosage regimes, they must take much care with the wording of patent application, publications and clinical trial reports in order to avoid vague formulations that could deter a dosage regime's application. The established vague formulation of future potential research or unproven factors can still affect the assessment of inventive step. Secondly, as far as possible, patentees should strive for an "improved technical effect". These have better chances of overcoming the hurdles of the inventive step assessment.

Another strategy is the combination of different types of dosage regimes (e.g. new dose with a new mode of administration). These cases seemed to be more likely to be held[96] to have an inventive step but also appear to overcome novelty and different steps of the inventive step requirement more successfully. Out of the 45 studied cases 67% concerned more than one dosage regime were held to have an inventive step in comparison to 50% of the cases that only involved one dosage regime, and were non-obvious. The prior art for the novelty assessment and closest prior art for the inventive step test is more likely to be "less similar" to the claimed invention, thereby resulting in a technical problem that makes it more likely that it will be held as non-obvious.

Overall comparisons between the different types of dosage regimes displayed in Figure 1 below indicate that, some types of dosage regimes are generally more successful than others. Whilst new formulations appear the most likely to be patented, regimes for new doses struggle the most. The reason for this is that most of them are rejected because they are obvious in the light of closest affiliated prior art or because the dose can be obtained through routine optimization. Comparing the cases concerning new doses that were held to have an inventive step and those that were not held to have an inventive step a number of observations could be made. These could then in return be incorporated in order to make a dose-related

dosage regime more likely to overcome the patentability requirements.

Firstly, cases which concern specific doses for sub-groups for which a separate dose range or regime has not yet been established appear to have higher chances in meeting the patentability requirements as was the case of patent EP2296686.[97] Secondly, new doses that focus on overcoming patient compliance appear to also be more successful as can be seen from for example the case of patent EP2265285.[98] Thirdly, new doses concerning active ingredients for which literature exists that suggests that there are particular difficulties concerning the application of pharmacokinetics to it, also have greater chances of overcoming the patentability requirements.[99] Therefore, whilst of course the chances of a new dose are not non-existent, it appears to be much more difficult to recieve such a dosage regime patent protection. Through the above-named adaptions, however, the chance of receiving a patent of the dose regime can be increased.

Comparison of the types Dosage Regime of the studied cases that were held to have an inventive step and those that did not

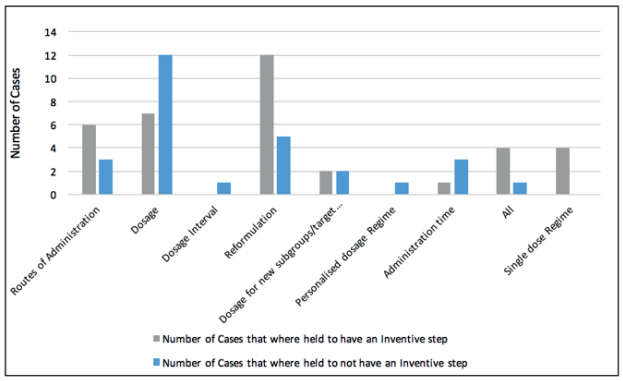


Figure 1

A dosage regime that appears to have high success rates in fulfilling the patentability requirements is a single dose regime. Out of the 4 cases that involved a single dose regime all cases were held to have an inventive step. This is firstly, because these cases are not considered to be generally derivable through routine optimization and secondly, because of their clear improvement of patient compliance that makes them automatically superior to other dose regimes. They, therefore, are likely to be held to have an "improved technical effect" without further required evidence. The EPO has accepted a general presumption that, where the administration of a drug is simplified, it will result in a greater degree in patient compliance and in return has an improved effect.[100] It is, there-fore, the factor that is the easiest to prove in order to establish an improved effect and is often not greatly affected by the prior art. Proving an improved effect due to fewer side effects or increased therapeutic effects is much harder and can involve the need for comparative experiments/evidence.

Lastly, also dosage regimes for sub-groups of patients could be seen as a strategy however it will depend greatly on whether the sub-group is new in regard to the prior art and is, therefore, a strategy which is much less predictable as the other above-named strategies. Nevertheless, it would be worth a try.

This article would, therefore, recommend that R&D is tailored towards dose regimes for single dose regimes, novel sub-groups, combining two types of dosage regimes or dosage regimes that focus on improving patient compliance as these types of dosage regimes are most likely to meet the requirements of patentability. Where however, in the process of research tailored into theses directions another dosage regime is derived, it is worth attempting to patent this.

[80] See for example: T 0259/ 15, Euro-Celtique S.A., Mundipharma Laboratories Gmbh, Napp Pharmaceutical Holdings Limited, Board of Appeal Of the Epo, 25.07.2017.

[81] Laboratoire Hha-Pharma and Family Health International V Generics (U.K.) Limited And Hexa/ Ag (Ep2419109) Decision Of The Opposition Division Of The Epo, 23.01.2018.

[82] Decision For Refusal Of Application By The Epo (Ep1931354), 30.01.2014.

[83] Gebro Pharma Gmbh V Ferring International Center S.A. (Ep1255557) Epo Board Of Appeal, 10.06.2009.

[84] Appendix A, Table 33 (See Eg. Glaxosmithkline Biologicals S.A., Rixensart (Be). V Dr. Wolfgang Bock (Ep1361890), Decision Of The Opposition Division Of The Epo, 23.12.2014).

[85] Akzo Nobel, Nl V Schering Ag (Ep0491415) Opposition Division Of The Epo, 24.04.2000.

[86] T 0619/12, Zoetis Services Llc V Intervet International B.V., Boehringer Ingelheim Vetmedica Gmbh and Merial Limited (Ep1474067), Decision Of The Board Of Appeal Of Epo, 14.07.2017; Genzyme Corporation V Generics [Uk] Limited (Ep2664334) Opposition Division Of Epo, 26.07.2017.

[87] T 0177/13, Warner Chilcott Company, Llc V Apotex Inc. (Ep1753395), Board Of Appeal Decision (11.06.2015) .

[88] Hexal Vs.Panion & Bf Biotech (Ep1931689), Epo, 27.07.2017.

[89] Decision To Refuse The Application By Epo(Ep2538945), 05.11.2015.

[90] T 0531/04, Schering Corporation V Alfa Wassermann S.P.A., Teva Pharmaceutical Industries Ltd., Sandoz Gmbh Appelt, Christian W. Meduna And Arzneimittelfabrik Gmbh (Ep0903148) Epo, 18.11.2015.

[91] Alk-Abello A/S V Merck Patent Gmbh, Mr. John Gerard Leeming And Stallergene Sa (Ep2265285), Decision Of The Opposition Division Of The Epo, 23.02.2016.

[92] The Decision To Refuse The Application By EPO (Ep2538945), 05.11.2015 (In this Decision the opposition division took the approach that everything could be derived by trial and error would constitute a routine optimization).

[93] Op. Cit, Fn.6.

[94] T 1409/06 F.Hoffmann-La Roche Ag V Teva Pharmaceutical Industries Ltd. (Ep0689437) 1.4.2009.

[95] G 0002/08 (Dosage Regime/Abbott Respiratory), Epo, 19.2.2010.

[96] Ibid.

[97] Gebro Pharma Gmbh V Ferring B.V. (Ep2296686), Epo, 03.01.2017.

[98] Alk-Abello A/S V Merck Patent Gmbh, Mr John Gerard Leeming And Stallergene Sa (Ep2265285), Decision Of The Opposition Division Of The Epo, 23.02.2016.

[99] Novartis Ag V Teva Pharmaceutical Industries Limited and Synthon Bv (Ep1556013), Opposition Division Decision Of Epo, 20.01.2012.

[100] Boehringer Ingelheim Vetmedica V Intervet International Bv And Eli Lilly And Company (Ep2281829) Opposition Division Decision, Epo, 17.08.2017; Genzyme Corporation V Generics [Uk] Limited (Ep2664334) Opposition Division Decision of The Epo, 26.07.2017.

3. INFRINGEMENT OF DOSAGE REGIME PATENTS AT NATIONAL LEVEL

In Germany and the UK both direct and indirect infringement exists. Both of these infringement types must, however, "strike a balance between the two competing factors [of]" a fair protection for the patent proprietor [and] a reasonable degree of legal certainty for third parties".[101] Due to the nature of dosage regimes, many difficulties have arisen in finding the correct balance between these two factors. This is especially the case where skinny labelling is involved. In order for a pharmaceutical product to be placed on the market in Europe it must receive market authorization, something that requires information on both indications and dosages through SmPC (summary of product characteristics), PIL (patient information leaflet) and the medicinal label.[102] Even though generic products must provide the same information as their reference medicine, an exception for second medical use patent protected products exists under article 10 and 11 of Directive 2001/83/EC[103] allowing generics to exclude the patent protected use. In practice, this means that the generic products enter the market for all indications and dosage regimes except the ones which are patent protected. This act is referred to as a skinny labelling or carving out. Where then this generic product is used for dosage regimes that are not authorized for, this use is called "off-label use".

Complicating matters further, the change in claim form of dosage regime patents from Swiss type claims to EPC 2000 claims also brought with it a level of uncertainty as to the potential difference in the scope of protection of the two. Establishing whether or not a difference in the scope of protection exists is fundamental to the assessment and establishment of infringement of a dosage regime patent.

3.1. Has the scope of protection of dosage regimes changed from Swiss-type claims to EPC 2000 form claims?

When examining the preparatory works of the EPC 2000 it becomes evident that the Swiss delegation, having proposed the final version of article 54(4), had the intention of using this article to simply codify the legal position of Swiss claims. This would mean that the new EPC 2000 claims would be equivalent to that of Swiss-type claims. As EPC 2000 claims however were a replacement of the uncodified Swiss-type claims, the EBA held in G2/08 that these claims were no longer necessary and therefore, no longer allowed. In this decision, however, the EBA also held that EPC claims "are most likely broader" due to the difference in claim category. Whilst at first these findings from the EBA appear to be in contradiction to the preparatory works stated above, they are in line with earlier case law, such as Mobil[104].

This issue was further assessed in regard to article 123(3), where the TBA held that changing a claim from Swiss-type to EPC 2000 claim was a breach of Article 123(3) as this was an increase in the scope of protection of the claim. This, therefore, means that the decisions T1780/12[105] and T250/05[106], concluded that product-related claims confer a larger scope of protection than Swiss-type claims (method-related). From the perspective of the EPO, EPC 2000 claims clearly grant a wider scope of protection. Therefore, it would be expected that current infringement cases decided the on basis of Swiss-type claims may may differ from future cases regarding EPC 2000 claims.

The position of the UK courts is far less clear. Whilst on one hand Arnold, J. in Warner-Lambert Company, LLC vs Actavis Group[107] cited the case-law of the EPO concerning the increased scope of protection, which could be seen as implicitly acknowledging that a difference in protection exists,[108] a clear connection between the two claim types was also made holding that the term "for" lay central to both claim constructions. The similarities in claim construction therefore could, on the other hand, indicate that the scope of protection would not necessarily be different between the two types.[109] Nevertheless, considering that Swiss-type claims are process claims and EPC 2000 claims are product claims, this difference could indicate in itself a difference in treatment in regards to the assessment of infringement. This is enhanced by the fact that under direct infringement they would be covered by different sub-sections of section 60 of the Patents Act 1977.[110] Product claims are covered by 60(1)(a) whilst process claims are covered by 60(1)(b)-(c). As there are differences in the wordings of these subsections, infringement proceedings may differ between dosage regimes covered by EPC 2000 product claims and Swiss-type claims. Hence, also the scope of protection may be different. However, it remains to be seen how UK courts will interpret these differences, not only in regard to the claim wordings as suggested above but also in their application to the different infringement sections.

In Germany, contrary to the approach taken by the EPO, the Bundesgerichtshof (hereafter BGH) in Pemetrexed[111] has held that there is no difference in the scope of protec-

[101] Actavis Uk Ltd V Eli Lilly & Co [2017] Uksc 48; [2018] 1 All E.R. 171.

[102] Regulation (Ec) No 726/2004 On Laying Down Community Procedures For The Authorization And Supervision Of Medicinal Products For Human And Veterinary Use And Establishing A European Medicines Agency (31.03.2004). Also See Directive 2001/83/Ec On The Community Code Relating To Medicinal Products For Human Use (06.11.2001).

[103] Directive 2001/83/Ec On The Community Code Relating To Medicinal Products For Human Use (06.11.2001).

[104] G 2/88, Mobil Oil Iii V Chevron Research, Epo, 11.12.1989.

[105] T 1780/12 Board Of Regents, The University Of Texas System, Epo, 30.1.2014.

[106] T 0250/05 The Brigham And Women's Hospital, Inc. V Air Products & Chemicals Inc. And L'air Liquide S.A., Epo 4.3.2008.

[107] Warner-Lambert Company, Llc Vs Actavis Group Ptc Ehf & Others [2015] Ewhc 72 (Pat).

[108] Potter Clarkson, 'Infringement Of Second Medical Use Claims In The Uk: The Patents Court Takes With One Hand But Gives With The Other' [2015] Lexology.

tion between Swiss-type claims and EPC 2000 claims. Both grant purpose-bound protection. The same was held in Kollagenase I[112], where the BGH held that irrespectively of the formulation, all claims which are concerned with second medical uses have as their subject-matter the specific medical use. The use is an inherent feature of the product, which the use is aimed at. According to the BGH, this correlates with the intended protection of EPC claims, making it clear that the two types of claims provide the same level of protection. Therefore, the current judgments that have been decided on the basis of Swiss-type claims.

3.2. The position in the United Kingdom

In order to understand both direct and indirect infringement in the case of dosage regimes, one must firstly understand the underlying practice of prescriptions in the UK. Generally, when a prescription is written in the UK, the doctor does not know whether the patent protected product or the active ingredient from another company is dispensed. This is because the pharmacist has the freedom to dispense either the patent protected product or a generic. When it comes to National Health Service (NHS) prescriptions, the pharmacist receives a lump sum reimbursement, which covers the price the pharmacy paid to the supplier as well as a small additional amount, a medicine margin. Therefore, the pharmacist may be motivated to dispense the cheapest generic drug in order to increase this medicine margin. However, where the prescription is not generic, the pharmacist does not have this freedom. In practice, this is nevertheless rarely the case.[113]

3.2.1. Direct infringement

As previously established, the fact that different subsections of Section 60(1) which deals with direct infringement apply to product claims and process claims, a great level of uncertainty exists in regards to legal position of infringement cases of EPC 2000 dosage regime patents. At the core of the entire section 60(1) lies however the interpretation as to what constitutes a part of a medicament. In Warner Lambert, the Court of Appeal established that a medicament is not completed at the moment of its formulation into the pharmaceutical composition[114], while it involves acts of both up- and downstream preparations. These could include for example drug packaging, labelling or patient information leaflets and providing medicaments with a wide definition for the purpose of the act.

However, in order to prove direct infringement of a Swiss-type claim by a manufacturer or supplier of a generic drug, the Court of Appeal made clear that it must be shown that these knew or could reasonably foresee the ultimate intentional use for the infringing purpose by the end user.[115] This conclusion was in the court's opinion, derived from the court's interpretation of the term "for" in Swiss-type claims. In this case, concerned with a second medical indication, the use of "Pregabalin for pain", the court concluded that where the doctor had prescribed the drug for the patented indication and the pharmacist dispensed a generic Pregabalin, knowing that it had been prescribed from the patented indication, the intentional element of the use would be met. This, however, meant that where the indication was not included in the prescription there could be no direct infringement. In practice, whilst dosage ranges and interval times are likely to be included on prescriptions, making it relatively easy to prove intent, patient group indications as well as personalised dosage regimes based on specific gene types are unlikely to be included by doctors on prescriptions making it almost impossible to prove direct infringement. The current system therefore only provides a potential protection for some types of dosage regime patents. Ironically, complicated dosage regime patents, which the UK has the greatest desirability in protecting (e.g. where a different dose is given each week or month) are for practical reasons often given to patients on separate paper rather than included on the prescription, making these the hardest to prove direct infringement for and hence enforce.

[109] Paul England And Anja Lunze, 'Infringement Of Second Medical Use Patents' [2015] Lexology.

[110] Christopher Burnett, 'Swiss Claims - Full Of Holes? - A.A. Thornton & Co' (Aathornton.Com, 2015) <Https://Www.Aathornton.Com/Swiss-Claims-Full-Of-Holes/> Accessed 13 May 2018.

[111] BGH, Pemetrexed Grur 2016, 921.

[112] BGH, Kollagenase I Grue 2014, 464.

[113] Paul England, 'Infringement Of Second Medical Use Patents In Europe And The Unified Patent Court: Table 1.' (2016) 11 Journal Of Intellectual Property Law & Practice.

[114] Warner-Lambert Company Llc V Generics (Uk) Ltd. (T/A Mylan) & Others (2016) Ewca Civ 1006 Para. 224.

[115] Apart From Obiter Mentions In Regards To Swiss Type Claim On The Problems Of Making Intention A Relevant Issue On Infringement By Jacob J In Bristol Myers Squibb [1999] R.P.C. 253, At 271–273 The Issue Of Intent Had Not Be Considered Further By The Courts.

In the same case, Warner-Lambert[116], the Court of Appeal further held that, it would however only be foreseeable that the pharmacist would dispense the generic drug for the protected indication in the absence of other factors, making it harder to prove direct infringement of dosage regime patents. In the present case, the superintendent pharmacist had been notified that the product of the defendant was not licensed for the treatment of pain. This was done close to the date when the defendant's product had entered the market. The court held that this did, in fact, add an additional factor to the assessment and concluded that as a result, it was not foreseeable when the marketing of Pregabalin took place. This would in practice mean that simply by making a statement excluding patented dosage regimes any generic company could avoid direct infringement of the dosage regime patent. Due to the fact that the EPC 2000 claims also include the term "for use" it would be extremely likely that knowledge or foreseeability is also required mutatis mutandis in those cases regardless of the fact that the assessment would be made under Section 60(1)(a) rather than Section 60(1)(c).

Whilst no clear direction was provided in regard to the liability of doctors, the Court of Appeal indicated in Warner-Lambert that due to the current legal framework of prescriptions, it is unlikely that doctors would be liable. Furthermore, whilst the counsel for Pfizer in Warner-Lambert[117] had indicated that doctors might be liable, they held in their closing remarks that even in their opinion this was not the case. The court, in summary, held that "it is very difficult to see how a doctor could be liable for infringement of a patent merely by writing a generic prescription for Pregabalin for pain since for all doctors would know the prescription could well be fulfilled by the pharmacist by dispensing Lyrica".[118] Considering the court's reasoning there appears to be no reason that this position would be changed through the application of EPC 2000 claims.[119] In regards to pharmacists, however, it would be expected, following the same reasoning, that where they knew the dosage regime was patent protected, in other words where the dosage regime is written on the prescription, they could be potentially liable.[120] This is because they would make use of the dosage regime under either 60(1)(c) in regards to Swiss-type claims or 60(1)(a) in regards to EPC 2000 claims. No dosage regime cases have however been decided in regards to pharmacists direct liability and therefore it must be seen how courts will deal with this issue over time. As the current legal position stands in the UK, it is extremely easy for generics to escape liability through skinny labelling.

In regard to reformulations, bioequivalence can create a threat to patent enforcement. This would be the case where the formulation of the potentially infringing product is slightly different from the patent but this change is immaterial. In other words, the changes of the formulation mean that products would not fall within the literal reading of the claims but as the changes do not alter the functions of the product, it achieves the same technical effect as the patent. The recent Supreme Court decision of Actavis vs. Eli Lilly[121] has clarified this by introducing the doctrine of equivalence and made its applicability to dosage regimes clear.

The case concerned Eli Lilly's Pemetrexed compound (Pemetrexed disodium) used in combination with vitamin B12 for the treatment of cancer. Actavis's products contained Pemetrexed diacid, Pemetrexed dictromethamine, and Pemetrexed dipotassium together with vitamin B12. Reformulating the "improver questions",[122] the Supreme Court held that there was a direct infringement of Actavis's products contrary to the Court of Appeal's findings.[123] This was proceeded through the reformulation of the second question of the test, which lowered the burden of proof of the patentee. Instead of asking whether it was obvious to the person skilled in the art, it now assumes that the person skilled in the art has the knowledge. Through this reformulation of the applicable test and questions, the court has clarified two important issues. Firstly, that variants fall within the claim under normal interpretation and secondly, that they are regardless considered an "immaterial variation". However, what has been left unclear is how wide this new doctrine of equivalents is and how far it is extending. This could, therefore, have the effect that there will be a greater period of uncertainty following this case.[124] However, from the perspective of a proprietor of a dosage regime patent, especially of a new formulation, this judgment should be highly welcomed. Whilst it is clearly beneficial for dosage regimes that concern a new formulation, it is unclear whether it will have any relevance for other types of dosage regimes.

3.2.2 Indirect infringement

Indirect infringement is dealt with under section 60(2) covering situations where one, without consent of the patent owner, "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." The test for article 60(2) therefore, contains a distinct knowledge requirement. It, therefore, resembles the newly introduced test under direct infringement for Swiss-type claims in part, which will most likely also be the applicable approach for EPC 2000 claims.[125] In Grimmer v Scott[126] it was established that this standard of knowledge is satisfied where at the time of supply or offer of supply the supplier knows or it is obvious in the circumstance. This knowledge requirement, however, does not contain any requirement of bad faith.[127]

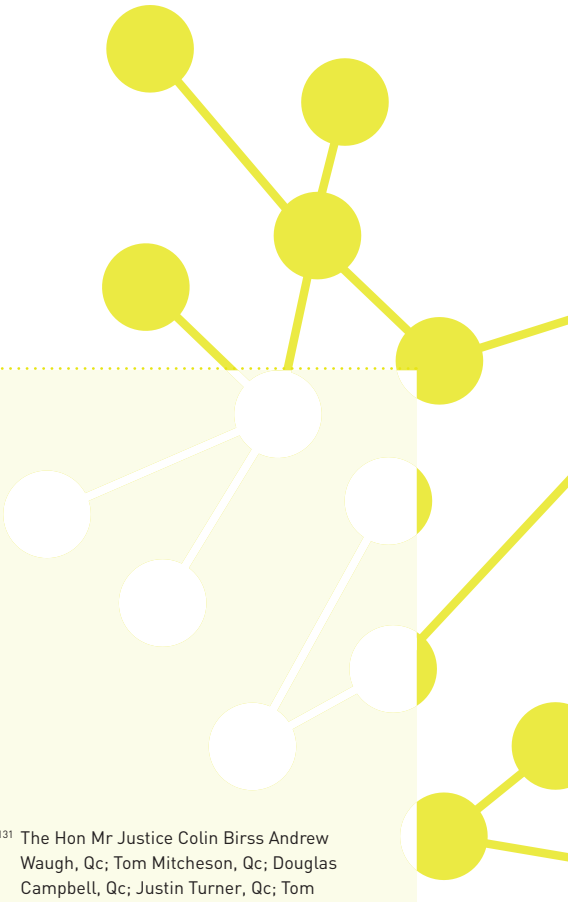
Other than requiring a degree of knowledge, article 60(2) also requires that the patent must have been "put into effect". This in regard to Swiss-type claims has caused some issues and has been the reason that the courts have been relatively reluctant in the UK until recently to interpret them in a way that would be put into effect downstream. At first instance in Warner-Lambert[128] the High Court had held that indirect infringement of a Swiss-type claim could not succeed as " there can only be infringement under section 60(2) if there can be infringement by the person supplied or by a user further down the chain of supply (although it is not necessary for there actually to be an

infringing act). This is not the case here since no wholesaler or pharmacist will use Lecaent to prepare a pharmaceutical composition."[129] This means in line with article 60(2), that the Swiss-type patent cannot be put into effect after the manufacturer or supplier has placed the medicine on the market.[130] However, the Court of Appeal held that it was arguable that "putting the invention into effect", may also refer joint action of a manufacturer who supplies the means to a party that than intentionally uses it for putting the invention into effect." It therefore becomes evident that the courts have generally unnecessarily melted together the "suitable for" feature of the claim with the "prepared for". This has had the effect that the courts appear to be very reluctant to grant indirect infringement to Swiss-type claims for dosage regimes or any other type of second medical use.

Compared to Swiss-type claims, the situation would appear to be more straightforward when it comes to EPC 2000 claims, this is because these are not the process of manufacture claims but particular product claims for the use in a particular therapy.[131] This means that, where a dosage regime in the EPC 2000 claim form offers to supply or supplies the product with requisite knowledge that at least some of the product in question will be used for a protected dosage regime, then infringement will arise from this. As the courts have held themselves, the vast majority, around 83% of all prescription are generic ones[132], it would therefore be foreseeable that doctors and pharmacists would prescribe and hand out a generic product for the patent protected dosage regime. This would mean that it would appear to be much easier to prove infringement of dosage regimes in the format of EPC 2000 claims than Swiss-type claims. Whether the courts will adopt this approach however, is left to be seen.

3.3. The position in Germany

The situation relating to prescription in Germany are substantially different from that in the UK, resulting in different potential infringement risks. In Germany, pharmaceutical companies and health insurers can enter into rebate agreements through §130a(8) of the German Social Law Book V. Where this is done, the pharmacist will only be reimbursed from the health insurers for a prescribed drug that they have dispensed when they must under §129(1) take these rebate agreements into account. It is through this section that the obligation to dispense that exists in Germany arises. This obligation requires the pharmacist to dispense the cheapest drug to an insured patient unless the doctor's prescription explicitly orders to provide a specific brand by striking out the "aut idem" field on the prescription form. There is however, little chance that this is done by doctors as they are motivated by budget controls to leave this field blank. In practice therefore, doctors generally allow this substitution. With regards to EPC 2000 claims the situation of infringement is much more certain in Germany than the UK, as it is clear that the current jurisprudence on Swiss-type claims will apply directly to EPC 2000 claims.



[116] op. cit, fn.106.
[117] Ibid.
[118] Ibid. Para 686.
[119] The Hon Mr Justice Colin Birss Andrew Waugh, Qc; Tom Mitcheson, Qc; Douglas Campbell, Qc; Justin Turner, Qc; Tom Hinchliffe, Qc, Terrell On The Law Of Patents (2nd Supplement) (18th Edn, Sweet & Maxwell 2018).
[120] S.J.R. Bostyn, 'Personalised Medicine, Medical Indication Patents And Patent Infringement: Emergency Treatment Required' [2016] Intellectual Property Quarterly.
[121] Actavis UK Limited and others v Eli Lilly and Company [2017] UKSC 48
[122] Improver [1990] Fsr 181, 189.
[123] It Did This By Considering Section 130(7) Of The Uk Patent Act Which Directly References To The Epc 2000. Article 69(1) Of Epc 2000 Concerning The Scope Conferred By The Claims. This Is Expanded By The Protocol, Especially Articles 1 (General Principles) And Article 2 (Equivalents).
[124] Tanvi Shah Jason Raeburn And Hiroshi Sheraton, 'Actavis V Eli Lilly: English Supreme Court Shapes Up Approach To Patent Infringement By Equivalents' [2018] European Intellectual Property Review.
[125] Matthew Fischer, 'Second Medical Indications And The Swiss-Form Claim: Taming Frankenstein's Monster: Part 2- Putting The Problem In Context' [2017] European Intellectual Property Review.
[126] Grimme Landmaschinenfabrik Gmbh & Co Kg V Scott (2010) Ewca Civ 1110; Also See Kci Licensing In & Smith &Nephew Plc (2010) Ewca 1260.
[127] Kennametal V Pramet (2015) R.P.C. 2 Ch D; Para 90 And 95.
[128] op. cit, fn.106.
[129] Ibid. Para 113.
[130] This Finding Was In Line With The Decisions At First Instance Of The Dutch Case: Novatis Ag V Sun Pharmaceutical Industries (Europe) Bv, District Court Oft He Hague, C/09/469148/Ha Za 14-770, 25th November 2015.
[131] The Hon Mr Justice Colin Birss Andrew Waugh, Qc; Tom Mitcheson, Qc; Douglas Campbell, Qc; Justin Turner, Qc; Tom Hinchliffe, Qc, Terrell On The Law Of Patents (18th Edn, Sweet & Maxwell 2018).
[132] Warner-Lambert V Actavis [2015] Ewhc 72 (Pat).

3.3.1. Direct infringement

§9 of the German Patent Act states that, the patentee shall alone be entitled to use the patented invention and outlines grounds upon which one can directly infringe a patent in Germany. Claims concerning dosage regimes are, under the current law considered as "zweckgebundenes Stoffpatent" and therefore they are conferred their protection through their "Zweckbindung" purpose limitation. As clarified in "Antivirusmittel"[133] it is this purpose limitation of the dosage regime, which is inventive and therefore, it is this purpose limitation for which protection exists. Where the drug is manufactured for a different dosage regime, no infringement can take place. It is this very nature of dosage regime claims that makes infringement, especially direct, at least to some extent problematic. "Antivirusmittel"[134] therefore held that there is no infringement of a patent where the use of the patent that is protected is neither aimed at nor achieved in a targeted way.

In order to assess whether or not the use was targeted or aimed at, the courts have developed through case law[135] the concept of "sinnfällige Herrichtung", which translates into English as "manifest arrangement". In essence, this is an "objective evidence that the drug was marketed with the intention that it can be used for the indication claimed in the patent".[136] Establishing a "sinnfällige Herrichtung" requires therefore that a close link between the product as marketed and the use that is patent protected. The Düsseldorf Court of Appeal has held that this can be achieved through a number of ways such as the drug's instruction manual that includes the description of the dosage regime, the formulation of the drug, dosage or provisions of ready-to-use preparations of a drug.[137] At the same time however, the court has also made it clear that whilst those are ways to establish "sinnfällige Herrichtung", information provided about the drug in marketing materials (e.g. advertisements or flyers) or explanation from salespeople that the product can be used in a protected way do to establish a close enough link and hence do not result in a direct infringement.

This narrow scope, however, was widened through the recent judgment Östrogenblocker[138] by the Civil Court of Appeal of Düsseldorf. Manifest arrangement can according to this case still be used to establish direct infringement it is no longer the only way of establishing it. This case concerned a dosage regime patent, which was developed for a specific patient group. This patient group, however, was smaller than that, which was indicated on the packaging of the defendant's product. The defendant's product, therefore, could also be used for the patented use according to its own labelling. With closer analysis of the underlying objective of §9 of the Patent Act, it concluded that as the defendant's product was objectively suited for the patented use it would not be appropriate to not find the act infringing. The case, therefore, can be seen to not only move away from the strict approach that existed before but also as having established a new test for the assessment of direct infringement for dosage regime patents. This requires the following 2-step analysis: "(1) the product must be suited for the patented use and (2) the distributor makes use of circumstances that ensure (comparable to a manifest preparation) that the offered or distributed product is used for the protected therapeutic use. The last requirement in return requires two sub-requirements: (1) the product is amply (not only sporadically) used for the patented use and (2) that the distributor knew this, respectively shutting their eyes to this knowledge."[139] The implications of this judgment however, still remain to be seen. Nevertheless, it is clear that the scope of direct infringement has been widened especially in regard to sub-target groups.

For new doses, a link must exist between relatively easy for generics to not directly infringe the patent through ensuring that the dose is neither indicated on the label (a form of skinny labelling) and that the pills or other routes of administration do not entail the exact amount. This could easily be done where the pills contain ½ of the patented dose. No case in Germany currently exists as to whether or not a single dosage regime produced not in one pill but multiple (perhaps even only two) where the instruction gives no indication of the use is limited to a single intake, would, in fact, be a directly infringing act. Following the current case-law, however, it would most likely be concluded that this would not, in fact, be a direct infringing act as the link between the product and the single dose patent would not be close enough. It appears that, even the outcome of Östrogenblocker would most likely not affect this outcome as long as the dose of the potential infringer's products are "lower" and therefore not directly suited for the intended dose. It appears that generics could easily by-pass direct infringement of these types of patents. In regard to sub-groups, Östrogenblocker has made it clear that it is possible to find a direct infringement as long as the sub-group is also part of the original use and did not make up a too small percent of the original group. 7 % of patents falling within the patented scenario where held too small of a percentage to constitute a suffi-

[133] "Antivirusmittel" (Grur 1987, 794).
[134] Ibid.
[135] Originally Established In Düsseldorf District Court, "Ribavirin" 4a 0 12/03, 24 February 2004 And Then Developed Further Through.
[136] Ibid.
[137] Düsseldorf District Court, "Ribavirin" 4a 0 12/03, 24 February 2004, Grur-Rr 2004, 19. Also See: Düsseldorf Court Of Appeal, "Cistus Incanus" 2u 54/11, 31 January 2013; Düsseldorf District Court, "Chronic Hepatitis C" 4a O 145/12, 14 March 2013.
[138] Bgh, 5 May 2017 – I-2 W 6/17 – Östrogenblocker.
[139] Ibid, 9.
[140] District Court Düsseldorf Grur Rr 2001, 2004.
[141] Bgh 1977 Gewerblicher Rechtsschutzund Urheberrecht (Grur) 652 – Benzolsufonylharnstoff.
[142] Case No X Zr 168/00, 2002 Grur 519 (Schneidmesser I), Para 30; Also See Case No X Zr 156/97, 1999 Grur 977, (Räumschild).
[143] Bgh X Zr 153/03, 13 June 2006— Deckenheizung.
[144] Ibid.
[145] "Düsseldorf District Court, "Ribavirin" 4a 0 12/03, 24 February 2004, Grur-Rr 2004, 19.
[146] Lg Hamburg, 2 April 2015 Published As Grur-Rr 2015, 330 (O 24/15; 327 O67/15;327 O143/15;327 O143/15;327 O132/15;327 O140/15; 327).
[147] 14 September 2015 - S 2 Kr 374/15 Er.
[148] 16 March 2015 - Vk2 - 7/15; Vprrs 2015, 0147.
[149] Court Of Appeal Düsseldorf- 1 December 2015, Az Vii-Verg 20/15.

cient scope. Single digit percentage ranges are therefore unlikely to result in a finding of direct infringement. Nevertheless, where a completely new population is found these can be directly excluded from skinny labelling and hence avoid direct infringement. It would appear that these cases would be left unchanged by Östrogenblocker. However, as the established test should be seen as a case by case analysis rather than a clear-cut principle it leaves much room for future possibilities. Furthermore it was also held by District Court of Düsseldorf that not the entire process/use of the patent must be copied.[140] If a dosage regime patent consisted of two different types of dosage regimes (e.g. a new dose at a new interval) it appears that it could be sufficient if only one is directly infringed.

New routes of administration, however, as well as reformulations are much more likely to be subject to direct infringement. This is because they are more concerned with the physical state of the medicament, which cannot be easily altered. Skinny labelling, therefore, is not an option where the first indication of the drug was in oral form and the patented dosage regime is for an intravenous (IV) application. These two regimes can be seen to be much more interlinked with the actual manufacturing process. New doses, intervals and administration times, on the other hand, are quantitative and hence do not need complete customization for the use. Customisation of the drug to the use is considered by law as a preparatory act which gives rise, according to Benzolsulfonylharnstoff' to a direct infringement claim.[141] Therefore dosage regimes that require customization provide better protection against direct infringement. Furthermore, new formulations patents are also protected by the German doctrine of equivalence. The BGH held in Schneidmesser I[142] that "a variant will infringe if (i) it solves the problem underlying the invention with modified but objectively equivalent means, (ii) this would be recognised by the person skilled in the relevant art, and (iii) that person focus[sing] on the essential meaning of the technical teaching protected in the patent would regard the variant as being equivalent to the solution offered by the invention". This gives extra protection against attempts of competitors to reach the same technical effect through immaterial "designing around" the patent.

3.3.2. Indirect infringement

Indirect infringement is covered by §10(1) of the German Patent Act which states that a

> *"patent shall further have the effect that, any third party shall be prohibited, in the absence of the consent of the proprietor of the patent, from supplying or offering to supply, within the territorial scope of this Act, persons other than those entitled to exploit the patented invention with means relating to an essential element of the invention for use within the territorial scope of this Act if the third party knows or if it is obvious from the circumstances that those means are suitable and intended for using that invention."*

The BGH took a relatively wide reading of this section in Deckenheizung[143] where they held that the indirect infringement through §10 not only covers situations where the buyer uses the patented product and the supplier knows this but also situations where the buyer intends to use this patented product.[144] For the purpose of dosage regimes, this would, therefore, mean that the drug that was supplied must have been suitable as well as intended to be used for the protected dosage regime. Even though it does not require the intention to be formed at the time of supply, this appears relatively difficult to prove in regard to dosage regimes. Additionally, it remains unclear as to whether high numbers of sales would be enough to show a necessary link between knowledge of the manufacturer or supplier and the end user.

Originally German case law was so narrrow in its interpretaion of dosage regimes that skinny labelling was in fact a safe harbour both for direct as for indirect infringement.[145] However, in five parallel proceedings before the Hamburg Regional Court concerning the use of Pregabalin, it was held that, carving out and skinny labelling does not grant complete protection against indirect patent infringement. The case concerned the product of Pregabalin, which did not in its labels include the patent protected uses and indications nor did it advertise that the products could be used for these purposes. Nevertheless, the companies did enter into rebate agreements with health insurers without carving out the patent protected uses. Due to these practices and laws, the District Court of Hamburg held that infringement was a foreseeable consequence. Whilst the court did not in detail discuss the arguments of the defendants that the prescription of doctors and pharmacists could not be attributed to them, considering the backdrop of social legal frame-work outlined previously it is clear that the pharmacists and doctors had little control over the infringing acts. The substitution was carried out more or less automatically. The court additionally, quite surprisingly, stated that manifestly arrangement may not be necessary for the infringed use, but nevertheless found it was present in this case. Leaving this question of the requirement of manifestly arrangement relatively unanswered has therefore given rise to a great level of uncertainty as to the real assessment of indirect infringement.[146] On the other hand, it also opened up the possibility for more patentee-friendly decisions.

Two further judgments were decided in the same ways. The Hannover Social Court[147] and 2nd Federal Procurement Chamber[148] both granted injunctions, however only on procurement law, requiring the insurer not to enter into rebate agreements, which contradict the patent law. It therefore appears that in regard to rebates the law is relatively clear: where a dosage regime patent exists this must be carved out of a rebate agreement. The scope has been widened and clarified even further by the Düsseldorf Court of Appeal.[149] Here the court held that, even entering into a tender procedure of rebates without restrictions constitute an indirect infringement. What remains unclear is how far the case-law will develop in regard to indirect infringement. What can be concluded however, is that law of indirect infringement in Germany is moving towards a patentee-friendly system that allowed a wider scope of protection for dosage regimes.

3.4. Conclusion

In conclusion, it can be seen that in both jurisdictions, a clash exists between the regulatory laws governing the health systems and prescriptions and patent law. Dealing with this clash has been difficult for the courts, as expressed by Arnold J in Generics v Warner-Lambert. This has resulted in the fact that in the UK a much greater uncertainty remains in regard to infringement of dosage regimes. Whilst the court in Warner-Lambert clarified some issues in regards to Swiss-type claims, it created equally as many.[150] It is, for example, clear that manufacturers can avoid liability through taking reasonable steps within their power, however, it is not clear what these reasonable steps must be or more importantly whether these steps need to be considered effective. The German courts have left the area of infringement far less unclear for the patentee, however, uncertainty remains for potential infringers. It will be left to be seen how far the German courts will go with expanding the protection of dosage regimes (and other second medical uses) in cases of indirect infringement through skinny labelling. As the law currently stands, dosage regimes are more enforceable in Germany than in the UK.

Whereas direct infringement is the preferred ground in the UK for dosage regime infringement proceedings as it promises a greater success chance than indirect infringement. In Germany the opposite appears to provide more opportunities to a patentee.

There are some important legal consequences of having to rely on indirect infringement rather than indirect infringement. Firstly, indirect infringement does not cover the manufacturing but only the offer or sale in Germany. Therefore, where a dosage regime is produced in Germany but sold outside of Germany, direct infringement would not protect the patentee against this. Secondly, in regard to indirect infringement, the damages can only be rewarded in regards to the extent to which the patentee could prove that the contested product was actually used for the claimed product. This in practice could be relatively hard especially with dosage regimes patents.

A desirable international shift towards greater consistency can however, also be observed through recent case law developments such as Actavis UK Ltd v Eli Lilly & Co[151]. The Supreme Court highlighted this in Schütz (UK) Ltd v Werit (UK) Ltd[152] stating that "complete consistency of approach" between different national courts of the EPC states "is not a feasible or realistic possibility at the moment", but nonetheless "it is sensible for national courts at least to learn from each other and to seek to move towards, rather than away from, each other's approaches". Therefore, it is clear that differences between the member states will remain, however a general trend towards greater harmonization can be observed. In regard to dosage regimes, this appears to mean that the UK is more willing to follow the more patentee-friendly approach of Germany. This should be greatly welcomed by the patentee or potential patentee of a dosage regime.

3.4.1. Suggestions to potential and current patentees of dosage regimes

Additionally, as it appears that sub-target groups and therefore, also sub-doses are easiest to bring infringement proceedings against in both Germany and the UK potential patentees are encouraged to direct their research into this field as to at least include this type of dosage regime within their patent claims. Due to the doctrine of equivalence in both systems infringement of new formulations also has a greater level of protection. On the other hand, administration time and interval regimes are the easiest for generic companies to avoid infringement proceedings in and therefore give the weakest protection. Where these are in combination with another regime, the success chances of an infringement proceeding are drastically increased. In conclusion, it should also be noted that as both the German and UK systems are moving towards greater patent protection, until the boundaries of the current laws are clearly defined, it may be worth attempting proceedings in the hope that the court continues on down this road of increased protection for patentees.

3.4.2. Suggestions for generics

In Germany, it would hence be suggested for generic companies to avoid entering into rebates or tenders and tender agreements unless all patented dosage regimes have been explicitly carved out and excluded. Health insurances are additionally advised to check the overlap of regulatory laws and patent law, as a clash will not guarantee protection against the latter. In the UK generics are advised to make an explicit announcement to pharmacies at the time of marketing that their drug is not suited for the patent protected dosage regimes. This act appears, as case law has shown to be sufficient to avoid infringement. As the position in regard to indirect infringement as to EPC 2000 claims is highly unclear, generics are advised to be careful in regards to skinny labelling, as a greater degree of desired harmonisation can be seen between the UK and Germany. Therefore, the UK may therefore follow the more patentee friendly approach of Germany in regard to indirect infringement.

[150] Matthew Fischer, 'Second Medical Indications And The Swiss-Form Claim: Taming Frankenstein's Monster - Part 3: The Franken-Cuckoo Comes Home To Roost' [2017] European Intellectual Property Review.

[151] op. cit, fn.101.

[152] Schütz (Uk) Ltd V Werit (Uk) Ltd (Nos 1 To 3) [2013] Bus Lr 565; [2013] Rpc 16 Para. 40.

[153] Agreement On The Unified Patent Court (Signed 19th Feburary 2013) (Upc) And Regulation (Eu) No 1257/2012 Of The European Parliament And Of The Council Of 17 December 2012 Implementing Enhanced Cooperation In The Area Of The Creation Of Unitary Patent Protection.

[154] 24(1)(E) In Full Compliance With Article 20, When Hearing A Case Brought Before It Under This Agreement, The Court Shall Base Its Decisions On National Law.

[155] 'Can You Protect Dosage Regimes In France? | Lexology' (Lexology.Com, 2018) <Https://Www.Lexology.Com/Library/Detail.Aspx?G=170e087c-E19d-4830-9ae8-A4ee-d5a78486> Accessed 11 May 2018.

4. FINAL REMARKS

Whilst theoretically dosage regimes are patentable under the EPC 2000, in practice, these patents appear to struggle in meeting the requirements under the convention. Many dosage regimes are therefore left unprotected. The problem, however, does not lie in overcoming the hurdle of novelty but in fact meeting the requirements of the inventive step requirement. Not only does the problem and solution approach, due to its strong focus on the closest prior art and problem reformulation, appear to not be the most appropriate approach for dosage regimes, the decisions within the EPO are also inconsistent. After a difficult and perhaps lengthy struggle at EPO level, dosage regimes continue to face problems at national level. Despite overlaps and the court's attention to further harmonization, the current legal position between Germany and the UK differs greatly. The abolishment of Swiss-type claims and the introduction of EPC 2000 claims added additional fuel into the fire. Not only is the scope of protection of these latter claim formats in regard to dosage regimes unclear but also different. In the UK this has additionally resulted in the fact that infringement proceedings and therefore patent enforceability is left completely unclear and unpredictable. This is highly detrimental to both current and potential patentees and competitors. Therefore, closing one door of uncertainty in G2/08 opened others.

Whilst a trend can be observed towards decreasing the hurdles that dosage regimes must overcome in order to be rewarded and retain a patent, the law remains highly unclear. It appears that whilst in theory dosage regimes are patentable, the position in practice has not changed drastically. Whilst before dosage regimes were being rejected on the basis of industrial application or method of treatment exclusions, they are now being rejected on the ground of lacking an inventive step as they are routine optimizations. This appears to be the case as a general presumption amongst the EPO and the UK courts that developing the dose of any drug is a simple routine optimization task, which is generally carried out. This approach, however, takes all the work and knowledge required to develop a dosage regime for granted, in inadequately rewarding the work and effort required.

Legal uncertainty is highly undesirable from the prospect of a patentee. However, this article has established strategies based on trends in current case law that may allow greater chances in the patentability of dosage regimes and tailoring of R&D budget allocations. In conclusion, therefore, patent applications should as far as possible be filed encompassing multiple dosage regimes (e.g. new dose and new route of administration). Furthermore, new formulations and single dose regimes should currently receive a high level of focus due to their greater chances of being patentable. As regimes for a new dose have relatively low chances of being patented, these should be focussed on improving patient compliance, concern a specific subgroup or be designed for drugs for which a particular difficulty exists. Additionally, sub-target and dose groups, as well as new formulations, are likely to receive better patent protection.

The clear lack of certainty requires, more adequate and detailed guidelines for assessment for the EPO. A greater need for consistency, clarity and transparency can be obtained by establishing clearer guiding principles in regard to how the inventive step requirement is to be assessed for dosage regimes. Additionally, patent law therefore should attempt as much as possible to seek a balance between the different stages of research: drug discovery and drug development. Adequately rewarding of both is the suggestion of this article. This would entail increasing the protection and enforcement of dosage regime patents and ensuring that first medical use patents are only granted protection for properties that are known at the time of filing. Ensuring such a balance is achieved would furthermore be in line with the social contract theory. Lastly, this article suggests revisiting the regulatory laws that appear in conflict with the patent law. The answer does not necessarily have to lie within the field of patent law.

The differences in invalidity and infringement proceedings between the UK and Germany signal potential difficulties in finding a common ground for the Unified Patent Court system. This is enhanced by the fact that, whilst prescription practices differed between Germany and the UK, in both cases the national laws of these interacts with the laws of patent law. Article 25 and 26 concerning infringement of the agreement on the Unified Patent Court[153], must according to Article 24(1)(e)[154] be read in line with national law. This article would, therefore, urge further research into this area in order to develop an appropriate starting point for the Unified Patent Court in regard to dosage regimes and appropriate methods of how this system will overcome the challenges caused by the quickly evolving law of dosage regimes at national level. In line with this suggestion, this article further calls for further research into different jurisdictions not covered by the article. One example of this would be France, where much uncertainty remains in regard to the exclusion from patentability of dosage regime claims.[155]

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