

Examination Guidelines for Patent Applications relating to Medical Inventions in the Intellectual Property Office

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6 Examination Guidelines for Patent Applications relating to Medical Inventions in the Intellectual Property Office

INTRODUCTION

- 1. These Guidelines set out the practice within the Intellectual Property Office as it relates to patent applications for medical inventions. The relevant legislation is the Patents Act 1977, as amended by subsequent legislation, and the Patents Rules 2007. The interpretation of this legislation has been informed by case law in the UK courts. It has also reflected the fact that judicial notice must be taken of international conventions (such as the European Patent Convention) and of decisions and opinions made under these conventions by the appropriate bodies. Accordingly, decisions taken by the UK courts relating to the 1977 Patents Act are binding on our practice, whilst EPO Board of Appeal decisions are strongly persuasive. UK court decisions under previous legislation may also be persuasive, depending on the extent to which that aspect of patent law had been changed by the 1977 Act. Existing Office practice, as set out in the <u>Manual of Patent Practice (MoPP)</u> and in decisions taken in Office hearings, has not been changed without good reason.
- 2. The Patents Act 2004, which received royal assent on 22 July 2004, amended the Patents Act 1977 in respect of medical inventions, to implement the European Patent Convention as revised in 2000 (EPC 2000). The Convention (and therefore the medical provisions of the Patents Act 2004) took effect on 13 December 2007. The Patents Act 2004 introduced a new Section 4A to the 1977 Act which states in Section 4A(1) that the invention of a method of treatment of the human or animal body by surgery or therapy, or a method of diagnosis practised on the human or animal body, is not patentable. This replaces the former Section 4(2), and thereby removes the "legal fiction" that such methods lack industrial application they are regarded as unpatentable in their own right.
- 3. In addition, Section 4A states that patents may be granted for a known substance or composition for use in medicine (Section 4A(3)), or for a specific medical use (Section 4A(4)). These provisions therefore explicitly allow patent protection for the first medical use of a known substance or composition (as previously, under the former Section 2(6)) and a second or further medical use. Prior to 13 December 2007, inventions relating to second medical uses could only be protected using the "Swiss-type" claim form of "the use of substance X for the manufacture of a medicament to treat disease Y". Section 4A(4) allows a simpler and more direct second medical use claim, of the form "substance X for use in the treatment of disease Y". Following the issue of our <u>Practice Notice</u> on second medical use claims on 26 May 2010, inventions relating to second medical uses may only be protected this way; the Office no longer accepts "Swiss-type" claims (see paragraphs 105-112)
- 4. It is very important to note that the changes introduced by the Patents Act 2004 have **not** led to any substantive change in what is and is not patentable in this field. Previous case law under the repealed Section 4(2) (or the equivalent Article 54(2) of the EPC) relating to the exclusions of methods of treatment by surgery or therapy, or methods of diagnosis practised on the human or animal body, continues to govern our practice under Section 4A(1). Similarly, case law relating to first medical use under the repealed Section 2(6) (or the equivalent Article 54(5) of the EPC) governs our practice under Section 4A(3). Moreover, the body of case law relating to Swiss-type second medical use claims remains relevant to our practice in relation to the new form of second medical use claim under Section 4A(4). Throughout these Guidelines, reference is made to decisions under the law as it stood before 13 December 2007; these decisions (other than where explicitly noted) are considered to be directly relevant to the law under the amended Patents Act.
- Any comments or questions arising from these Guidelines should be addressed to Richard Sewards, Room 2Y52, Intellectual Property Office, Concept House, Cardiff Road, Newport, South Wales, NP10 8QQ (Telephone: 01633 813536).

BASIC PRINCIPLES

- 6. Patent applications in the medical field must meet the same requirements as applications in all other fields of technology; that is, they must be new, inventive and capable of industrial application, and the claims must clearly define the scope of the invention and be supported by the description. The invention must not fall wholly within the excluded categories defined in Section 1(2), and its commercial exploitation must not be contrary to public policy or morality.
- 7. In addition, patenting in the medical field is constrained by the exclusion from patentability of methods of treatment of the human or animal body by therapy or surgery, or methods of diagnosis performed on the human or animal body, under Section 4A(1) of the Patents Act 1977 (as amended), which states that such methods are not patentable. This exclusion applies only to methods of treatment and diagnosis and not to the materials used in such methods, as explicitly stated in Section 4A(2).
- 8. In addition, the definition of novelty for substances or compositions used in methods of treatment is addressed by Sections 4A(3) and (4). Section 4A(3) states that a substance or composition which is itself already known is regarded as novel "for use in" any method of treatment or diagnosis prohibited by Section 4A(1), provided that the substance or composition has not been known to be used in any such method before ("first medical use"). Section 4A(4) states that a substance or composition for use in a **specific** treatment, provided that the substance or composition has not been known for that specific use before ("second medical use").
- 9. Much of the case law relating to patenting in the medical field has focussed on boundaries between, on the one hand, the exclusion of methods of treatment from patents, and on the other hand the patentability of the materials used in such treatments, and in particular the first or subsequent medical uses of substances or compositions.

"[The exclusion] has the limited purpose of ensuring that the actual use, by practitioners, of methods of medical treatment when treating patients should not be the subject of restraint or restriction by patent monopolies. The difficulty is to decide whether the restraint concerns a method of treatment as opposed to that which is available for treatment."

Bristol-Myers Squibb v Baker Norton Pharmaceuticals [2001] RPC 1 (Court of Appeal)

10. There are an increasing number of patent applications in the medical field which relate to the use of biotechnological inventions for medical purposes, for example through gene therapy. Any such applications will also need to meet the requirements of Schedule A2 to the Act. The <u>Examination Guidelines for Patent</u> <u>Applications relating to Biotechnological Inventions in the Intellectual Property Office</u> set out the practice of the UK Intellectual Property Office in these areas. Our practice in relation to chemical inventions, including those relating to pharmaceuticals, is set out in the <u>Examination Guidelines for Patent Applications relating to Chemical Inventions in the Intellectual Property Office</u>

METHODS OF TREATMENT OR DIAGNOSIS

11. Methods of treatment by therapy or surgery or methods of diagnosis performed directly on the human or animal body are unpatentable, as set out in Section 4A(1) of the Patents Act 1977 (as amended):

"A patent shall not be granted for the invention of— (a) a method of treatment of the human or animal body by surgery or therapy, or (b) a method of diagnosis practised on the human or animal body."

Section 4A(1) of the Patents Act 1977 (as amended by the Patents Act 2004)

12. Section 4A(1) replaced the previous Section 4(2), now repealed, which stated that such methods "shall not be taken to be capable of industrial application". Similarly, the equivalent Article 53(c) of the EPC 2000 replaced the repealed Article 52(4), which also related to industrial application. It had been clearly stated that the purpose of Section 4(2) (and Article 52(4)) was to prevent medical or veterinary practitioners being restrained or hampered in their practice by patent legislation.

"The intention of Article 52(4) EPC...is only to free from restraint non-commercial and non-industrial medical and veterinary activities."

- G 05/83 EISAI/Second medical use OJEPO 1985, 64
- 13. The exclusion of medical methods on grounds of lack of industrial applicability under Section 4(2) was therefore a "legal fiction" designed to achieve a public policy objective, as medical and veterinary activities are clearly industries. Section 4A(1) removes this legal fiction and simply states that these methods cannot be patented.
- 14. Section 4A(1) does not prevent the patenting of materials or compositions used in such methods, as explicitly stated in Section 4A(2):

Subsection (1) above does not apply to an invention consisting of a substance or composition for use in any such method.

Section 4A(2) of the Patents Act 1977 (as amended by the Patents Act 2004)

This replaced the repealed Section 4(3), which stated that substances and compositions for use in medical and veterinary methods are capable of industrial application.

15. Not all methods of treatments of the human or animal body are excluded; only those that fall within the scope of the terms "therapy" or "surgery". In addition, claims to methods of diagnosis are only objectionable if they are performed directly on the human or animal body. This is discussed in more detail in the subsequent sections.

THERAPY

Definition of "therapy"

16. The definition of therapy used by both the UK courts¹ and the EPO² includes both treatments to cure or prevent disease, and so methods of, for example, vaccination of healthy individuals are considered to be methods of treatment by therapy and thus unpatentable. In *Unilever (Davis's) Application*¹ it was stated that therapy should be construed as the medical treatment of disease, including preventative treatment as well as curative treatment. Moreover, therapy encompasses methods of alleviating symptoms as well as curative treatments for a disease^{3 4 5}. In deciding whether a treatment can be considered to be "therapy", the broad definition applied by the EPO in T 24/91⁶ and T 58/87⁷ should be used:

"...any treatment which is designed to cure, alleviate, remove or lessen the symptoms of, or prevent or reduce the possibility of contracting any disorder or malfunction of the animal body"

T 24/91 THOMPSON/Cornea OJEPO 1995, 512

17. Veterinary treatment of a diseased or injured animal is regarded as therapy and it was pointed out in *Unilever* (*Davis's*) Application¹ (at pages 229-230) that therapy cannot have a different meaning for humans and animals. Similarly, the EPO Board of Appeal in T 116/85⁸ held that therapeutic methods practised on farm animals are not patentable, and this applies regardless of who performs the method.

Therapeutic methods: form of claims

- 18. The following formats of claim are all considered to define methods of treatment by therapy, and are thus unpatentable under Section 4A(1):
 - i) The treatment of (medical condition Y) with (substance X).
 - ii) The use of (substance X) to treat (medical condition Y).
 - iii) (Substance X) when used to treat (medical condition Y).
 - iv) The use of (substance X) as a pharmaceutical.

In G 05/83⁹, the Enlarged Board of Appeal of the EPO decided that claims to "the use of X to treat Y" were indistinguishable from claims to "the treatment of Y with X", and this was upheld by the Patents Court in *John Wyeth's and Schering's Applications*¹⁰. These cases established that "Swiss-type" second medical use claims of the format "the use of X in manufacture of a medicament to treat Y" were acceptable. However, since the implementation of the medical provisions of the Patents Act 2004, second medical use inventions can be protected by claims of the form "substance X for use in the treatment of disease Y", and following the decision of the EPO Enlarged Board of Appeal in G 02/08¹¹ and the release of our <u>Practice Notice</u> on 26 May 2010, "Swiss-type" claims are no longer allowable (see below, paragraphs 105-112).

- 3 T 81/84 RORER/Dysmenorrhoea OJEPO 1988, 202
- 4 Schultz's Application BL O/174/86

- T 1599/09 COVIDIEN
 T 24/91 THOMPSON/Cornea OJEPO 1995, 512
- 7 T 58/87 SALMINEN/Pigs III [1989] EPOR 125
- 8 T 116/85 WELLCOME/Pigs I OJEPO 1989, 13
- 9 G 05/83 EISAI/Second medical use OJEPO 1985, 64
- 10 John Wyeth's and Schering's Applications [1985] RPC 545
- 11 G 02/08 ABBOTT RESPIRATORY/Dosage regime OJEPO 2010, 456

¹ Unilever (Davis's) Application [1983] RPC 21

² T 19/86 DUPHAR/Pigs II OJEPO 1989, 24

⁵

19. A claim to the use of a substance "as a pharmaceutical" (claim (iv) above) is interpreted as a method claim to the use of the substance in therapeutic treatment, rather than simply a claim to its use in a pharmaceutical formulation. This is in accordance with the general rules for construction of claims in this format, as described in <u>MoPP 2.16</u>. Where appropriate, amendment to acceptable first or second medical use claims should be sought for claims of this type. The use of a substance as an adjuvant or immunostimulant may be acceptable if restricted to non-therapeutic uses, as adjuvants are often used to produce antibodies in animals for experimental use, as well as in therapy.

Guidelines for determining whether a method is "treatment by therapy"

20. It is useful to consider whether the method would normally be carried out by a medical professional such as a doctor or vet. Section 4A(1) is intended to prevent medical or veterinary practitioners being restrained or hampered in exercising their professional skills by patent rights, and so a claimed method which does not impact on a practitioner's medical discretion is likely to fall outside the scope of Section 4A(1)^{12 13}. This principle was also applied (in relation to both therapy and surgery) in *Virulite's Application*¹⁴, where the Hearing Officer held that the "fundamental test" for inventions in this field is whether the patent, if granted, would interfere with the work of a medical or veterinary practitioner in their treatment of patients. A method in which a laser was used to modify a synthetic lenticule implanted on the cornea, on the other hand, was considered to be unpatentable, in part because it would be performed by or under the supervision of a medical practitioner due to the health risks concerned⁶.

"The intention underlying [Article 52(4)] is to ensure that nobody who wants to use the methods specified in this Article as part of the medical treatment of humans or animals should be prevented from this by patents. Such medical treatments need not necessarily be carried out by physicians...However, where, in view of the health risks connected with such a treatment, a claimed method of treatment has to be performed by a physician or under his supervision, it will normally fall within the exclusion..."

T 24/91 THOMPSON/Cornea OJEPO 1995, 512

21. However, this consideration is not decisive, and the purpose and inevitable effect of the invention are more important. If a method has no therapeutic purpose or effect (for example in methods for collecting bodily fluids for analysis etc), then the fact that it may be carried out by a doctor does not render it unpatentable^{15 16}. Conversely, methods for treating diseases in farm animals are excluded, even if the method may routinely be carried out by the farmer rather than the vet.

"...if a claimed method requires the treatment of an animal body by therapy, it is a method which falls within the prohibition on patentability set out in Article 52(4) EPC. It is not possible as a matter of law to draw a distinction between such a method as carried out by a farmer and the same method as carried out by a veterinarian, and to say that the method when carried out by a farmer is an industrial activity and therefore patentable... and when carried out by a veterinarian is a therapeutic treatment not patentable under Article 52(4)."

T 116/85 WELLCOME/Pigs I OJEPO 1989, 13

¹² T 245/87 SIEMENS/Flow measurement OJEPO 1989, 171

¹³ T 426/89 SIEMENS/Pacemaker OJEPO 1992, 199

¹⁴ Virulite's Application BL O/058/10

¹⁵ T 329/94 BAXTER/Blood extraction method OJEPO 1998, 241

¹⁶ T 1165/97 ULTRAFEM/Feminine hygiene device [2002] EPOR 384

Furthermore, the fact that a method may be carried out by patients on themselves does not render a therapeutic method patentable⁵. This is consistent with the view of the Enlarged Board of Appeal in G 01/07¹⁷ that the exclusions under Art.53(c) EPC (and therefore s.4A(1)) are not solely limited to methods which might hinder a doctor or vet in their practice:

"There is, however, no term in Article 53(c) EPC which would allow concluding that hampering of the practitioner's freedom is a prerequisite for the exclusion to apply in the individual case considered. The only condition defined in Article 53(c) EPC for a claim to be excluded from patentability is that it contains subject-matter being a method for treatment of the human or animal body by surgery or therapy or a diagnostic method."

G 01/07 MEDI-PHYSICS/Treatment by surgery OJEPO 2011, 134

In view of this clear statement from the Enlarged Board of Appeal, the question of whether a claimed method would hamper a medical or veterinary practitioner's freedom can only be considered an important guide in determining whether a method is excluded under s.4A(1), rather than a "fundamental test" as suggested in *Virulite's Application*¹⁴.

22. Although both prevention and cure of diseases are considered to be therapeutic, there must be a direct link between the treatment and the condition to be treated or prevented. Methods of hygiene are not considered therapeutic even though they may result in a reduced incidence of infection. In *Commonwealth Scientific & Industrial Research Organization's Application*¹⁸, the Hearing Officer held that a method for the destruction of wool follicles in the skin of a wool-bearing animal was not directly linked to a disease state to be cured or prevented, even though it could have the indirect effect of reducing parasite infestation. In addition, methods of sterilising non-living surfaces (such as surgical devices) are not considered to be methods of treatment by therapy. In T 611/09¹⁹ the use of an anti-bacterial citrate solution inside a catheter was not considered to constitute a method of treatment by therapy as – even when the catheter was inserted – the citrate could not exert its anti-bacterial effect in the patient's body, as the citrate would be inactivated on contact with blood.

Claims to both therapeutic and non-therapeutic methods

- 23. There are many instances where claims may potentially include within their scope both patentable and non-patentable methods. For example, a claim to "a method for inhibiting the coagulation of blood by contacting the blood with a carrier containing compounds X and Y" could include a method of treating the blood in a patient as part of a therapeutic method (not patentable), and also a method of treating stored blood in a bottle (patentable). In cases where it is unambiguously clear from the specification that the claims relate only to patentable methods, then no amendment is required.
- 24. If it is apparent from the specification that the claims could cover non-patentable embodiments of the method then amendment is required to clearly limit the claim to methods which are patentable, and if necessary to amend the description to clarify that therapeutic methods do not form part of the invention.

19 T 611/09 ASH ACCESS TECHNOLOGY

¹⁷ G 01/07 MEDI-PHYSICS/Treatment by surgery OJEPO 2011, 134

¹⁸ Commonwealth Scientific & Industrial Research Organization's Application BL O/248/04

- 25. The EPO Enlarged Board of Appeal in G 01/03²⁰ considered whether, and under what circumstances, an "undisclosed disclaimer" - that is, one where neither the disclaimer nor the subject matter excluded by it may be allowable. The Enlarged Board held that an undisclosed disclaimer to exclude unpatentable subject material, including methods of treatment by therapy or surgery, or methods of diagnosis practised on the human or animal body, is in principle allowable and does not necessarily constitute added matter. This principle was applied in the specific medical context by the Enlarged Board in G 01/07¹⁷ and subsequent decisions^{21 22}. The Enlarged Board's later decision in G 02/10²³ confirmed that the subject matter remaining in the claim after the introduction of the disclaimer must be disclosed in the application as filed, whether or not the disclaimer itself is disclosed in the application. This is in accordance with UK Office practice, which is explained in more detail in MOPP 14.126-14.127. Therefore if claims are limited, either by disclaimer or otherwise, to patentable methods, there must be support in the description for a non-therapeutic method - if there is not, then the amended claim will constitute added matter, as well as being objectionable through lack of support. In ICI (Richardson's) Application²⁴ a claim was made to a method of producing an anti-oestrogenic effect in a human, but excluding any method of treatment by therapy. It was considered that the specification did not describe any application of the method other than in the treatment of breast cancer or infertility, and so the claim was rejected. The words "cosmetic" or "non-therapeutic" in a claim to a method of treatment are generally acceptable as sufficient limitation²⁵; the use of the phrase "preimplanted", to disclaim a surgical method step in an otherwise patentable method, is also allowable¹⁷. Of course, if a claim is amended to "cosmetic methods", there must be disclosure of such methods in the application as filed. If there is not, then the amended claim will constitute added matter, as well as being objectionable through lack of support. Any disclaimer needs to exclude therapeutic methods and leave the scope of the remaining monopoly clear. A disclaimer which merely uses the words of the Act is considered to leave the scope of the monopoly unclear²⁴.
- 26. Moreover, it must be possible to distinguish the therapeutic and non-therapeutic effects of a claimed method. If the non-therapeutic effect is inseparable from the therapeutic effect, or if it is merely a secondary consequence of the therapy, then the invention is unpatentable, regardless of the wording used. For example, it has been held in both the UK courts and the EPO that it is not possible to claim a cosmetic method for the removal of plaque from teeth, as such a method will inevitably have therapeutic benefits in preventing tooth decay and gum disease.

"...the claimed use of a lanthanum-containing composition for cleaning plaque and/or stains from human teeth... will always inevitably have a therapeutic effect (at least in the prophylactic sense) as well as a cosmetic effect. Thus the invention as here claimed is not directed solely to a cosmetic effect, but is also necessarily defining 'a treatment of the human body by therapy' as well"

T 290/86 ICI/Cleaning plaque OJEPO 1992, 414

The EPO Technical Boards of Appeal have applied these criteria in, for example, T 1680/08²⁶, where it was held that a method of optimising an artificial respiration system (performed while the system was in use) was inextricably linked to the therapeutic use of the respiration system in keeping the patient alive, and so the claim was not allowable.

²⁰ G 01/03 PPG/Disclaimer OJEPO 2004, 413

²¹ T 385/09 LELY ENTERPRISES

²² T 266/07 WISCONSIN ALUMNI RESEARCH FOUNDATION

²³ G 02/10 SCRIPPS/Disclaimer OJEPO 2012, 376

²⁴ ICI (Richardson's) Application [1981] FSR 609

²⁵ T 36/83 ROUSSEL-UCLAF/Thenoyl peroxide OJEPO 1986, 295

²⁶ T 1680/08 BÖHM

- 27. On the other hand, if the effects are separable, then the existence of a possible therapeutic use should not prevent a cosmetic or other non-therapeutic method from being patentable. For example, a treatment may be therapeutic or cosmetic depending on the subject being treated. This distinction was accepted in the case of an appetite suppressant²⁷ and an antibacterial skin treatment²⁵. A similar distinction between therapeutic and non-therapeutic uses of the same method was made in T 584/88²⁸, wherein a treatment of snoring was regarded as either therapeutic in cases where the snoring was harmful to health, or non-therapeutic if the snoring was merely troublesome. In this case it was accepted that it was difficult to draw a precise boundary between harmful or merely troublesome snoring, but this did not prevent a method claim from being accepted for the latter (and a second medical use claim for the former).
- 28. The way these general principles have been applied by the courts and the EPO Boards of Appeal to specific, contentious areas is discussed below.

Therapeutic and non-therapeutic methods: specific examples

i) Cosmetic treatments

29. Purely cosmetic treatments of the skin and hair are patentable. These may include cosmetic methods of strengthening hair and nails (following Joos v. Commissioner of Patents²⁹), and cosmetic methods to prevent hair loss³⁰. In Virulite's Application¹⁴ the Hearing Officer observed that the removal of wrinkles caused by ageing had no conceivable therapeutic benefit, and so a cosmetic method claim for removing wrinkles by phototherapy was allowed. Methods of protecting the skin by simply blocking UV radiation are not considered to be therapy, but where a method includes physiological protective effects against UV-associated damage then it is considered to be therapeutic (T 1077/93³¹). In this case the Technical Board decided that the cosmetic and therapeutic aspects of the claimed method of protecting skin were "inevitably linked, such that each one necessarily develops together with the other and such that it is impossible to separate them". The argument that the treatment was effectively directed towards natural ageing of the skin, and was therefore not therapeutic, was rejected on the grounds that "a natural process of cell degeneration loses its physiological normality when it develops in an abnormal manner, and in particular faster than its normal process". A similar view was taken by the Board of Appeal in T 67/02³², wherein a "non-therapeutic" method of prevention of skin ageing was held (on the facts of the case) to be inseparable from therapeutic effects acting on the skin. In the same case however, the use of the same agent to protect the lips (eg. from sunburn) was held to be a purely cosmetic application with no therapeutic benefit. The use of a composition for the local treatment of comedones (blackheads) was regarded as a cosmetic method of non-medical body hygiene, although when applied for the treatment of acne this would be regarded as therapeutic²⁵.

ii) Removal of parasites

- 30. Methods of treating or preventing infestation of internal parasites are regarded as therapy; the argument that the host animal is unaffected and that it is only the parasites that are being killed and that therefore this is not therapy of the animal body, has been rejected³³. Treatment of parasites residing on the skin of a human or animal is considered to be therapy (T 116/85⁸). The Board of Appeal in this decision explicitly rejected the view that a treatment of an ectoparasite infection was therapeutic in the case of "permanent" ectoparasites residing in the skin, and not in the case of "temporary" ectoparasites residing on the skin. Treatment of, for example, head lice, is therefore considered therapeutic, despite the decision made under the 1949 Act in *Stafford-Miller's Application*³⁴.
- 31. However, the procedure must be **directly** related to the treatment or prevention of parasite infestation to be excluded. A procedure to remove hairs from the skin of an animal, which had the indirect effect of reducing the incidence of blowfly strike, was held to be non-therapeutic¹⁸.

²⁷ T 144/83 DU PONT/Appetite suppressant OJEPO 1986, 30

²⁸ T 584/88 REICHART/Anti-snoring means [1989] EPOR 449

²⁹ Joos v. Commissioner of Patents [1973] RPC 59

³⁰ T 453/95 REDKEN

³¹ T 1077/93 L'OREAL /Protection against UV [1997] EPOR 546

³² T 67/02 BEIERSDORF

³³ Ciba-Geigy's Application BL 0/35/85

³⁴ Stafford-Miller's Application [1984] FSR 258

iii) Oral care

32. Methods for the removal of dental plaque, or preventing the formation of plaque are considered to be therapeutic and thus unpatentable. All such methods have the effect of treating or preventing dental caries, and have been refused on these grounds under the 1949 Act^{35 36} and under the previous Section 4(2) of the 1977 Act³⁷. In EPO decision T 290/86³⁸ it was found that the inherent therapeutic effect of removing plaque could not be separated from the purely cosmetic effect of improved appearance of the teeth, and so restriction of such a claim to a cosmetic method is not possible. On the other hand, "treatment of halitosis" was not considered to be a method of treatment by therapy (as it could only in extreme cases be considered a disease)³⁹.

iv) Pain, fatigue and addiction

33. The relief of pain is considered to be therapeutic, even where the pain has no pathological cause:

"Irrespective of the origin of pain, discomfort or incapacity, its relief, by the administration of an appropriate agent, is to be construed as 'therapy'..."

T 81/84 RORER/Dysmenorrhoea OJEPO 1988, 202

- 34. However, in T 385/09²¹ the Board of Appeal rejected the argument that any alleviation of discomfort is by definition therapeutic in this case a claim to a non-therapeutic method of cooling farm animals (for example, to encourage them to enter a milking stall) was allowed. In addition, in T 469/94⁴⁰ it was held that a method of reducing the perception of fatigue (for example, following exercise) was not comparable with the relief of pain, discomfort or incapacity, and could be considered to be non-therapeutic when carried out on healthy individuals, although there were clearly therapeutic uses of the treatment as well.
- 35. Methods of treatment of addiction or withdrawal symptoms, including methods to help stop smoking, are considered to be therapeutic.

v) Obesity, weight reduction and fitness

36. Methods of weight reduction for purely cosmetic reasons, including the suppression of appetite, are patentable. In T 144/83²⁷ a claim to a "method of improving the bodily appearance of a non-opiate-addicted mammal" was considered allowed insofar as it related to cosmetic weight loss only. It was recognised that the method could also be used for therapeutic effects such as the treatment of obesity. Claims to such methods therefore need to clearly relate to cosmetic weight loss only. Similarly, a method for "enhancing skeletal muscle performance of normal healthy subjects" was considered to be non-therapeutic by virtue of its limitation to healthy subjects⁴¹

vi) Contraception, abortion and fertility treatment

37. Claims to methods of abortion, termination of pregnancy or induction of labour are considered to be unpatentable treatments, as they will always be carried out under medical supervision (see UpJohn (Kirton's) Application⁴² - 1949 Act). This applies regardless of the reasons for performing these methods.

³⁵ Oral Health Products (Halstead's) Application [1977] RPC 612

³⁶ Lee Pharmaceuticals' Applications [1975] RPC 51

³⁷ ICI Ltd's Application BL O/73/82

³⁸ T 290/86 ICI/Cleaning plaque OJEPO 1992, 414

³⁹ T 675/11 COLGATE-PALMOLIVE

⁴⁰ T 469/94 MIT

⁴¹ T 1230/05 BIOENERGY

⁴² UpJohn (Kirton's) Application [1976] RPC 324

- 38. Methods of contraception are not considered to be therapeutic, and may be patented (following the decision under the 1949 Act in *Schering's Application*⁴³). Pregnancy is not an illness or disorder, and so its prevention is not regarded as therapy. This has been confirmed in decisions of the EPO Boards of Appeal^{44,45}. However, contraceptive methods are excluded under Section 4A(1) if they contain a therapeutic element⁴⁴. In T 1635/09⁴⁶ this principle was applied to a low dosage contraceptive, on the grounds that the improvement over the prior art was in the reduction of side effects, rather than any increase in efficacy, and the claim was refused as being a method of treatment by therapy. However, unlike in T 820/92⁴⁴, it was not alleged that any element of the composition served to actively reduce the side-effects; instead, the lower dosage resulted in reduced side effects compared to the prior art. This would appear to be simply a safer way of carrying out a non-therapeutic contraceptive method, and so we would not follow this approach. Methods of contraception are not considered to lack industrial application merely because they are for "private and personal use". The private use of such a method would not constitute an infringement of a patent according to Section 60(5) of the Patents Act 1977, and so a patent to such a method is allowable (notwithstanding the EPO decision in T 74/93⁴⁵).
- 39. Methods of treatment of infertility, including methods utilising *in vitro* fertilisation, are considered to be therapeutic. Moreover, the implantation of an *in vitro* fertilised embryo would, in most cases at least, be considered to be a surgical process and thus not patentable (as was the case in *Occidental Petroleum's Application*⁴⁷). In addition, the implantation of a human embryo would constitute a "commercial or industrial use" of such an embryo, and so would be unpatentable under Schedule A2 of the Patents Act.

vii) Methods utilising implanted devices

40. If a claimed method has a therapeutic purpose or effect then it is unpatentable under Section 4A(1) even if the direct effect of the method is targeted on a non-living object such as an implant. A method of operating a pacemaker in which its output to the heart was adjusted was rejected as being a method of treatment by therapy in T 82/93⁴⁸. The applicant's argument that this was a "technical operation performed on a technical object" was considered to be irrelevant. On the other hand, a method of controlling the input energy to a pacemaker, which had the effect of minimising the energy requirements of the device but did not affect the output to the heart was accepted⁴⁹. Similarly, a method for measuring the flow of a drug from an implant, which did not actually control the flow, was held to be non-therapeutic¹².

47 Occidental Petroleum's Application BL O/35/84

⁴³ Schering's Application [1971] RPC 337

⁴⁴ T 820/92 GENERAL HOSPITAL/Contraceptive method OJEPO 1995, 113

⁴⁵ T 74/93 BRITISH TECHNOLOGY/Contraceptive method OJEPO 1995, 712

⁴⁶ T 1635/09 BAYER SCHERING/Composition for contraception OJEPO 2011, 542

⁴⁸ T 82/93 TELECTRONICS/Cardiac pacing OJEPO 1996, 274

⁴⁹ T 789/96 ELA MEDICAL/Therapeutic method OJEPO 2002, 364

viii) Treatments performed outside the body

41. A therapeutic treatment of the human or animal body is unpatentable under Section 4A(1) even if the actual treatment takes place outside the body, as in an extracorporeal blood dialysis or filtration method (Calmic Engineering's Application⁵⁰ (1949 Act) and Schultz's Application⁴). In the latter case it was observed that the words "practised on the human or animal body" relate only to methods of diagnosis, and not methods of treatment by therapy or surgery. Similarly, the addition of anticoagulants in an ex vivo blood processing system, and the ex vivo removal of immunoglobulins using a binding agent, wherein the blood was returned to the patient were considered to be therapeutic by the EPO in T 1075/06⁵¹ and T 2003/08⁵² respectively. However, methods of treating blood removed from the body are only regarded as therapeutic where the method includes - explicitly or implicitly - the return of the blood to the patient. In particular, if the blood is returned to the same body in a continuous or "closed loop" process then the method will be regarded as therapeutic, whether or not the claim explicitly includes the re-infusion step. Where the blood treatment is separated from the subsequent use of the blood - for example where it is stored for use in treating another patient, or the same patient at later date, it may be patentable⁵³. In addition, a method of preparing a dialysis solution which was carried out "on line" (i.e. while the patient was connected to the dialysis system) was not considered therapeutic as the solution in question did not ever come into contact with the patient's blood - it was merely a component of the dialysis solution⁵⁴.

ix) Treatment of stock animals

- 42. The treatment of stock animals in order to improve their meat or other products, eg. milk yields, or to improve their growth by administration of substances or compositions in their food is not regarded as therapy, even if the substances concerned may have therapeutic benefits. However, where an increase in meat yield or other industrial benefit is merely an inevitable consequence of improved health through therapeutic treatment, then such a method is unpatentable. Claims have been rejected for this reason to methods involving general immunostimulation⁵⁵ or through a specific effect on a pathogen⁵⁶.
- 43. On the other hand, a claim to the non-therapeutic use of antibiotics may be acceptable if the effect on meat or milk production is not a mere consequence of improved health. The test used in T 774/89⁵⁷ was that a nontherapeutic method would be expected to show an improvement on the normal condition of the subject, rather than merely restoring an animal to a normal, healthy condition. In such cases, the non-therapeutic effects must be distinguishable from the therapeutic benefit, and any therapeutic methods must be specifically disclaimed (see paragraphs 23-27 above).

SURGERY

44. Decisions of the UK courts, Intellectual Property Office Hearing Officers and EPO Boards of Appeal concerning the interpretation of the term "methods of surgery" in section 4A(1) of the Act and Article 53(c) have considered the nature of the procedure in question, its purpose, and by whom the method is carried out.

Methods of surgery: the nature of the procedure

45. The dictionary (OED) definition of surgery is the treatment of the body by incision or manipulation. It is therefore not limited to cutting the body but includes manipulation such as the setting of broken bones or relocating dislocated joints (sometimes called "closed surgery"), and also dental surgery. Furthermore, in *Occidental Petroleum's Application*⁴⁷, it was observed that a method of implanting an embryo could still be viewed as surgery even if the method did not require incision. Similarly, a method comprising the insertion of devices into the respiratory cavities of the body (without incision) was also considered to be surgical by the EPO⁵⁸.

58 T 05/04 CAMTECH

⁵⁰ Calmic Engineering's Application [1973] RPC 684

⁵¹ T 1075/06 FENWAL

⁵² T 2003/08 EDWARDS LIFESCIENCES

⁵³ T 144/04 ARUBA INTERNATIONAL

⁵⁴ T 794/06 GAMBRO LUNDIA

⁵⁵ T 780/89 BAYER/Immunostimulant OJEPO 1994,797

⁵⁶ T 438/91 MEIJI/Feeds [1999] EPOR 333

⁵⁷ T 774/89 BAYER

46. In T 35/99⁵⁹ a very broad interpretation of the term "methods of surgery" was put forward, which included any physical interventions on the body in which maintaining the life and health of the subject was of paramount importance. This was distinguished from those interventions which result in the death of the subject (e.g. slaughter of farm animals or sacrifice of laboratory animals), which are not excluded. This followed the Technical Board of Appeal decision in T 182/90⁶⁰, which stated that the definition of surgery includes (amongst other things) "endoscopy, puncture, injection, excision and catheterisation". However, the Enlarged Board of Appeal in G /01/07¹⁷ held that such a broad interpretation of "method of surgery" was unjustifiable, given the advances in medical techniques. Although the Enlarged Board did not provide an authoritative definition of the term "methods of surgery", it did state that a method should be excluded if it constitutes a substantial physical intervention, which entails a significant health risk even when carried out by a medical professional, and subsequent Technical Board of Appeal decisions have followed this approach.

"A ... method ... which comprises or encompasses an invasive step representing a substantial physical intervention on the body which requires professional medical expertise to be carried out and which entails a substantial health risk even when carried out with the required professional care and expertise, is excluded from patentability as a method for treatment of the human or animal body by surgery pursuant to Article 53(c) EPC"

G 01/07 MEDI-PHYSICS/Treatment by surgery OJEPO 2011, 134

- 47. Therefore, in deciding whether a claimed method is objectionable under s.4A(1) on the grounds that it is a method of surgery, examiners should be satisfied that the method is invasive, requires professional skill and carried a potential risk. For example, a simple injection method, either for taking a small blood sample or introducing a composition would not be regarded as a method of surgery, as it would involve relatively low levels of technical expertise. On the other hand, a method which requires more specialist medical skills or carries a significant risk, such as a lumbar puncture to deliver epidural injections, or puncturing veins and extracting blood for blood donation or blood processing^{51 61}, is unlikely to be patentable. In deciding whether a claimed method of introducing an agent (such as a pharmaceutical or contrast agent) is surgical in nature, it is the risk of the invasive procedure, and not the risk of any side effects of the agent, that should be considered¹⁷.
- 48. Methods which define the implanting or insertion of devices by surgical means are clearly unpatentable as in the cases considered in *Allen's Application*⁶² and T 05/04⁴⁹. The same applies for methods which control a surgical device, for example a surgical robot, in a manner which impacts on the body⁶³. However, methods of attaching exoprostheses to the skin using an adhesive were found to be patentable in T 635/08⁶⁴. Claims to methods involving the internal operation of implanted devices, or the interaction between the implanted device and the operator or external control system, are not objectionable if they do not relate to the implantation of the device, and do not impact on the body. The fact that the device needs to have been implanted by surgical means prior to performing the claimed method does not render the claim unpatentable^{65 66}. On the other hand, where the claimed method necessarily **encompasses** a surgical step (even if this step is not explicitly claimed), then it will be objectionable in T 429/12⁶⁷ it was held that a method of producing dental apparatus was unpatentable because the method encompassed an indispensable step of fixing a "reference element" (such as a screw) to the jaw bone by surgical means.

60 T 182/90 SEE-SHELL/Blood flow OJEPO 1994, 641

65 T 09/04 KONONKLIJKE PHILIPS ELECTRONICS

67 T 429/12 DENTAL VISION

⁵⁹ T 35/99 GEORGETOWN UNIVERSITY/Pericardial access OJEPO 2000, 447

⁶¹ T 1695/07 TRANSONIC SYSTEMS

⁶² Allen's Application BL O/59/92

⁶³ T 2102/12 INTUITIVE SURGICAL OPERATIONS

⁶⁴ T 635/08 DOW CORNING FRANCE

⁶⁶ T 1102/02 MAQUET CRITICAL CARE

49. The Enlarged Board of Appeal in G 01/07¹⁷ held that a method (such as an imaging method) which is not itself surgical but is useful for or during surgery, or which allows a surgeon to make a real-time decision during a surgical intervention, is not a method of surgery as such. In addition, it was held that if the surgical step was omitted from a claim, for example by use of a disclaimer, then this could overcome an objection under Art.53(b) EPC (s.4A(1)). Nevertheless, the claims must adequately define the invention, and so if a surgical step is an essential feature of the invention (rather than being simply a necessary prerequisite) then disclaiming or omitting the surgical step may lead to an objection under s.14(5)⁶¹. In T 2102/12⁶³ it was held that a claimed imaging method was inextricably linked to the "unclaimed" surgical method, and so the claim was considered unclear. Furthermore, a disclaimer directed to "such uses that comprise or encompass an invasive step representing a substantial physical intervention on the body of a human or an animal which requires professional medical expertise to be carried out and which entail a substantial health risk even when carried out with the required professional care and expertise" (taking the wording from G 01/07) was considered unclear, as it would be require the skilled person to evaluate whether any such use met these conditions and so left the boundaries of the claim uncertain⁶⁸.

Methods of surgery: purpose

50. The definition of surgery used in applying Section 4A(1) relates to the nature of the treatment, and not its purpose. The exclusion of methods of surgery is not limited to therapeutic surgery; methods of surgery for cosmetic purposes, or other non-therapeutic purposes such as sterilisation, are not patentable.

"...surgery can be curative of the disease or diseased conditions, or prophylactic, that is, preventative of diseased conditions, as for example, where an appendix or tonsils may be removed before any diseased condition starts up, and surgery may even be cosmetic without being curative or preventative. So that the subsection it seems to me is saying that any method of surgical treatment, whether it is curative, prophylactic or cosmetic, is not patentable."

Unilever (Davis's) Application [1983] RPC 219 (NB remarks on surgery were obiter)

51. This remains the practice of the Intellectual Property Office with respect to cosmetic surgery, and is also in line with EPO practice following the Enlarged Board's decision in G 01/07¹⁷:

"Hence, the Enlarged Board concludes that the meaning of the term "treatment by surgery" is not to be interpreted as being confined to surgical methods pursuing a therapeutic purpose."

G 01/07 MEDI-PHYSICS/Treatment by surgery OJEPO 2011, 134

This overturned previous EPO practice as established in the decision by the Technical Board of Appeal in T 383/03⁶⁹, where it was decided that the only surgical methods which are excluded from patentability are those potentially suitable for "maintaining and restoring the health, the physical integrity, and the physical well-being of a human being or animal, and to prevent diseases." In this case, a method of hair removal by optical radiation was held to be surgical in character, but nonetheless patentable as its purpose was purely cosmetic. This type of procedure would not in any case be considered to be surgical in nature under UK Office practice. (Indeed, it is very similar to the procedure in *Commonwealth Scientific & Industrial Research Organization's Application*¹⁸, in which method claims were granted, although the question of whether this was a surgical method was not considered at the hearing). The EPO Technical Board of Appeal has applied the practice established in G 01/07¹⁷ in, for example, T 1213/10⁷⁰. In this case a method of measuring *in vivo* enzymatic activity which included a surgical step of using a "penetration device" such as an endoscope to introduce a substrate to an organ in the body was excluded as being a method of surgery despite the applicant's argument that the method was carried out for analytical rather than therapeutic purpose.

68 T 1487/09 BIOLASE

- 69 T 383/03 GENERAL HOSPITAL/Hair removal method OJEPO 2005, 159
- 70 T 1213/10 SONY

Methods of surgery: who carries out the method?

- 52. The Enlarged Board in G 01/07¹⁷ stated that whether a method is excluded or not as a "method of surgery" cannot depend on who carries it out, not least because of the changing medical roles in healthcare systems. Nevertheless, the Board did consider that the exclusion is intended to cover methods which require professional medical skills, and so the level of medical skill needed to perform a method can be a useful guide in determining whether a method is excluded or not. In general, any operation on the body which requires the skill or knowledge of a surgeon or other medical practitioner is regarded as being surgery, whether or not it is therapeutic. A method of embryo implantation which required the intervention of a surgeon or veterinary surgeon was held to be a surgical method, regardless of its purpose (Occidental Petroleum's Application⁴⁷). In this case, it was stated that "if a method requires a surgeon for its execution then it must be surgery." However, in Allen's Application⁶² (which related to a method of inserting implanted markers into the body for NMR or CT scans) it was held that this did not mean that a method which did not necessarily require a surgeon could not be considered to be surgery. A physical intervention which required the medical skills of, for example, a nurse, could still be regarded as surgery. Similarly, methods of dental surgery require specialist dental skills and so are not patentable. If a method does not require medical skills or knowledge, on the other hand, (such as, for example, a method for cosmetic ear-piercing, or a method of tattooing the body) then it would not be excluded as a method of surgery. In T 663/02⁷¹ it was held that tasks which are likely to be delegated or are carried out on such a routine basis as to be thought commonplace, with a low health risk, may be patentable. This case also reinforced the notion that consideration of the surgical aspect is separate from any possible therapeutic effects of what, exactly, is introduced.
- 53. Similarly, the setting of bones is carried out by doctors and is considered to be surgical in nature, while making and applying a plaster cast is normally carried out by a technician and would not be regarded as surgery. A method of making a plaster cast would also not be treated as therapeutic, as the therapy resides in holding the bone in position while it heals and this occurs after the method of making the cast is complete. Methods of making artificial limbs or taking measurements or making casts are therefore not regarded as surgery or therapy.

DIAGNOSIS

Definition of diagnosis

54. Diagnosis is the determination of the nature of a medical condition, usually by investigating its history, aetiology and symptoms and by applying tests. Diagnosis in itself is an intellectual exercise which is not patentable in view of Section 1(2)(c). Section 4A(1) however relates to <u>methods</u> of diagnosis practised on the human or animal body. Diagnosis includes a negative finding that a particular condition can be ruled out, as well as a positive identification of a disease⁷². However, determination of the general physical state of an individual (for example, for a fitness test) is not considered to be diagnostic if it is not intended to identify or uncover a pathology.

The meaning of "methods of diagnosis"

- 55. Typically, the process of diagnosis involves a number of steps leading towards identification of a condition. The EPO Enlarged Board of Appeal in G 01/04⁷³ characterised these steps as being;
 - (1) the examination and collection of data;
 - (2) comparison of the data with normal values;
 - (3) recording any deviation from the norm; and finally
 - (4) attributing the deviation to a particular clinical picture.

If a claimed method includes all these steps, and thereby makes it possible to identify a clinical state (e.g. identifying a disorder and/or enabling the doctor to decide on a particular course of treatment), it clearly constitutes a method of diagnosis. (In practice, if the method includes the first measurement step, and the final deductive step, then the intermediate steps may be implied.)

⁷¹ T 663/02 PRINCE

⁷² T 807/98 ST JUDE

⁷³ G 01/04 Diagnostic methods OJEPO 2006, 334

56. Alternatively, claims may be directed towards methods which are of value in diagnosis, but which do not in isolation enable a full diagnosis to be made. Examples include methods of internal imaging or methods of taking samples for subsequent *in vitro* analysis. Where a claimed method does not encompass all the steps necessary to enable a diagnosis to be made, then it is not considered to be a "method of diagnosis" and is not excluded from patentability under Section 4A(1). In G 01/04⁷³ the EPO Enlarged Board of Appeal decided that the term "method of diagnosis" should be interpreted narrowly. Only a method which comprises all of the 4 steps listed above, and therefore allows the identification of a pathological condition, falls within this definition.

"The method steps to be carried out prior to making a diagnosis as an intellectual exercise... are related to examination, data gathering and comparison.... If only one of the preceding steps which are constitutive for making such a diagnosis is lacking, there is no diagnostic method, but at best a method of data acquisition or data processing that can be used in a diagnostic method..."

G 01/04 Diagnostic methods OJEPO 2006, 334

- 57. This decision led to a significant change in practice in this Office and the EPO. We had adopted a broader definition of a method of diagnosis, based on the decision of the EPO Technical Board of Appeal in T 964/99⁷⁴. In that case it was held that all methods practised on the human or animal body which related to diagnosis or which were of value for the purposes of diagnosis were excluded. Thus, a method of taking a sample from the body for the purpose of medical examination was held to be an unpatentable method of diagnosis. The Enlarged Board in G 01/04⁷³ overturned this interpretation, and instead endorsed the narrow definition used in the earlier decision T 385/86⁷⁵, relating to a method of determining temperature and pH by magnetic resonance imaging. A method of taking a sample, or determining internal temperature or pH, does not in itself identify a condition, and so it is no longer considered to be a method of diagnosis. (This is also consistent with the earlier UK Office practice prior to T 964/99, which followed T 385/86 and the decision under the 1949 Act in *Bio-Digital Sciences' Application*⁷⁶).
- 58. A method performed on the body which does not enable a disease to be identified, but which may be of value in diagnosis is therefore not excluded under Section 4A(1). For example, a method of imaging using CT scanning⁶⁵, a method of measuring blood glucose⁷⁷ and a method of assessing tissue viability by measuring total haemoglobin, oxygen saturation and hydration⁷⁸ were all considered to provide only intermediate results which did not enable a diagnosis to be made. In *Aueon's Application⁷⁹* the Hearing Officer held that a method of analysing a sample from a tumour to determine the status of a plurality of markers and using this method to interrogate a database of drug treatment options, to identify and rank drug treatment options, was not a method of diagnosis as it did not include steps (3) and (4) as identified in G 1/04 (though the method would not have been excluded regardless under s.4A(1) as it was not practised on the body)
- 59. A method practised on the body (see paragraphs 62-66 below) which includes all of the steps leading to a diagnosis should be objected to under Section 4A(1). This is usually clear-cut if the claim relates to the identification of a specific condition. In addition, it may be apparent from the description that a claimed method does in fact result in a diagnosis, even if the words of the claim do not specify a specific disease. In T 125/02⁸⁰, the measurement of nitrogen monoxide levels in exhaled air was used to identify "impaired respiratory function". The description indicated that the method allowed a particular course of treatment to be selected, and so the claimed method was considered to encompass all the steps leading to a diagnosis.
- 60. In T 1016/10⁸¹ it was argued that the detection of an "amyloidogenic disorder" was merely an intermediate finding as this terms includes a range of disorders, and further tests would be needed to identify precisely which disorder and so determine a course of treatment. The Technical Board held that the term "particular clinical picture" used in G 01/04 to define step (4) was broader than identification of a single disease or determining the course of treatment, and so encompassed the identification of a class of disorders such as amyloidogenic disorders.

- 75 T 385/86 BRUKER/Non-invasive measurement OJEPO 1988, 308
- 76 Bio-Digital Sciences' Application [1973] RPC 668
- 77 T 330/03 ABBOTT LABORATORIES
- 78 T 41/04 NATIONAL RESEARCH COUNCIL OF CANADA
- 79 Aueon's Application BL O/248/13
- 80 T 125/02 AEROCRINE
- 81 T 1016/10 GENERAL HOSPITAL

⁷⁴ T 964/99 CYGNUS/Diagnostic device OJEPO 2002, 4

61. It should be noted that Section 14(5)(a) requires that the claims adequately define the matter for which the applicant seeks protection. If an essential step of the method is omitted (including the final, deductive step) then the claim may not adequately define the invention⁷³. In addition, if one of the steps (such as the final deductive step) is deleted by amendment, then it must be considered whether the amendment adds matter if the entire teaching of the application as filed related to the diagnostic method in its entirety⁸². However, this does not mean that the claim must explicitly refer to every detail of the process. In particular, a claim to a diagnostic method performed *in vitro* on a sample taken from the body does not need to explicitly include the step of obtaining the sample (unless the invention actually lies in the method of obtaining the sample from the body).

The meaning of "practised on the body"

- 62. Section 4A(1) states that methods of diagnosis practised on the human or animal body cannot be patented. *In vitro* diagnostic tests, performed on blood or other samples removed from the body, are therefore patentable. Furthermore, to be excluded from patentability, diagnostic methods must be carried out on the living human or animal body. A method carried out on a dead body, for example to determine the cause of death, would not be objectionable.
- 63. Moreover, diagnostic methods may encompass both *in vivo* and *in vitro* steps. If the claimed method includes new and inventive technical steps performed *in vitro* then the method as a whole is not considered to be practised on the body. The Enlarged Board in G 01/04⁷³ considered whether all, or just one of the steps leading to a diagnosis had to be performed on the body for a method to be excluded. It was concluded that a method is only excluded if all of the **technical** steps in a method are practised on the human or animal body.

"if... some or all of the method steps of a technical nature... are carried out by a device without implying any interaction with the human or animal body, for instance by using a specific software program, these steps may not be considered to satisfy the criterion "practised on the human or animal body", because their performance does not necessitate the presence of the latter. By the same token, this criterion is neither complied with in respect of method steps carried out in vitro in a laboratory."

G 01/04 Diagnostic methods OJEPO 2006, 334

- 64. In practice, the key question is whether the examination and collection of data is practised on the body. As discussed above, a method is only considered to be a "method of diagnosis" if it has all the steps (1) to (4) listed in paragraph 55 leading to a diagnosis ie examination and collection of data, comparison of the data with normal values, recording any deviation, and attributing the deviation to a particular clinical picture. If the method includes all these steps, and the examination stage step (1) is practised on the body, then objection should be made under Section 4A(1).
- 65. Formally, the practice set out in G 01/04⁷³ is that for each of these 4 steps, there are two questions. Firstly, is this a technical step? For each **technical** step, the 2nd question is to ask whether the step is practised on the body. The method is not patentable if all the technical steps are practised on the body, but is patentable if any of these 4 steps are technical in nature but are carried out away from the body. In practice, the first step of examination and collection of data is the only one that may be "practised on the body", and is (in most cases at least) the only "technical" step. The final deductive step of determining the condition is a purely intellectual exercise carried out by the doctor or vet, and so is not considered to be a technical step. In most cases, the comparison of data with standard values and recording of any deviation (steps 2 and 3) are also not technical features, and so are irrelevant for deciding whether the claim is objectionable. Moreover, in T 1197/0283 it was held that any additional or preparatory steps (other than these 4) are irrelevant - the claim may still be objectionable even if these additional steps are both technical and *in vitro*. Thus in this case the claimed method for diagnosing glaucoma was held to be unpatentable despite the fact that it included a technical process of producing images prior to presenting them to the patient – i.e. preparatory to step (1) – and technical data analysis steps between steps (1) and (2), none of which were practised on the body. Similarly, in T 143/04⁸² and T 1016/10⁸¹ methods of diagnosing disorders such as Alzheimer's disease which included automated data analysis or signal processing steps between steps (1) and (2) were held to be unpatentable as the initial measurement step was practised on the body.

66. To decide whether a particular step in a method is "practised on the human or animal body", the key test is whether the step requires the presence of the patient to perform it. It is irrelevant whether the procedure is invasive, or capable of causing harm to the patient⁷³. For example, in T 125/02⁸⁰, the first step was the measurement of the nitrogen monoxide content during exhalation. As this step required the presence of the patient, it was considered to be a technical step practised on the human body. The other steps of the method – comparison with standard values, finding of a deviation, and attribution of the deviation to a clinical picture – were all held to be non-technical in nature, and so the claim in question was considered to be an unpatentable method of diagnosis.

Who performs the method?

67. The question of whether a claimed method is excluded under Section 4A(1) depends on whether it falls within the definition of a "method of diagnosis" (paragraphs 55-61), and whether it is "practised on the human or animal body" (paragraphs 62-66). It is not dependent on who carries out the method, or whether a physician needs to be present.

"whether or not a method is a diagnostic method within the meaning of Article 52(4) EPC should neither depend on the participation of a medical or veterinary practitioner, by being present or by bearing the responsibility, nor on the fact that all method steps can also, or only, be practised by medicinal or non-medicinal support staff, the patient himself or herself or an automated system."

G 01/04 Diagnostic methods OJEPO 2006, 334

At most, if a doctor is required to be present for a given step then this would appear to imply that the step is performed on the body. However, the decision of the Enlarged Board in G 01/04⁷³ makes it clear that this is not a decisive factor in determining whether a method is excluded or not. This contrasts with the decision of the Technical Board in T 655/92⁸⁴, where a method of NMR imaging included a step of injecting contrast agents into the body. These agents carried the risk of side effects, including potentially fatal anaphylactic shock, and so the method required the involvement of medical as well as technical staff. It was therefore held that this was a diagnostic method falling within the scope of the exclusion. In view of the clear direction given by the Enlarged Board in G 01/04, this reasoning is no longer relevant.

Diagnosis: summary of examination practice

68. To determine whether to object that a claim defines an unpatentable method of diagnosis practised on the human or animal body, a simplified test based on the reasoning of G 01/04⁷³ and subsequent EPO decisions may be used, at least at first instance. First, the examiner must consider whether the method includes (explicitly or implicitly) both a measurement or examination step, and a deductive step of determining the disease or clinical picture (steps (1) and (4) as set out above). If this is the case, then the second question is whether the measurement or examination step is "practised on the body" – the simple test for this is whether the patient has to be present during this step. If (and only if) the answer to both questions is "yes", an objection should be made.

Diagnostic methods and Section 1(2)

- 69. Diagnostic methods typically include steps of data analysis and interpretation. This may include steps which fall into the excluded categories defined in Section 1(2); in particular mathematical methods (Section 1(2)(a)), or methods of performing a mental act or computer programs (Section 1(2)(c)). In such cases, the four-step approach set out by the Court of Appeal in *Aerotel/Macrossan*⁸⁵ should be followed to determine patentability;
 - (1) properly construe the claim;
 - (2) identify the actual contribution;
 - (3) ask whether it falls solely within the excluded subject matter; and
 - (4) check whether the actual or alleged contribution is actually technical in nature.

This approach to assessing patentability under Section 1(2) should be taken regardless of whether the original diagnostic method is carried out *in vitro* or *in vivo*. In *Aueon's Application*⁷⁹, it was argued that a method of diagnosis could not be excluded under s.1(2) as G 1/04⁷³ made it clear that such methods **are** inventions (unlike the categories in s.1(2), which are considered not to be inventions), albeit inventions which are excluded under s.4A(1) if they are practised on the body. The Hearing Officer concluded that the method in question was not a method of diagnosis, and so did not need to come to a view on this question.

In vivo testing of drugs etc.

70. In vivo methods of testing pharmacological efficacy or toxicity of drugs, or experimental methods of investigating diseases in animals are not considered to be methods of diagnosis as defined in Section 4A(1). However, if the method would cause suffering to the animal and the application does not disclose any potential medical use or medical research benefit, then objection may be made that the method is incapable of industrial application, and moreover that the commercial exploitation of such a method would be contrary to public policy or morality (Section 1(3)).

MULTI-STEP METHODS INVOLVING A SURGICAL, THERAPEUTIC OR DIAGNOSTIC STEP

- 71. Section 4A(1) states that a patent shall not be granted for an invention of a method of treatment of the human or animal body by surgery or therapy or a method of diagnosis performed on the human or animal. Unlike section 1(2) of the Act, there is no proviso in s.4A(1) that methods are only excluded "to the extent that a patent or application for a patent relates to that thing as such". The EPO Enlarged Board of Appeal on G 01/07¹⁷, confirming a body of earlier EPO case law (e.g. T 820/92⁴⁴ and T 35/99⁵⁹), held that any multi-step method which includes a step comprising a method of surgery or therapy step is excluded from patentability. The claimed method in question in G 01/07 encompassed the step of injecting contrast media into the heart and as such was considered to fall within the exclusion, although it was also held that the claim could be saved by disclaiming the surgical step using the phrase 'pre-implanted' or similar. A similar conclusion was reached in T 266/07²².
- 72. In view of this settled view of the EPO Boards of Appeal, where a claimed method involves a number of steps, one or more of which constitutes a method of therapy or surgery (as defined above), then objection should be raised under s.4A(1). This means that, for example, a claim to a method of manufacturing a pharmaceutical, and then using it to treat a disease, is objectionable as a method of treatment by therapy. In addition, a method of producing a transgenic animal which includes a surgical method of embryo transplantation is also objectionable under s.4A(1). This is consistent with Hearing Officer's decision in *Occidental Petroleum's Application*⁴⁷, where amendment of a claim to a surgical embryo transplantation method to a claim to a "method of enhancing the production of thoroughbred mammalian animal stock" (which still encompassed the surgical step) did not save the application from refusal. The invention was held to be to a method of surgery, and thus unpatentable. If the claim includes an unpatentable surgical or therapeutic step, then it is considered unpatentable even if the technical contribution lies elsewhere in the method⁶¹.

73. The principle that one excluded step renders the whole claim unpatentable does not apply to methods of diagnosis practiced on the body, following the decision in G 01/04⁷³. As discussed above (see paragraphs 55-66) the Enlarged Board in this decision held that diagnostic methods are inherently multi-step methods, and claims are only excluded if they include all the steps necessary for making a diagnosis, and all the new and inventive technical steps are practised on the body.

APPARATUS FOR SURGERY, THERAPY OR DIAGNOSIS

- 74. Claims to medical apparatus are allowable in the same way as claims to non-medical apparatus. However, the exclusion of methods of surgery, therapy or diagnosis performed on the human body means that claims to such apparatus "when used" in such a method are not patentable. In other words, while a surgical instrument is patentable, it cannot derive novelty from the way it is intended to be used in a surgical method⁸⁶. Similarly, a claim to a pacemaker, which was characterised in part by its method of use, was rejected in T 82/93⁴⁸.
- 75. Moreover, it is not possible to claim the first or second medical use of apparatus. Sections 4A(3) and 4A(4) are restricted to substances and compositions, and cannot be used to protect apparatus. This has been confirmed in respect of first medical use claims by the UK courts (*National Research & Development Corporation's Application*⁸⁷), and similarly it has been held in this decision and by EPO Boards of Appeal that second medical use claims are not allowable with respect to apparatus⁸⁸ or prostheses^{89 90}. The rationale for this distinction given in T 227/91⁸⁸ was that compositions are expended in use, and so any new use is correlated with an expansion in the manufacture of the composition for this purpose. This does not apply to surgical apparatus, where there is the possibility of repeated and different uses of the same item. This practice was confirmed by the Technical Board of Appeal in T 1099/09⁹¹ and T 2369/10⁹²; in both cases a request to refer a question relating to the allowability of second medical use claims for medical devices to the Enlarged Board of Appeal was refused on the grounds that there was no ambiguity in the EPC or the case law to resolve.
- 76. A method of assembling or manufacturing a device or system inside the body which requires surgical steps is not patentable, as held by the Technical Board of Appeal in T 775/97⁸⁹. In this decision, the Board further held that this exclusion also applied to a product-by-process claim wherein the process of manufacture required a surgical step:

"...no European patent can be granted with claims directed to a new and even possibly inventive way of using devices, in particular endoprostheses, involving a treatment by surgery. This is equally true in the case of product claims defined by a construction which is only arrived at in the human or animal body following a surgical method step."

T 775/97 EXPANDABLE GRAFTS/Surgical device [2002] EPOR 24

77. However, more recent decisions^{61 93} have held that product claims which do not define any method steps are not excluded under Art. 53(c) EPC (S.4A(1)), even where they define products which are only obtained in their completed form following surgical methods. In T 1407/08⁹³ the Board said that such product claims were patentable even if they were expressed as product-by-process claims, where the manufacturing process included one or more surgical steps, as the claim protected the product only and not the process used to manufacture it; this appears to be inconsistent with the second sentence of the quoted passage from T 775/97⁸⁹. Moreover, a claim to a product can in fact be regarded as protecting the method used to produce it, as a product claim is infringed under s.60(1)(a) if a person "makes" the product. Pending clarification from the courts, it remains our practice that if a claimed product can only be manufactured by performing a method of surgery then it is objectionable under s.4A(1); in such a case it would not be possible to work the invention without performing an excluded method.

⁸⁶ Visx v Nidex [1998] FSR 405

⁸⁷ National Research & Development Corporation's Application BL O/117/85

⁸⁸ T 227/91 CODMAN/Second surgical use OJEPO 1994, 491

⁸⁹ T 775/97 EXPANDABLE GRAFTS/Surgical device [2002] EPOR 24

⁹⁰ T 213/07 TAYSIDE FLOW TECHNOLOGIES

⁹¹ T 1099/09 COLOPLAST

⁹² T 2369/10 CYBERONICS

⁹³ T 1407/08 BARONE

78. While the use of a device in surgery, therapy or diagnosis performed on the human body is unpatentable, the existence of functional features (for example, defining a prosthesis in relation to the human anatomy) in a product claim does not in itself transform the claim into a method claim⁹⁴. However, such a claim may be open to objection on clarity grounds, as being defined by its desired result.

FIRST MEDICAL USE

Section 4A(3)

79. In order to alleviate the effects of the Section 4A(1) prohibition on the claiming of methods of medical treatment, Section 4A(3) of the Patents Act 1977 (as amended by the Patents Act 2004) states that:

"In the case of an invention consisting of a substance or composition for use in any such method, the fact that the substance or composition forms part of the state of the art shall not prevent the invention from being taken to be new if the use of the substance or composition in any such method does not form part of the state of the art."

Section 4A(3) of the Patents Act 1977

- 80. This replaced the similarly-worded Section 2(6) of the Patents Act 1977, which was repealed by the Patents Act 2004. The words "any such method" refers to any method rendered unpatentable by Section 4A(1); ie a method of treatment of the human or animal body by surgery or therapy, or a method of diagnosis practised on the human or animal body. Under this section, and the equivalent Article 54(4) of the EPC 2000, a substance or composition which is itself already known is regarded as novel "for use in" a method of treatment prohibited by Section 4A(1) provided that the substance or composition has not been known to be used in any such method before. This provides an exception to the general rule of anticipation that once a substance or composition is known for whatever purpose then it cannot be patented again for another purpose, because it is old.
- 81. Section 4A(3) protects the **first** medical use only. However, Section 4A(4) allows further, specific medical uses for a known substance or composition to be claimed, using the same basic format. This is discussed in more detail in the next section. First medical use claims are normally used in cases where the substance is known. However, first (and second) medical use claims are acceptable for new compounds, for example, as a fall-back in the event of a prior disclosure of the compound coming to light after grant⁹⁵.
- 82. The case law relating to first medical use under the repealed Section 2(6) (or the equivalent Article 54(5) of the EPC 1973) continues to govern our practice under Section 4A(3). The exception to this is the case law relating to the novelty of claims of the form "substance X, for use in treating disease Y", which is now governed by Section 4A(4) as discussed below.

First medical use - forms of claim

- 83. A claim to the first medical use of a known substance or composition may broadly claim any therapeutic use. Such claims may have the wording:
 - i) (Substance X) for use in therapy; or
 - ii) (Substance X) for use as a medicament.

Obviously no single drug is suitable for treating all diseases. Nonetheless, this broad form of first medical use claim is allowable for the first medical use of a substance or composition, providing there is support in the form of evidence for at least one medical use (see paragraphs 97-102). The question of the allowability of this broad form of medical use claim was considered by the EPO Board of Appeal in T 128/82⁹⁶. It was decided that claims which did not state the specific therapeutic purpose were allowable if the substance in question had not been used in therapy, even if the specification only disclosed a single therapeutic use. It was argued that, as the inventor of a new chemical compound is granted absolute protection for all uses of the compound, an inventor who for the first time makes a known compound available for therapy should be able to gain protection over the whole field of therapy.

84. In addition, the first (or subsequent) medical use of a known substance or composition may be protected by a specific medical use claim of the form:

(Substance X) for use in the treatment of (medical condition Y).

Following the implementation of the EPC 2000 by the Patents Act 2004, claims of this form are treated as second medical use claims for the purpose of novelty, under Section 4A(4). In other words, they are only anticipated by the use of X for the specific purpose of treating disease Y. This represented a change in UK and European patent practice; formerly, a claim of this type was considered to be anticipated by **any** medical use of the substance or composition^{10 97}. This type of claim is discussed in more detail in the next section. However, essentially the distinction between "first" and "second" medical use claims is artificial; both types of claim are considered to be limited in scope to the substance when prepared for the defined use (whether general or specific), and both types of claim are only anticipated by the use of the substance or composition for the purpose (whether general or specific) defined in the claim. Therefore much of the case law concerning the construction of medical use claims, the criteria for assessing novelty and inventive step, and the requirements for sufficiency and support, applies equally to first or second medical use claims. The vast majority of the case law has concerned second medical use claims, and so the detailed discussion of these issues is considered in the following section, but this case law and the practice derived from it may need to be considered in examining applications relating to the first medical use of a known substance or composition. Case law specifically relating to first medical use claims is highlighted in the present section.

85. Claims of the form "the use of (substance X) in therapy" or "the use of (substance X) as a medicament" are **not** first medical use claims; these are unpatentable method of treatment claims, as discussed in paragraphs 18-19.

First medical use and Section 4A(1)

- 86. It is a general principle that a substance or composition cannot be protected by Section 4A(3) unless the method for which it is to be used is prohibited by Section 4A(1) (cf Articles 54(4) and 53(c) of the EPC 2000). The two Sections run hand-in-hand, and if the substance or composition is known in itself (but is not known for use in surgery, therapy or diagnosis) and the method falls foul of Section 4A(1), then a claim to the substance or composition for use in the method is protected by Section 4A(3) against an objection of lack of novelty. The meanings to be given to "surgery", "therapy" and "diagnosis" in Section 4A(1) therefore apply equally to Section 4A(3). Since non-surgical, purely cosmetic methods are not considered to be therapeutic, a substance or composition for use in a cosmetic method cannot be protected by Section 4A(3). However, an application may include both claims to the first medical use of a compound for therapeutic purposes, and claims to cosmetic methods using the compound (as in T 36/83²⁵). Moreover, known compositions or substances cannot derive novelty under Section 4A(3) in a claim worded as a first medical use claim where there is no disclosure of actual prophylactic or therapeutic effect achieved beyond, for example, the maintenance of a healthy diet⁹⁸.
- 87. EPO case law in relation to both first⁹⁹ and second medical use claims (see paragraph 123 below) indicates that protection for medical uses of known substances or compositions is only available for the use of a substance or composition as an active agent in medicine. The use of a known substance or composition as an inactive carrier or excipient for a therapeutic agent cannot therefore be protected by a first medical use claim. This represents a change to the practice set out in previous editions of these Guidelines.

Searching and assessing novelty and inventive step of first medical use claims

- 88. A first medical use claim of the form "(substance X) for use in therapy" would be anticipated by any prior use of the substance in therapy. The search should nevertheless be focussed on the use(s) disclosed in the application, as amendment of the claim to the second medical use format is likely if any prior medical use is found.
- 89. As discussed below in paragraphs 124-125, it has been established in the case law that a claim to a substance or composition "for use in treating disease Y" is construed as "suitable and intended for" the claimed treatment. It therefore follows that a first medical use claim to a substance or composition "for use in therapy" is construed as the substance or composition suitable and intended for a therapeutic use in humans or animals.
- 90. The disclosure of the effective use of the claimed substance or composition in the therapeutic treatment or prophylaxis of any medical condition will therefore anticipate a claim to the substance or composition for use in therapy. The substance or composition does not need to cure the disease or treat all patients with it, but it must have some beneficial effect. A claim to the first medical use of a compound is anticipated by its prior use in therapy, even if the only previous use was in association with another compound. However, the EPO Technical Board of Appeal in T 1758/07⁹⁹ held that the prior use of a composition to simply improve the palatability of a therapeutic agent did **not** anticipate a first medical use claim for the same composition. This case indicates that first and second medical use claims are not anticipated by the prior use of the agent in question as an inactive carrier or excipient for a therapeutic agent.
- 91. As medical use claims are construed as being limited to the **intentional** treatment of disease, the disclosure that the substance in question has previously been administered or ingested (for example, in a food product) would not anticipate a first medical use claim if there was nothing in the prior art to indicate any therapeutic benefit, even though this may have occurred inherently.

- 92. As with other fields of technology, for a prior art document to anticipate a first medical use claim it must meet the two requirements of prior disclosure and enablement. The disclosure requirement was summarised by Lord Hoffmann in *SmithKline Beecham's (Paroxetine Methanesulfonate) Patent*¹⁰⁰ (NB this case did not relate to medical use claims) as follows: "anticipation requires prior disclosure of subject-matter which, when performed, must necessarily infringe the patented invention". For this reason, a research paper which discloses experiments which show an activity which would make the substance or composition suitable for use in therapy, or discloses *in vitro* testing for such a use, but does not explicitly or implicitly disclose such a use does not anticipate a first medical use claim. Such disclosures of experiments and tests might of course be used as a basis for an obviousness objection under Section 3. Furthermore, a general statement of the medical use of a large class of chemical substances does not necessarily anticipate a first medical use claim to a specific compound falling within the class¹⁰¹.
- 93. Where there is an explicit statement of a therapeutic use, it is not always necessary for this to be accompanied by actual clinical evidence of a therapeutic effect to meet the disclosure requirement, at least, for novelty. A document (typically a patent document) which states that the substance is used in therapy without describing actual clinical data may therefore be cited for novelty. It would then be open to the applicant to challenge whether such a statement constitutes an enabling disclosure, as discussed further in paragraphs 128-130. The EPO Board of Appeal in T 1031/00¹⁰² rejected a first medical use claim on grounds of novelty, where the experimental data provided in the application was considered to be the same as that in a published research paper. It was not argued that the prior art paper explicitly disclosed the invention as claimed. Instead, it was argued that there was no new technical feature provided in the application the only new feature was the assertion of a therapeutic use. However, it is not clear whether this prior art would have met the test for disclosure in UK law as set out in *SmithKline Beecham's (Paroxetine Methanesulfonate) Patent*¹⁰⁰. In such a case, if a novelty objection could not be made due to a lack of explicit disclosure then the claim is likely to fall on grounds of either inventive step or support and/or sufficiency as discussed in relation to second medical use claims in paragraphs 142-143.

Plurality

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94. If a substance or composition has not previously been used in medicine, a number of general and/or specific surgical, therapeutic or diagnostic uses may be independently claimed in the one application without objection to plurality of invention.

Combined therapies

95. A first medical use claim to the use of two different agents (both of which are known in the prior art for therapeutic use separately) for simultaneous, separate or sequential use in therapy is considered novel, if there has been no disclosure of the use of the two agents together in therapy. However, it should be noted that the inventiveness of claims of this type needs to be scrutinised carefully, to determine whether the claim represents a mere collocation of known elements - see paragraphs 227-230 below.

"The Board also takes the view that combined products intended under Article 54(5) EPC for therapeutic, surgical or diagnostic methods also include compositions in which the components are presented side by side and can therefore be applied simultaneously, separately or at intervals to one and the same human or animal body."

T 09/81 ASTA/Cytostatic combination OJEPO 1983, 372

First medical use and apparatus

96. Section 4A(3) is restricted to substances and compositions; apparatus cannot be so protected⁸⁷.

First medical use claims: support and sufficiency

- 97. The requirements for support and sufficiency of medical use claims are discussed in full at paragraphs 195-216 as the case law in this area primarily relates to second medical use claims to the treatment of specific diseases and conditions. Much of this case law is also directly applicable to first medical use claims. However, as discussed above, it has been established that where an invention relates to the **first** medical use of a known substance or composition, the inventor is entitled to a broad claim to the substance "for use in therapy". Therefore no objection should be made that such a claim lacks support across its full scope, or is insufficient due to undue claim breadth, if the application provides credible evidence of the efficacy of the claimed agent or agents to treat any one or more diseases (though such an objection can of course be made if the claim is unduly broad in terms of the claimed substances or compositions).
- 98. A claim to the first medical use of a known substance or composition should be supported by evidence of its likely efficacy in therapy, surgery or diagnosis. In the absence of any such evidence, the claim is merely speculative and objection should be raised under s.14(5)(c). This requirement for first medical use claims follows from the logic of the decision by the Patents Court in *Prendergast's Applications*¹⁰³. This case concerned support for Swiss-type second medical use claims. It was held that, as the claims are distinguished from the prior art by their use, this use must be supported by evidence. The Hearing Officer in *F. Hoffmann La Roche's Application*¹⁰⁴ applied the same reasoning to claims in the first medical use format the essential feature of such claims is the intended use and so there must be support for it. The form of evidence is not critical; the application may provide *in vivo* or *in vitro* data, and *in silico* modelling data may be sufficient if it is considered to provide a credible basis for support. In *F. Hoffmann La Roche's Application*, the evidence was in the form of sequence homology with related genes and proteins; on the facts of the case it was held that this provided credible support for a medical use for a nucleic acid, but not for the protein coded by it. The Hearing Officer in *Lalvani et al's Applications*¹⁰⁵ followed this reasoning and also concluded that first medical use claims require evidence to support them.
- 99. Furthermore, if the application is not considered to render any medical use plausible, an objection of lack of sufficiency under s.14(3) may also be raised. The case law in relation to sufficiency of second medical use claims is discussed at paragraphs 196-205. In addition, a lack of any evidence for a therapeutic utility for antibodies to a newly-discovered receptor (of unclear function) was held to render a first medical use claim in respect of such antibodies insufficient in T 604/04¹⁰⁶.
- 100. It should be made clear in the examination report whether the objection (under either s.14(5)(c) or s.14(3)) relates to all or only some of the claimed agents. In the former case, the objection is likely to be fatal to the application, if the agents in question are already known. The evidence in support of medical use claims must be provided in the application as filed, and this objection cannot be overcome by later-filed results. A warning, e.g. in the form of an examination opinion, should therefore be provided at the search stage if the main claims relate to the first medical use of a known substance or composition, and no data is provided.
- 101. Moreover, if the application claims priority from an earlier application which does not provide evidence to render any medical use plausible, then it should be assumed at search and examination stage that a claim to the medical use of a known substance or composition is **not** entitled to a priority date based on the earlier application see paragraph 210. If the examiner considers it inherently implausible that the claimed composition could possibly have any therapeutic activity, then an objection of lack of industrial applicability, in addition to lack of sufficiency, may be raised as discussed in paragraph 211.

106 T 604/04 GENENTECH

¹⁰⁵ Lalvani et al's Applications BL O/220/13

102. In cases where a first medical use claim is included as a subsidiary claim to a *per se* claim to the substance or composition, then - as a general rule - if the substance or composition claim is new, inventive and supported by the description, further consideration of support for the medical use claim(s) is not necessary as a matter of practicality. Of course attention should be paid to any claims which were filed later than the application to check that they are supported by the description (see <u>MoPP 18.43</u>).

SECOND MEDICAL USE

Section 4A(4)

103. Section 4A(3) of the Patents Act 1977 allows patent protection for the first medical use of a known substance or composition, in the same way as the now-repealed Section 2(6). Section 4A(4), on the other hand, allows for the protection of further, specific uses of a known substances or compositions ("second medical use"), and has no equivalent in the Patents Act prior to implementation of the EPC 2000.

"In the case of an invention consisting of a substance or composition for a specific use in any such method, the fact that the substance or composition forms part of the state of the art shall not prevent the invention from being taken to be new if that specific use does not form part of the state of the art"

Section 4A(4) of the Patents Act 1977

104. The effect of this section (and the equivalent Article 54(5) of the EPC 2000) is that a claim to a known substance or composition for a **specific** medical use is considered to be novel if the substance or composition has not previously been used for that specific purpose, even if it has been used for other medical methods. This section for the first time introduces a statutory mechanism for the protection of inventions relating to second or further medical uses, and allows them to be defined using the same direct claim format as first medical use claims. However, it is important to note that **Section 4A(4) has not changed the boundaries of what is and is not patentable**, as for many years previously second medical use inventions were patentable through the "Swiss-type" claim format. A large body of case law in both the UK courts and the EPO has helped to define the scope, requirements and limits of Swiss-type second medical use claims. It was the express intention of the legislators, in drawing up both the EPC 2000 and the 2004 Act, that the new provisions were not intended to lead to any change in what is and is not patentable, and so the case law concerning Swiss-type claims is considered (with a very few exceptions which are highlighted below) to apply equally to the new form of second medical use claims.

Second medical use: claim format

105. Before implementation of the EPC 2000, second or further medical uses of a known substance or composition could only be protected by a claim to the use of the substance for the manufacture of a medicament for a specified medical use. If the use of the compound for the specified medical purpose was new, then such a claim was considered to be novel even if the same substance had previously been used in medicine for a different purpose before. This type of claim is known as a "Swiss-type" claim, as they were first allowed by the Swiss Patent Office. The protection of second medical uses by Swiss-type claims was allowed by the Enlarged Board of Appeal in G 05/83⁹, and this was followed by the Patents Court in *John Wyeth's and Schering's Applications*¹⁰.

- 106. Since the implementation of the medical provisions of the EPC 2000 on 13 December 2007, applicants have been able to protect inventions relating to second medical uses through the simpler and more direct claim form "substance X for use in the treatment of disease Y". This form of claim is referred to henceforth as the "EPC 2000" claim form, to distinguish it from the "Swiss-type" claim form where necessary. Initially, applicants were allowed to claim inventions relating to second medical uses using either the EPC 2000 format, the Swiss-type format, or both, pending guidance from the UK courts and/or the EPO Boards of Appeal. In 2010, the EPO Enlarged Board of Appeal issued its decision on G 02/08¹¹: this addressed, amongst other questions concerning second medical use claims, whether there were any special considerations applicable when interpreting and applying Articles 53(c) and 54(5) of the EPC 2000 (equivalent to sections 4A(1) and 4A(4)). The Enlarged Board considered that Swiss-type claims were accepted in G 05/83⁹ as the only possible means of protecting inventions relating to second medical uses in order to fill a loophole in the provisions of the EPC 1973. Article 54(5) of the EPC 2000 and section 4A(4) of the Act fill this loophole by explicitly allowing claims to the further specific use of a known drug, and so the Board held that the reason for this judge-made or "praetorian" law no longer exists. It was therefore decided that Swiss-type claims for the second or further medical use of a known substance or composition should no longer be allowed. However, the Board set out transitional provisions such that this only applies to new applications filed at the EPO more than 3 months after the publication of the decision in the Official Journal - the EPO therefore only reject Swiss-type claims in applications with an earliest priority date of 29 January 2011 or later. For applications with an earlier priority date, the EPO allow applications with both forms of second medical use claims, following the decision in T 1021/11¹⁰⁷, which reversed the earlier decision of T 1570/09¹⁰⁸ which held that applications could only include one or the other form of claim.
- 107. Following the decision of the Enlarged Board in G 02/08¹¹, the Office issued a <u>Practice Notice</u> on 26 May 2010, which sets out the Office practice on second medical use claims. In view of the desirability of maintaining conformity with EPO practice as established in Board of Appeal decisions in this field, the Office no longer allows claims in the Swiss format, and so any claims in this format must either be deleted or replaced by EPC 2000 claims of the form "substance X for use in the treatment of disease Y". This applies to both new and pending applications, regardless of their filing or priority date. While it is recognised that this is inconsistent with the transitional provisions set out in G 02/08, there is no clear legal basis under UK patent law for treating new and pending applications differently following a change in the interpretation of the statutes.
- 108. Examiners should therefore object to second medical use claims in the Swiss format on grounds of lack of clarity. Specifically, Swiss-type claims are considered to be unclear because, although they define a method of manufacturing a medicament, the invention does not in fact relate to the method of production but instead relates to the intended use of the medicament. As stated in G 02/08¹¹, there is no functional relationship between the feature conferring novelty (the intended use) and the claimed manufacturing process. As s.4A(4) now allows a simpler and clearer form of second medical use claim, there is no longer a reason to allow the more ambiguous Swiss form of claim. Lack of clarity is not one of the grounds for revocation under s.72, and so this practice does not have any bearing on the validity of patents already granted and including Swiss-type claims.
- 109. The only form of second medical use claim that is now allowable is the "EPC 2000" format:
 - i) "Substance X for use in the treatment of medical condition Y".

Under Section 4A(4) this claim is only anticipated by the prior use of substance X to treat disease Y. Prior to implementation of the EPC 2000, this form of claim was held (in *John Wyeth's and Schering's Applications*¹⁰, and *Sopharma's Application*⁹⁷) to be anticipated by any medical use of the substance in question.

110. The following types of claim are **not** acceptable second medical use claims:

ii) "The use of substance X in the manufacture of a medicament for the treatment of medical condition Y." *This is the usual form of Swiss-type claim.*

iii) "The use of substance X in the preparation of an anti-Y agent in ready-to-use drug form for treating or preventing medical condition Y." *The expression "in ready-to-use drug form" was intended to mean "as presented for sale", ie packaged, as explained in the Hearing Officer's decisions in John Wyeth's Application, cited in John Wyeth's and Schering's Applications¹⁰.*

iv) "The use of substance X in the manufacture of an anti-Y agent in a package together with instructions for its use in the treatment of medical condition Y."

v) "A process for the manufacture of a medicament for use in the treatment of medical condition Y, characterised by the use of substance X."

All of claim forms (ii) to (iv) were considered to be allowable by the Patents Court in *John Wyeth's and Schering's Applications*¹⁰, although claims (iii) and (iv) have rarely been used. Claims in any of these forms are objectionable on grounds of clarity as discussed above. The EPO Board of Appeal in T 958/94¹⁰⁹ considered that claim form (v) was an acceptable alternative to the Swiss form of claim. It is also now objectionable on grounds of clarity for the same reasons.

111. The following types of claim are also not acceptable as second medical use claims:

vi) "The use of substance X in the treatment of disease Y". *This is an unpatentable method of treatment claim.*

vii) "Commercial package containing as an active pharmaceutical agent compound X together with instructions ... for treating condition Y". *If the pharmaceutical use of X is already known, the claim is only distinguished from the prior art by the content of the instructions, and this represents a mere presentation of information and thus not a patentable invention under Section 1(2)(d).*

The interpretation of claims (vi) and (vii) given above was set out by the Patents Court in *John Wyeth's and Schering's Applications*¹⁰ and remains current practice.

112. The examples above all relate to situations where the applicant wishes to protect the use of a known substance X to treat a specified disease Y. However, claims written in the EPC 2000 second medical use format may be used in a variety of more complex scenarios. These are discussed at greater length in the following sections of these Guidelines, but examples are provided below of the types of claim that may occur with a reference to the detailed discussion of such instances:

viii) "Substance X for use in a cosmetic method of treating the skin." *This is not a second medical use claim as the new use is not excluded under s.4A(1), and so will not be novel if substance X is known – see paragraphs 116-123.*

ix) "Substance X for use in the treatment of disease Y by administration of a dosage of 0.1-1mg." / "Substance X for use in the treatment of disease Y by intravenous administration." The drug is used to treat the same disease as in the prior art, but using a new dosage regime or method of administration – see paragraphs 151-165.

x) "Substance X for use in the treatment of disease Y in patients showing over-expression of receptor Q". The drug has been used to treat the same disease as in the prior art, but the specific patient group is defined – see paragraphs 166-169.

xi) "Substance X for use in the treatment of disease Y by inhibiting the activity of receptor Q". The new use is defined, at least in part, by the mechanism of action by which the disease is treated – see paragraphs 170-176.

xii) "Substance X for use in the treatment of disease Y with reduced immuno-suppression". *The new use is defined, at least in part, by an unexpected advantage such as reduced side-effects – see paragraph 177.*

xiii) "Substance X for use in the treatment of disease Y as measured by an increased time to progression of disease". The new use is defined, at least in part, by the level of efficacy achieved and/or the method used to determine efficacy – see paragraph 178.

xiv) "Substance X for use in the treatment of diseases associated with over-expression of receptor Q." / "Substance X for use in inhibiting activity of receptor Q." *The disease to be treated, or the therapeutic use, is defined in mechanistic rather than clinical terms* – see paragraphs 179-181.

xv) "Substance X for use in the treatment of disease Y by combined, sequential or separate administration with substance N." *The new use relates to the combined use of two or more agents – see paragraphs 182-184.*

xvi) "Substance X for use in the extra-corporeal treatment of blood to treat disease Y." *The new use relates to a treatment performed on blood or tissue outside the body – see paragraphs 185-186.*

xvii) "An inhibitor of receptor Z, for use in the treatment of disease Y". The active agent is defined in functional rather than chemical terms – see paragraphs 188-189.

xviii) "A prosthetic device Z, for use the treatment of disease Y". The "active agent" is a device or piece of apparatus – second medical use claims can only protect the new use of a substance or composition, and so this claim will not be novel if device Z is known – see paragraphs 192-194.

"Swiss-type" and "EPC 2000" claim forms: scope, conflict and added matter

113. It was clearly stated, in both the preparations for the EPC 2000, and the passage of the 2004 Act, that the new provisions were not intended to lead to any change in what is and is not patentable. Nevertheless, Swiss-type and EPC 2000 second medical use claims are different in claim category and this has implications for their scope in relation to infringement. Specifically, Swiss-type claims are "purpose-limited" process claims - both the Patents Court (in Generics v Warner-Lambert¹¹⁰) and the Court of Appeal (in the earlier interim decision of Warner-Lambert v Actavis¹¹¹) have confirmed that Swiss-type claims are process rather than product claims. EPC 2000 format claims, on the other hand, are "purpose-limited" product claims. This means that direct infringement of a Swiss-type claim would constitute an infringement under s.60(1)(b) or (c), whereas direct infringement of an EPC 2000 second medical use claim would constitute an infringement under s.60(1)(a). There are also likely to be differences in the scope of the claims in relation to indirect infringement under s.60(2) - these issues were considered in detail in relation to Swiss-type claims by Arnold J in Generics v Warner-Lambert¹¹⁰, but he emphasised that his conclusions related to Swiss-type claims only – the scope of protection of EPC 2000 second medical use claims has not yet been tested in the court. Such infringement issues fall outside the scope of these Guidelines, and are discussed further in MoPP 60.16.1 and 60.19.2. However, it is clear that the scope of the two forms of claims is not identical; it was suggested in G 02/08¹¹ that the EPC 2000 form is likely to be broader in scope.

- 114. Regardless of the wording or scope of the claim, the technical disclosure (i.e., a new medical use for a substance or composition) is the same, and so where an application is filed with Swiss-type claims, replacement of these claims with the corresponding medical use claims in the new format does not constitute added matter. However, in view of the potentially broader scope of the EPC 2000 form, a request to make a post-grant amendment to replace Swiss-type claims with EPC 2000 form claims is unlikely to succeed - in T 250/05¹¹² it was held that a post-grant amendment from a Swiss-type claim to the EPC 2000 claim form would extend the scope of protection and thus would not be allowable under Art. 123(3) EPC (equivalent to s.76(3) (b)). However, this might be permissible if the granted patent includes a per se (or first medical use) claim to the product in addition to a Swiss-type claim to its use - in this instance the scope of any EPC 2000 second medical use claim would appear to fall wholly within the scope of the per se or first medical use claim.
- 115. The Boards of Appeal in T 1780/12¹¹³ and T 879/12¹¹⁴ highlighted this difference in scope and claim category between Swiss-type and EPC 2000 form second medical use claims. In both cases it was concluded that where a divisional application included the EPC 2000 claim form, and the granted parent claimed the same medical use in the Swiss form, this did not constitute "double-patenting". No objection should therefore be raised under s.18(5) or s.73(2) to conflict between applications including EPC 2000 second medical use claims and granted GB or EP patents which protect the same medical use solely through Swiss-type claims.

Second medical use and Section 4A(1)

116. Second medical use claims to substances or compositions can only derive novelty from their intended use if the use is in a medical method excluded under Section 4A(1).

"It is to be clearly understood that the application of this special approach to the derivation of novelty can only be applied to claims to the use of substances or compositions intended for use in a method referred to in Article 52(4) EPC."

G 05/83 EISAI/Second medical use OJEPO 1985, 64

- 117. This means that the second medical use claim format cannot be used to protect the new use of a known substance in, for example, non-surgical cosmetic or hygiene methods¹⁸, or sterilisation of non-living surfaces or liquids¹⁹ A claim to "substance X for use in cosmetic method Y" is therefore not limited by its intended use, and will not be new if substance X is known. Similarly, a second medical use claim "for the treatment of halitosis" was refused on the grounds that this is not a pathological condition³⁹, and the Hearing Officer in Lalvani et al's Applications¹⁰⁵ considered that "for lactation" and "for bone health maintenance" did not constitute therapeutic uses according to s.4A(1) and so interpreted the claims as being claims to the composition "suitable for" such a use.
- 118. An application may include both claims to the second medical use of a compound for therapeutic purposes, and claims to cosmetic or other patentable methods using the compound, providing the therapeutic and nontherapeutic methods are supported and distinguishable (as in T 584/8828, relating to therapeutic and nontherapeutic treatments for snoring). On the other hand, where any non-therapeutic effects are inseparably linked to (or a consequence of) the therapeutic effects, then (as discussed in paragraph 26) a method claim would be unpatentable under s.4A(1) and so a second medical use claim to a new use which encompasses both effects may be protected under s.4A(4)¹¹⁵.
- 119. As discussed below, second medical use claims may be defined in part by their mode of administration, or the patients to whom they are administered. However, definition in these terms alone (e.g. "for enteral feeding"), without specifying any actual therapy, does not define a new medical use and so in such cases the claim would be construed as a substance or composition "suitable for" such a use¹¹⁶.

- 114 T 879/12 GENENTECH
- 115 T 495/10 K. U. LEUVEN

T 1278/12 N.V. NUTRICIA 116

- 120. Although the Enlarged Board of Appeal referred only to "therapeutic" methods in its decision in G 05/83⁹, second medical use claims may be used to protect the use of a known substance or composition in any method falling within the exclusion of Section 4A(1). For example, in T 655/92⁸⁴, a Swiss-type claim was allowed for the use of a compound, previously used for therapeutic treatment, as a reagent in a diagnostic method performed directly on the human body.
- 121. Second medical use claims are acceptable whether or not the substance is known or has been used in therapy previously. There is no requirement for evidence concerning prior medical use to be included in the specification¹¹⁷.
- 122. If an application includes unpatentable method of treatment claims, such as "the use of X to treat Y", amendment of these claims to convert them into second medical use claims does not constitute added matter. However, in T 1635/09⁴⁶, post grant amendment of a method claim (to contraception) to a second medical use claim was refused on the grounds that it would extend the scope of protection. This situation would only be likely to arise if (as in this case) a granted patent with method claims was held to be excluded under s.4A(1)/Art.53(c) in post-grant proceedings.
- 123. In T 1099/09⁹¹ and T 2003/08⁵² it was held that second medical use claims can only be used to protect the use of a known substance or composition as an active agent. The use of a known substance or composition as an inactive carrier or excipient for a therapeutic agent cannot therefore be protected by a second medical use claim.

Determining novelty and inventiveness of second medical use claims

i) Construction of "for use in treating disease Y"

- 124. The Court of Appeal in *Bristol-Myers Squibb v Baker Norton Pharmaceuticals*¹¹⁸ held that the words "for treating disease Y" should be construed as "suitable for trying to treat disease Y", since the skilled person would realise that drugs which are suitable for treatment will not always have a 100% success rate. However, drugs which are perceived as being suitable for treatment, but actually have no effect, do not fall within the scope of the claim. Furthermore, the therapeutic effect must be discernible¹¹⁹, and it must be more than a mere placebo effect¹²⁰. In *Regeneron Pharmaceuticals v Genentech*¹²¹ the Patents Court followed the view of the EPO Technical Board of Appeal in T 609/02¹²², that "the actual achievement of the therapeutic effect is a functional technical feature of the claim, as opposed to a mere statement of purpose or intention", and it was held that this applied to both Swiss-type and EPC 2000 form claims. This interpretation was endorsed on appeal¹²³. Recent case law has indicated that the criteria for determining whether the therapeutic effect has in fact been achieved may vary depending on the nature of the condition and the disclosure of the specification; in *Eli Lilly v Janssen v Alzheimer Immunotherapy*¹²⁴ it was held (on the facts of the case) that the primary criterion for efficacy was success in a Phase 2 clinical trial, whereas in *Generics v Warner-Lambert*¹¹⁰ it was not limited to treatment of humans.
- 125. Moreover, the "for use" element of a medical use claim has a limitation beyond mere suitability for the treatment in question. In *Hospira v Genentech (2014)*¹²⁵ Birss J held that "for" in a second medical use claim means "suitable and intended for" in other words, second medical use claims have a mental element. The second part of this definition was further refined (in the context of infringement) by the Court of Appeal in *Warner-Lambert v Actavis*¹¹¹ to mean that the manufacturer knows, or can reasonably foresee, that the drug will be intentionally used for the claimed therapeutic purpose this interpretation was applied to the assessment of novelty and inventive step by the Patents Court in *Hospira v Genentech (2015)*¹²⁶.
- 117 T 143/94 MAI/Trigonelline OJEPO 1996, 430

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¹¹⁸ Bristol-Myers Squibb v Baker Norton Pharmaceuticals [2001] RPC 1

¹¹⁹ Teva v Merck [2009] EWHC 2952; [2010] FSR 17

¹²⁰ Pfizer's Patent [2001] FSR 16

¹²¹ Regeneron Pharmaceuticals v Genentech [2012] EWHC 657

¹²² T 609/02 SALK INSTITUTE

¹²³ Regeneron Pharmaceuticals v Genentech [2013] EWCA Civ 93 [2013] RPC 28

¹²⁴ Eli Lilly v Janssen Alzheimer Immunotherapy [2013] EWHC 1731 [2014] RPC 1

¹²⁵ Hospira v Genentech [2014] EWHC 1094

¹²⁶ Hospira v Genentech [2015] EWHC 1796
ii) Novelty

- 126. In light of this construction, what is needed to anticipate a second medical use claim to the use of a substance or composition to treat a specified condition? Clearly, the actual disclosure of the effective clinical treatment of the disorder by the agent in question will anticipate. In addition, experimental data showing that an animal with the condition in question was successfully treated with the specified agent would constitute anticipation, unless the claim was limited to treatment of humans. If the compound in question has been used in the treatment of the specified disease, then this will anticipate the claim even if the treatment was not effective for all patients¹¹⁸. Moreover, the treatment does not need to cure the disease, or treat all aspects of the disease, but it must have some beneficial effect¹²³. The claim would be anticipated by any prior use of the compound to treat the disease in question, even if the only previous use was in association with another compound¹²⁰. However, the previous use of the compound purely as an inactive carrier or excipient for a therapeutic agent does not anticipate a second medical use claim, as held in T 1758/07⁹⁹.
- 127. As second medical use claims are construed as being limited to the **intentional** treatment of the disease, the fact that the prior art use of the substance to treat a different condition may have inherently treated or prevented the claimed disease in some patients does not constitute an anticipation if the prior art does not disclose the new therapeutic use. As the Court of Appeal in *Warner-Lambert v Actavis*¹¹¹ said, in relation to a second medical use claim to the use of a known drug to treat pain:

"The therapeutic treatment is of course new because, and only because, it is carried out with the intention of producing the new therapeutic effect. The prior use of the compound may have in fact produced the effect, for example if a patient taking it for GAD or epilepsy was at the time experiencing pain as well. This demonstrates, to my mind, that it is the intention for which the compound is administered which is at the heart of the invention."

Warner-Lambert v Actavis [2015] EWCA Civ 556; [2015] RPC 24

- 128. As with other fields of technology, there are two requirements for anticipation, prior disclosure and enablement, and the requirements for each must be met. In *SmithKline Beecham's (Paroxetine Methanesulfonate) Patent*¹⁰⁰, Lord Hoffmann summarised the disclosure requirement as follows: "anticipation requires prior disclosure of subject-matter which, when performed, must necessarily infringe the patented invention". For that reason, a research paper that merely discloses experiments which show an activity suggesting the specified use, or disclosing *in vitro* testing for such a use, but does not explicitly or implicitly disclose the actual use would not anticipate a second medical use claim for the specified medical use. However, where there is such a disclosure, it is not always necessary for this to be accompanied by actual clinical evidence of a therapeutic effect to meet the disclosure requirement, at least, for novelty. In T 241/95¹²⁷, it was stated that "a pharmacological effect or any other effect such as a behavioural effect observed either *in vitro* or in animal models is accepted as sufficient evidence of a therapeutic application if for the skilled person this observed effect directly and unambiguously reflects such a therapeutic application". On the other hand, as held by the Patents Court in *Regeneron Pharmaceuticals v Genentech*¹²¹, the disclosure that the agent in question **might** have the claimed therapeutic effect does not enable the skilled person to directly and unambiguously deduce that it will have the claimed effect and so this does not meet the disclosure requirement for anticipation.
- 129. A document which states that the substance is used to treat the particular disease without describing actual clinical data may therefore be cited for novelty such statements are common in patent documents, as discussed in T 1001/01¹²⁸.

"...it is common practice that a patent literature document, in order to be an enabling disclosure of a medical indication for pharmaceutically active compounds ... does not necessarily need to include either clinical tests (Phase I, II or even III) or in vivo human assays."

T 1001/01 SMITHKLINE BEECHAM

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It would then be open to the applicant to challenge whether such a statement constitutes an **enabling** disclosure. In *Merck Sharp & Dohme v Ono*¹²⁹ (a case concerning a second medical use claim to the use of a particular antibody to treat cancer) a prior art patent document included the disclosure of the antibody in question and claims to its use to treat cancer amongst other disorders, together with evidence of an immune-regulatory role *in vitro* and *in vivo*, but without any data or models relating specifically to cancer. It was held that this document met the disclosure requirement for novelty, but not the enablement requirement. The reason was that Birss J considered that **plausibility** is an aspect of enablement of medical use claims – in order to be an enabling disclosure, the prior art has to make the claimed effect plausible, and on the facts of the case he held that it did not. Nevertheless, at first instance at least, a novelty objection should be raised if there is a clear disclosure in a prior art document of the use of the agent to treat the disease in question, unless it is clear to the examiner that the disclosure is not enabling (for example, if the condition is only referred to as part of a long list of diseases with no evidence to make the use plausible).

- 130. The EPO Board of Appeal in T 1031/00¹⁰² rejected both first and second medical use claims on grounds of novelty, where the experimental data provided in the application was considered to be the same as that in a published research paper. It was not argued that the prior art paper explicitly disclosed the invention as claimed, Instead, it was argued that there was no new technical feature provided in the application the only new feature was the assertion of a therapeutic use. While this prior art would appear to meet the test for enablement, it is not clear whether it would have met the test for disclosure as set out in *SmithKline Beecham's (Paroxetine Methanesulfonate) Patent*¹⁰⁰. In such a case, if a novelty objection cannot be made due to a lack of explicit disclosure then the application is likely to fall on grounds of either inventive step or support and/or sufficiency as discussed below in paragraphs 142-143.
- 131. It should be noted that the disclosure that an agent is being evaluated in clinical trials for a condition does not necessarily constitute evidence of therapeutic use¹³⁰. It was pointed out in T 715/03¹³¹ that successful completion of Phase I trials merely demonstrates an acceptable safety profile, and so the mere disclosure that a compound is undergoing Phase II trials does not indicate any therapeutic effect unless results are provided. Phase II trials are intended to investigate efficacy as well as safety, and so in many cases the disclosure that a drug has entered phase III trials may be considered to be implicit disclosure of therapeutic efficacy in phase II trials. However, this is not always the case in *Hospira v Genentech (2015)*¹²⁶, the claimed combination of drugs had not been tested in phase II trials, as both drugs had been shown to be effective individually in treating breast cancer. The disclosure (without providing results) that the combination had entered Phase III trials was therefore not considered novelty-destroying, both in the Patents Court in this case and at the EPO Technical Board of Appeal in T 1859/08¹³². Clearly, however, a disclosure that a drug has entered clinical trials for the specified use is likely to be relevant for inventiveness, and in fact the Patents Court in *Hospira v Genentech (2015)* found that the claim was obvious.

iii) Inventive step

132. As in all fields of technology, when determining inventive step the four step test set out in *Windsurfing International v Tabur Marine*¹³³, as reformulated in *Pozzoli v BDMO*¹³⁴ should be used. The four step approach of *Windsurfing/Pozzoli* is intended to address the concept of inventive step without the benefit of hindsight, by ensuring that the examiner assesses the invention through the eyes of the person skilled in the art, with the benefit of his common general knowledge. The inventive concept of the claim in question is then construed, and the differences between the state of the art and the inventive concept of the claim are identified. This then enables the examiner to approach the final step and ask "is it obvious". Section 3 of MoPP discusses these steps in detail, and therefore each step of this test is not discussed in detail here. Instead this section will focus on the specific issues raised in determining whether there is inventiveness in a claim to a new medical use for a known substance or composition, in light of the construction of such claims as discussed above.

129	Merck Sharp & Dohme v Ono [2015] EWHC 2973
130	T 158/96 PFIZER/Sertraline [1999] EPOR 285
131	T 715/03 PFIZER
132	T 1859/08 GENENTECH
133	Windsurfing International v Tabur Marine [1985] RPC 59
134	Pozzoli v BDMO [2007] EWCA Civ 588

133. Clearly, just as the new medical use can provide novelty to a claim to "substance X for use in treating disease Y", it can also provide inventiveness, as is made explicit in *Teva v Merck*¹¹⁹:

"If the new medicinal purpose is a sufficient distinction to provide for novelty, it must equally be a relevant distinction for the purpose of assessing inventive step."

Teva v Merck [2009] EWHC 2952, [2010] FSR 17

134. Furthermore, it was held in *Teva v AstraZeneca*¹³⁵ that for the new use to be considered inventive, the specification must provide reasons – not previously known or recognised – why the agent is likely to be effective in the new use:

"Where, as here, a patent is sought in relation to a new use of an existing drug or combination of drugs, patent protection will only be justified if the patentee discloses sound reasons, not recognised or known before, for thinking that new use will be effective to seure the object for which it is put forward"

Teva v AstraZeneca [2014] EWHC 2873

In other words, the specification must provide a contribution to the art beyond a mere proposal to treat a new condition. As discussed below in paragraphs 196-209, if the specification does not provide any such "sound reasons", then it is objectionable on grounds of lack of support or sufficiency, and this is likely to be the primary objection in such cases. Nevertheless, the technical contribution of the specification is taken into account in assessing inventiveness of selection inventions as discussed in paragraph 140 below.

135. Very often in the case law relating to new medical uses of known substances or compositions, the final step in the *Windsurfing/Pozzoli*^{133 134} test – assessing whether the invention is obvious – is framed as a question as to whether it would be obvious to try to use the agent for the claimed purpose. As discussed in *MedImmune v Novartis*¹³⁶ (although this case did not relate to medical use claims), in pharmaceuticals and biotechnology there may be many possible avenues to explore with little indication which, if any, will prove fruitful. Nevertheless, particularly given the potential rewards of inventing a successful treatment, they are pursued, and this would plainly not happen if the prospects of success were so low as not to make them worthwhile. But denial of patent protection in all such cases would act as a significant deterrent to research. For this reason, obviousness in these circumstances is only found where it is considered obvious to try with a reasonable or fair expectation of success, and the Court of Appeal gave some general guidance as to how this might be assessed:

"Whether a route has a reasonable or fair prospect of success will depend upon all the circumstances including an ability rationally to predict a successful outcome, how long the project may take, the extent to which the field is unexplored, the complexity or otherwise of any necessary experiments, whether such experiments can be performed by routine means and whether the skilled person will have to make a series of correct decisions along the way."

MedImmune v Novartis [2010 EWCA Civ 1234, [2013] RPC 27

- 136. This approach was endorsed in relation to a second medical use claim by the Court of Appeal in Regeneron Pharmaceuticals v Genentech¹²³, and has been applied by the courts in many decisions since then. In Actavis v Eli Lilly (2015)¹³⁷, it was pointed out that logically the question of whether the new use is obvious to try should be addressed first, and then, if necessary, whether there would be a reasonable expectation of success. On the facts of the case it was decided that it was not obvious to try to use the agent in question for the new use at all, and had it been there would have been no expectation of success. "Success" in second medical use cases means achieving the claimed therapeutic effect - as discussed above in paragraph 124, the criteria by which this would be assessed may vary according to the disclosure in the specification, and so what exactly the skilled person is said to be "trying" may also vary. In some cases, such as Hospira v Genentech (2014)¹²⁵ and Teva v AstraZeneca¹³⁵, the question was whether it would be obvious to undertake a clinical trial with a fair expectation of success, whereas in Generics v Warner-Lambert¹¹⁰ and Merck Sharp & Dohme v Ono¹²⁹ the question was whether it would be obvious to perform specified animal tests with a fair expectation of success. In Hospira v Genentech (2015)¹²⁶, Arnold J considered some of the factors which would determine whether it was obvious to run a clinical trial with a reasonable expectation of success. These included: the level of motivation to find a new or improved treatment for the condition; whether the trial would be of routine design; whether it would be technically difficult (as opposed to merely time-consuming and expensive); what risk to patients it would present; the failure rate in such trials; whether the specification overcame any "lions in the path" that would have deterred the skilled person from carrying out the trial; and how promising the skilled person would consider the prior art disclosure to be in light of the common general knowledge.
- 137. The principle that an invention can only be considered "obvious to try" if there would have been a reasonable expectation of success applies regardless of the extent of experimental evidence supporting the new use. As discussed below (paragraphs 196-209), second medical use claims must be supported by evidence of the likely effectiveness of the claimed treatment, and so in the absence of any such evidence the claim should be objected to as being speculative. However, providing this threshold test is met, the examiner should not apply a different test for obviousness depending on the amount of evidence provided in the specification, or determine the inventive concept on the basis of the supporting evidence rather than the claims. This follows from the decision of the House of Lords in *Conor Medsystems v Angiotech Pharmaceuticals*¹³⁸, which reversed the decision of the Patents Court¹³⁹ and the Court of Appeal¹⁴⁰.
- 138. This case concerned a drug-coated stent, and so was not a first or second medical use claim, but the case is relevant to medical use claims as it related to the choice of pharmaceutical agent used in the device, and the likely efficacy and safety of that drug for a specific therapeutic use. The case revolved around the question of whether it would be "obvious to try" to coat a stent with paclitaxel (Taxol^{RTM}) to prevent restenosis (the proliferation of cells around the stent). The Patents Court¹³⁹ held that the technical contribution disclosed in the application was critical in determining the question to be asked; whether it was merely necessary to show that the substance was an obvious candidate for testing without any expectation of success, or whether it was necessary to show that the skilled person must have had an expectation of success sufficient to induce him to use it in practice. The House of Lords¹³⁸ rejected this distinction:

"But there is in my opinion no reason as a matter of principle why, if a specification passes the threshold test of disclosing enough to make the invention plausible, the question of obviousness should be subject to a different test according to the amount of evidence which the patentee presents to justify a conclusion that his patent will work."

Lord Hoffmann Conor Medsystems v Angiotech Pharmaceuticals [2008] RPC 28

139. In this case there was evidence provided in the application as filed that Taxol^{R™} was a particularly effective antiangiogenic agent, and the invention was based on the principle that inhibition of angiogenesis could be used to prevent restenosis. The House of Lords accepted that the absence of any evidence to support a speculative claim could lead to an objection of lack of support or insufficiency (quoting the decision in *Prendergast's Applications*¹⁰³), but held that this requirement should not be confused with the requirement for inventiveness¹³⁸.

¹³⁸ Conor Medsystems v Angiotech Pharmaceuticals [2008] RPC 28

¹³⁹ Angiotech Pharmaceuticals' Patent [2006] RPC 28

¹⁴⁰ Angiotech Pharmaceuticals v Conor Medsystems [2007] RPC 20

- 140. Moreover, it cannot be argued that a prima facie obvious selection of a particular compound or treatment is rendered inventive by a surprising effect, in the absence of any evidence for or disclosure of that effect in the application as filed. In this respect, we would take a different view from that of the Technical Board of Appeal in T 36/04¹⁴¹. In this case, a second medical use claim relating to the administration of two agents in a specified order was granted on the basis of information obtained after filing showing an unexpected benefit of administration in that sequence, even though the specification as filed gave no hint that the order of administration was of importance. In assessing the inventiveness of any such selection invention, the question to be asked is whether the invention makes a technical contribution or is merely an arbitrary selection. If it is merely an arbitrary selection then the invention is obvious. This reasoning follows the Court of Appeal's decision in Dr Reddy's Laboratories v Eli Lilly¹⁴² and the EPO Board of Appeal decision in T 939/92¹⁴³, and was applied in respect of a second medical use claim in Teva v AstraZeneca¹³⁵.
- 141. The examination of selection inventions is discussed in greater detail in MoPP 3.88-3.93 and the Examination Guidelines for Patent Applications relating to Chemical Inventions in the Intellectual Property Office.
- 142. If the experimental evidence provided in support of the specified use is essentially the same as that provided in the prior art, then the application is likely to fail on grounds of either inventiveness on the one hand or support and/or sufficiency on the other. As discussed above, in Teva v AstraZeneca¹³⁵ the Patents Court held that the specification must provide reasons not previously known or recognised why the agent is likely to be effective in the new use. This is sometimes referred to as an obviousness/insufficiency "squeeze". In Teva v Merck¹¹⁹, Hospira v Genentech (2014)¹²⁵ and Accord Healthcare v Medac¹⁴⁴, the Patents Court held that the claims in guestion were not inventive, but had they been found inventive then they would have been invalid for insufficiency. In Hospira v Genentech (2014), Birss J held that if the evidence in the prior art was not enough to make it obvious for the skilled person to conduct a clinical trial of the claimed dosage regime, then the (very similar) experimental evidence in the patent would not be enough to render the claimed effect plausible and so the skilled person would again not conduct a trial. He also stated as a general principle:

"...the patentee can hardly argue, and the Court or Patent Office is unlikely to accept, that a mere prior proposal is not enough to invalidate the claim if all that is present in the specification of the patent is a mere proposal followed by a use claim."

Hospira v Genentech [2014] 1094

143. However, in Actavis v Eli Lilly (2015)¹³⁷, Carr J held that the standard for "plausibility" in relation to sufficiency was different from, and lower than, the "reasonable expectation of success" test used in the context of obviousness, and so rejected an obviousness/insufficiency squeeze argument and held that the patent in question was valid. In this case, unlike the cases referred to in the previous paragraph, there was no suggestion at all in the prior art that the substance in question might be useful for the claimed purpose i.e. treatment of attention deficit/hyperactivity disorder (ADHD), and so perhaps unsurprisingly it was not considered obvious without the benefit of hindsight. The rationale provided in the patent as to why the agent was likely to be effective to treat ADHD had not previously been recognised, and on the facts of the case it was considered to render the use plausible. In the later decision of Accord Healthcare v Medac¹⁴⁴, the patentee argued that a new dosage regime would not have been obvious because of the skilled person's concern about possible side effects. Birss J held that if this was the case, the patent in suit contained neither experimental evidence nor any reasoning that would suggest that this concern was unwarranted, and this was distinguished from Actavis v Eli Lilly (2015) where the patent did at least include some reasoning. He therefore held that there was indeed a "squeeze" between plausibility for insufficiency and obviousness. The requirements for sufficiency and support are discussed further in paragraphs 196-209.

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- 144. If the agent in question in a second medical use claim has been used to treat a related condition, then this disclosure may form the basis of an inventive step objection. This will obviously have to be dealt with on a case-by-case basis, but some guidance may be derived from the decision of the EPO Board of Appeal in T 913/94¹⁴⁵. The first question to be asked is whether the diseases have a common origin, causative factors or mechanism. If this is the case, then this does not automatically mean that the claim lacks inventiveness. However, if the symptoms of the disease already treated in the prior art are shared with, and are more serious than, the claimed condition, then this strongly suggests that the agent will be effective in the latter case as well.
- 145. In relation to cancer treatments, the Board of Appeal in T 385/07¹⁴⁶ argued that different types of cancer have very different causes and characteristics, and there are no "magic bullets" which successfully treat all cancers. The disclosure that a particular treatment is effective against one or more cancer types would not normally indicate a "reasonable expectation of success" in the treatment of an unrelated form of cancer. Nevertheless, this will need to be assessed on the facts of the case, as there are cancer treatments which exert their effect by targeting a mechanism common to many, if not all cancers one such treatment was at issue in *Merck Sharp & Dohme v Ono*¹²⁹.
- 146. Following the decision of the Court of Appeal in *Actavis v Merck*¹⁴⁷, second medical use claims which are defined by a new dosage regime (where the substance or composition, and the disease treated, are both known in the prior art) are in principle allowable. In this decision, Jacob LJ highlighted the fact that investigating dosage regimes is standard practice in the art, and so only in an unusual case (such as the existence of a technical prejudice pointing away from the claimed dosage regime) would a new dosage regime alone confer inventiveness to a claim.

"...nearly always such dosage regimes will be obvious – it is standard practice to investigate appropriate dosage regimes. Only in an unusual case such as the present (where... treatment for the condition with the substance had ceased to be worth investigating with any dosage regime) could specifying a dosage regime as part of the therapeutic use confer validity on an otherwise invalid claim."

Jacob LJ, Actavis v Merck [2008] RPC 26

In a review of an Office Opinion, the Hearing Officer in *InterMune's Patent*¹⁴⁸ held that the above comments provided useful guidance on determining obviousness, rather than establishing a binding legal principle that there is a general presumption that there must be a clear technical prejudice pointing away from the claimed dosage regime to confer validity on such a claim. Nevertheless, on the facts of the case the Hearing Officer declined to overturn the Opinion that the patent lacked inventive step.

147. In Hospira v Genentech (2014)¹²⁵ the inventiveness of a new dosage schedule for an anti-cancer drug was considered. Birss J rejected the argument that the skilled person would not consider the new schedule, pointing out that the skilled person would be aware that changes to dosage regimes were a routine aspect of the development of existing drug treatments. He also held that there was nothing in the prior art or the common general knowledge to suggest the new dosage regime should not be trialled, and so it would be obvious to run a small clinical trial of the new schedule – on the facts of the case he considered that it would have a reasonable expectation of success. This decision was upheld at the Court of Appeal¹⁴⁹, where it was pointed out that it was not necessary for the skilled person to know the new dosage schedule would work – all that was required was that the prospects of success were sufficiently good to warrant a small clinical trial. Similarly, in *Novartis v Focus*¹⁵⁰ and *Accord Healthcare v Medac*¹⁴⁴, it was considered obvious to conduct trials of the claimed dosage regimes and in both cases the patents were revoked for lack of inventive step. In *Accord Healthcare v Medac*, it was held that the skilled team would include a drug formulator as well as a clinician and it would be obvious to the formulator to investigate dosages to reduce undesirable effects (in this case, injection pain).

 145
 T 913/94 EISAI/Medicament for gastritis [2001] EPOR 362

 146
 T 385/07 PHARMA MAR

 147
 Actavis v Merck [2008] RPC 26

 148
 InterMune's Patent BL O/163/16

 149
 Hospira v Genentech [2015] EWCA Civ 57

150 Novartis v Focus [2015] EWHC 1068

148. The earlier decision of the Hearing Officer in *Advance Biofactures of Curacao's Application*¹⁵¹ illustrates some of the factors which might, exceptionally, lead to a new dosage form being considered both novel and inventive. The active agent was present at substantially higher concentration than the prior art, and it was impossible in practice to deliver the required dose with the prior art solutions. Moreover, the person skilled in the art would have considered this higher concentration to have unacceptable side effects, and the concentrated composition was successful in treating a group of patients who did not benefit from treatment with the prior art compositions.

Second medical use claims - the new use

i) Treatment of a new disease or condition

- 149. The decisions of the EPO Enlarged Board of Appeal in G 05/83⁹ and the Patents Court in *John Wyeth's and Schering's Applications*¹⁰ established that the use of a substance for a "new and inventive therapeutic application" could (prior to G 02/08¹¹ and the release of our <u>Practice Notice</u> on 26 May 2010) be protected by a Swiss-type claim, while Section 4A(4) allows such a use to protected by the direct form of second medical use claim. Typically, second medical use claims are used to protect the use of a substance or composition in the treatment of a specified disease, where it had previously been used for the treatment of a different disease. Providing the use of the substance in the treatment of the specified disease is not known, such claims are considered to be novel.
- 150. It may be more difficult to determine whether a second medical use claim is novel if the new use is the treatment of a specific form of a disease, where the prior art discloses (or appears to disclose) the treatment of a wider class of diseases. Examples considered by the EPO Boards of Appeal include the use for treating pancreatic cancer of an agent known for the treatment of a variety of other cancers¹⁴⁶, adenocarcinoma of the ovary as opposed to ovarian cancer in general¹²⁸, and hormone refractory prostate cancer as opposed to prostate cancer in general¹⁵². As a general principle, a general disclosure of a class does not anticipate a claim to a specific member of that class. Nonetheless, a novelty objection should be made if the prior art disease class appears to encompass the specific disease claimed, and, **either** the specific disease is referred to in the prior art document as being treatable with the substance in question, **or** it may reasonably be implied that the prior art does disclosure for the disease in question in the three cases referred to above, the EPO decided that the specific use was in fact novel. Nevertheless, it should be emphasised that the mere discovery that a treatment is particularly effective in one particular sub-group of disease patients, does not render a claim novel if the substance has clearly been used to treat this sub-group (amongst others) in the prior art.

ii) New method, time, frequency or dosage of administration

151. Second medical use claims which are distinguished from the prior art solely by the dosage regime used, or the mode of administration, are considered to be patentable if the claimed use is both new and inventive, with the proviso that if the claim is considered to be directed at the activity of the doctor rather than the manufacturer, it may be objectionable under Section 4A(1). This follows from the decision of the Court of Appeal in *Actavis v Merck*¹⁴⁷, which led to a significant change in Intellectual Property Office practice in this field.

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152. In this case, the disputed claim was as follows;

The use of [finasteride] for the preparation of a medicament for oral administration useful for the treatment of androgenic alopecia in a person and wherein the dosage amount is about 0.05 to 1.0 mg.

Finasteride was a known drug (used for treating prostate conditions), which had in the past been proposed as a treatment for alopecia, but at a dosage at least 5mg – the only new feature of the claim was thus the reduced dosage. The Court of Appeal held that the claim was valid, as it was novel, inventive and not excluded as a method of treatment by therapy¹⁴⁷. This overturned the decision of the Patents Court¹⁵³ that this claim lacked novelty, and was a method of treatment excluded under Section 4(2) of the Patents Act 1977. These two grounds for invalidity both stemmed from the earlier decision of the Court of Appeal in the *Taxol* case (*Bristol-Myers Squibb v Baker Norton Pharmaceuticals*¹¹⁸), which had governed UK patent practice in relation to dosage regimes and similar second medical use claims prior to the more recent Court of Appeal decision in *Actavis v Merck*¹⁴⁷.

153. The claim in question in Bristol-Myers Squibb v Baker Norton Pharmaceuticals¹¹⁸ had the wording;

"Use of taxol and sufficient medications to prevent severe anaphylactic reactions, for manufacturing a medicamentation for simultaneous, separate, or sequential application for the administration of from 135 mg/m2 up to 175 mg/m2 taxol over a period of about 3 hours or less as a means for treating cancer and simultaneously reducing neutropenia."

The Court of Appeal held that this claim defined an improvement in the method of administering an existing treatment; it did not define a new and inventive therapeutic purpose (Taxol^{R™} was known to treat cancer). In particular, it was noted that all the claimed steps were in fact directed at actions taken by the doctor, tailored to the individual patient, rather than being directed at the manufacturer.

"The claim is an unsuccessful attempt to monopolise a new method of treatment by drafting it along the lines of a Swiss-type claim. When analysed it is directed step-by-step to the treatment. The premedication is chosen by the doctor, and administered prior to the taxol according to the directions of the doctor. The amount of taxol is selected by the doctor as is the time of administration. The actual medicament that is said to be suitable for treatment is produced in the patient under supervision of the medical team. It is not part of a manufacture."

Aldous LJ, Bristol-Myers Squibb v Baker Norton Pharmaceuticals [2001] RPC 1

- 154. Following this decision, the practice of the Intellectual Property Office was to treat second medical use claims which defined the new use in terms of the mode of administration, or the quantity, frequency or timing of dosage, as being unpatentable methods of treatment, disguised by drafting in the second medical use format. Moreover, such claims were also considered to lack novelty over the prior use of the substance to treat the same disease at a different dosage or by a different method of administration.
- **155.** This interpretation of the *Taxol*¹¹⁸ decision was supported by the Patents Court in *Merck's Patents [Alendronate]*¹⁵⁴ (upheld by the Court of Appeal¹⁵⁵). In this case, a Swiss-type claim based on a new dosage regime (a single weekly administration of 70 mg of alendronate as opposed to daily administration of 10mg) was considered to be an unpatentable method of treatment.
- 156. However, the Court of Appeal in *Actavis v Merck*¹⁴⁷ took the view that the *Taxol*¹¹⁸ case provided no clear *ratio decidendi* that a second medical use claim lacks novelty if the only difference between it and the prior art is a new dosage regime. There was therefore no binding precedent to consider in respect of novelty, and the Court concluded that a second medical use claim solely distinguished by a new dosage regime is novel over the use of the substance to treat the same disease at a different dosage. Second medical use claims which define a new dosage regime or mode of administration should therefore be considered novel, even if this is the only new feature of the claim. This does not, of course, mean that such a claim will necessarily be inventive see paragraphs 146-148.
- 153 Actavis v Merck [2007] EWHC 1311
- 154 Merck's Patents [Alendronate] [2003] FSR 498
- 155 Merck's Patents [Alendronate] [2004] FSR 330

157. The Court of Appeal in *Actavis v Merck*¹⁴⁷ accepted that there was a clear *ratio* from the *Taxol*¹¹⁸ case that the claim at issue defined an unpatentable method of treatment. However, the dosage-specific claim of *Actavis v Merck* was considered to be directed at the manufacturer, and so was distinguished from the claim in *Taxol* which defined a series of steps performed by the doctor.

"So Aldous LJ decided the method of treatment point on a very narrow ground indeed. It was that if in essence the claim is merely to a method of treatment it is bad. The claim in the present case is far from that. It is in its essence directed at the manufacturer. The doctor's only involvement will be in prescribing for the treatment of aa the 1mg pill made by an alleged infringer. We do not regard Aldous LJ's ratio as binding in its effect so far as the general case of dosage specific Swiss form claims or so far as this case is concerned."

Jacob LJ, Actavis v Merck [2008] RPC 26

- **158.** In addition to distinguishing the facts of the case from *Taxol*¹¹⁸, the Court of Appeal in *Actavis v Merck*¹⁴⁷ decided (unusually) that it was not in any case bound to follow its own, earlier decision. The reason the Court of Appeal gave for departing from its own precedent was that the *Taxol* decision was inconsistent with the "settled view" of European patent law as interpreted in EPO Board of Appeal decisions.
- **159.** The EPO has historically taken a more liberal view of what constitutes a "new therapeutic use" than the UK courts. For example, claims were accepted in which the prescription regime of the treatment was specified¹⁵⁶ and where the distinguishing feature was mode of administration¹⁵⁷. On the other hand, in T 56/97¹⁵⁸, a Swiss-type claim defined by an amount of thiazide diuretic "with the range of 7-25% by weight of the predetermined diuretic effective dose" was refused as a method of treatment. In this case, the Board noted that the predetermination of the "diuretic-effective dose", and the determination of the dosage for achieving the desired result, required the exercise by the medical practitioner of his professional skill. However, in the later decision T 1020/03¹⁵⁹ it was held that the new therapeutic use may relate to **any** new and inventive use falling within Article 52(4) (equivalent to the now-repealed Section 4(2)). The claim in question was distinguished by the precise timing of an intermittent course of treatment over a period of several weeks, and this decision was followed in subsequent Technical Board of Appeal decisions.
- **160.** As a result of this, the Court of Appeal in *Actavis v Merck*¹⁴⁷ held that the approach taken in T 1020/03¹⁵⁹ represented the "settled view" of the EPO on this issue. This was confirmed by the decision of Enlarged Board of Appeal in G 02/08¹¹; which considered the following specific questions:

1. Where it is already known to use a particular medicament to treat a particular illness, can this known medicament be patented under the provisions of Articles 53(c) and 54(5) EPC 2000 for use in a different, new and inventive treatment by therapy of the same illness?

2. If the answer to question 1 is yes, is such patenting also possible where the only novel feature of the treatment is a new and inventive dosage regime?

- 3. Are any special considerations applicable when interpreting and applying Articles 53(c) and 54(5) EPC 2000?
- 161. The Enlarged Board's decision on the third question is discussed above (see paragraph 106). In answer to the first two questions, the Board decided that a medicament could be protected under Art. 54(5) EPC for use in a different method of treating the same disease as the prior art, and this could include uses where the dosage regime is the only new feature.

157 T 51/93 SERONO

¹⁵⁸ T 56/97 TAKEDA

¹⁵⁹ T 1020/03 GENENTECH/Method of administration of IGF-I OJEPO 2007, 204

"Thus, the new use within the meaning of Article 54(5) EPC need not be the treatment of another disease."

G 02/08 ABBOTT RESPIRATORY/Dosage regime [2010] 10 OJEPO 456

- 162. In view of the decisions in Actavis v Merck¹⁴⁷ and G 02/08¹¹, second medical use claims defined by a new dosage forms, or new modes of administration (for example, intramuscular as opposed to intravenous injection) should therefore not be objected to under Section 4A(1) as being an unpatentable method of treatment. It was pointed out in Actavis v Merck that manufacturers have to provide detailed information relating to uses and dosages with their medicines, and so such a claim can fairly be said to be directed at the manufacturer, rather than the doctor. Moreover, a new dosage regime may necessarily result in the use of a wholly different composition, for example, where the active agent is present at a different concentration compared with the prior art¹⁵¹.
- 163. The Court of Appeal in Actavis v Merck¹⁴⁷ took care to identify the narrow ratio in the Taxol¹¹⁸ case and distinguish the claim in question (and typical dosage regime claims in general) from it, and so it is not clear that the Court considered that the ratio in Taxol was no longer relevant. However, since the decisions in Actavis v Merck¹⁴⁷ and G 02/08¹¹ were issued in 2010, no subsequent decisions of the UK Courts have suggested that either form of second medical use claim can be construed as defining an unpatentable method of treatment by therapy further UK court cases relating to new dosage regimes are discussed in paragraph 147. Moreover, in discussing the infringement scope of Swiss-type second medical use claims, Arnold J in Generics v Warner-Lambert¹¹⁰ held (at 683) that the invention defined in Swiss-type claims is, by definition, a process of manufacture (limited to the intended use) rather than a method of treatment. The infringement scope of EPC 2000 second medical use claims has not yet been tested, but as it is accepted that they are "purpose-limited" product claims rather than method claims it would appear less likely still that they could be construed as defining unpatentable methods.
- 164. However, objection may be raised if the claimed use includes a surgical, therapeutic or *in vivo* diagnostic step which is not in fact directly connected to the administration of the agent in question. In T 566/07¹⁶⁰, the Technical Board of Appeal rejected a claim to the use of a dye "for staining a retinal membrane … in a method for performing retinal membrane removal" on the grounds that the claimed use of the dye solely related to staining the retina, and not to the surgical removal of the retina. This was considered to be an entirely separate surgical method step (even though it was worded as part of the second medical use) and so the claim was rejected under Art. 53(c) as defining a method of treatment by surgery. Similarly, in T 1075/09¹⁶¹ a second medical use claim to a new use of LH (luteinising hormone) which included the words "and wherein folliculogenesis is induced by the administration of FSH [follicle stimulating hormone]" was considered to define both a second medical use for LH and a method step of administering FSH, and so included an unpatentable method of treatment. This objection was overcome by amending the claim to define a new use of FSH and LH, with defined steps of administering each hormone.
- 165. Notwithstanding the settled view of the EPO that a new use can relate to a new method of administering the same agent to treat the same disease, the Technical Board of Appeal in T 174/07¹⁶² held that a negative feature of the method of administration (that the substance be administered and nature left to take its course) did not provide novelty over prior art in which further steps were taken following administration.

iii) New patient group

- 166. A second medical use claim may, in limited circumstances, rely for novelty and inventive step solely on the type of patient to be treated, despite the fact that the active agent and disease treated have already been associated in the prior art. This type of claim was first considered in T 19/86². It was held that the use of a known vaccine for preventing a known disease constituted a second medical use which could be protected by a Swiss-type claim when the type of animal treated (sero-positive pigs) was different from that previously treated in the art (sero-negative pigs). Similarly, in T 893/90¹⁶³, the use of a composition to treat bleeding in non-haemophiliac humans was not anticipated by its use in treating bleeding in haemophiliac patients.
- 160 T 566/07 MELLES
- 161 T 1075/09 LABORATOIRES SERONO
- 162 T 174/07 GENVEC
- 163 T 893/90 QUEEN'S UNIVERSITY KINGSTON

- 167. The Technical Board of Appeal in T 233/96¹⁶⁴ set out a number of conditions for this type of second medical use claim. Firstly, the new patient group must be clearly distinct from the subjects treated in the prior art, and the two groups must not overlap. Secondly, the distinction must not be arbitrary, but must be based on a functional relationship between the physiological or pathological characteristics of the new group and the therapeutic effect. In T 108/09¹⁶⁵, the Technical Board of Appeal considered whether the feature that a cancer patient had been previously treated unsuccessfully with another agent could provide novelty. The Board noted that the development of resistance to anti-cancer agents leads to physiological changes in the tumour, and so the post-treatment patients would have a different pathology to the pre-treatment patients, and this was a genuine difference in the new patient group. The Board distinguished this from a mere presentation of information about the medical history of the patient. This implies that a feature of the patient group with no physiological or pathological relevance (for example, the mere fact that the patients have been previously been the subject of a genetic test) could not form the basis of a valid patient group selection. If, for example, "for use in treating cancer in patients with genotype ABC" does not confer novely because patients with that genotype (amongst others) have already been treated with the same agent, then a claim to the use of the agent "for use in treating cancer in patients with a positive result in a test for genotype ABC" would also not be novel.
- 168. Notwithstanding the earlier decision in T 233/96¹⁶⁴, the EPO have held that the new patient group can overlap with, or be a subset of, the patients treated in the prior art. In T 1399/04¹⁶⁶ a known treatment for hepatitis C virus (HCV) was used to treat patients infected with a high titre of the HCV-1 subtype. This claim was considered new and inventive, despite the fact that over half of HCV-infected patients fell within this category. UK Office practice is that a second medical use claim to an agent for use in the treatment of a disease in a specific patient group is not new if the agent has already been used to treat the same group of patients amongst others, with the same disease. Insofar as this may depart from EPO practice, this is based on the decision of the Patents Court in the Taxol case (Bristol-Myers Squibb v Baker Norton Pharmaceuticals¹⁶⁷), that a new piece of information about an advantage, or how a treatment worked, did not constitute an invention if it did not lead to a new use. This aspect of the decision was upheld at appeal¹¹⁸ and was not challenged in Actavis v Merck¹⁴⁷. The discovery that the treatment works particularly well for a group of patients does not therefore render such a claim novel if that same group of patients has already in fact been treated for the disease with the same agent. This is merely the discovery of an advantageous property of a known treatment. Nonetheless, a general disclosure that an agent may be used to treat a disease does not necessarily anticipate a specific claim to the treatment of a subgroup of patients with the disease, unless it can be shown that treatment of this subgroup is explicitly or inherently disclosed in the prior art (see paragraph 150).
- 169. A related aspect to patient groups is a claim distinguished by the clinical circumstances in which the drug is administered. In *Teva v AstraZeneca*¹³⁵ the use of an inhaled preparation to treat asthma in both regular maintenance therapy and "rescue" therapy for treating acute attacks was considered novel (but not inventive) over the previous use of the preparation in maintenance therapy only. Second medical use claims may therefore also be used to protect treatment of patients in a new and inventive clinical situation.

iv) New mechanism or technical effect

- 170. Second medical use claims which relate to the same therapeutic purpose as the prior art, but are solely distinguished by claiming a different technical effect or mechanism of action, should be rejected as lacking novelty; how a treatment works is irrelevant.
- 171. This question was considered by the Patents Court in the *Taxol* case (*Bristol-Myers Squibb v Baker Norton Pharmaceuticals*¹⁶⁷). It was held that a new piece of information about how a treatment worked did not constitute an invention if it did not lead to a new use; this aspect of the decision was upheld by the Court of Appeal¹¹⁸.

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"All you have is more information about the old use. In due course no doubt more information about the exact mode of action of Taxol will emerge. No-one could obtain a patent for its use simply by adding "for" at the end of the claim and then adding the newly discovered details of the exact mode of action."

Jacob J, Bristol-Myers Squibb v Baker Norton Pharmaceuticals [1999] RPC 253

This decision was followed by the Patents Court in *El-Tawil's Application*¹⁶⁸, where a claim was considered to relate to a combination of newly discovered technical effects, and newly discovered advantages of a known treatment, neither of which conferred novelty. Furthermore in *Actavis v Janssen Pharmaceutica*¹⁶⁹ the Patents Court held that a second medical use claim relating to the use of a substance for "potentiating the effects of [other] blood pressure reducing agents" was not novel because the agent had already been disclosed for use in treating hypertension in combination with other agents as defined in the claim, and the "potentiation" would have occurred inherently in the prior art use – this was merely more information about the mechanism of action of a known treatment.

- 172. These decisions contrast with the decision in T 290/86³⁸ that a second medical use claim can derive novelty from a new technical effect (in this case, strengthening of tooth enamel as opposed to removal of plaque), even where the condition to be treated and the agent are the same. This was based on the decision of the Enlarged Board of Appeal in G 02/88¹⁷⁰, which held that a claim to the use of a known substance to achieve a new technical effect is novel if the technical effect has not previously been disclosed, even if it may have inherently taken place in a prior art method. The UK courts have interpreted G 02/88 narrowly, such that a use claim based on a newly discovered technical effect can only be considered novel if it leads to a new use which is clearly different from the old use. The Patents Court in *Taxol*¹⁶⁷ and in *Actavis v Janssen Pharmaceutica*¹⁶⁹ considered both G 02/88 and T 290/86 and declined to follow the Technical Board's approach in the latter case. Similarly, in a non-medical case, *Tate & Lyle Technology v Roquette Frères*¹⁷¹ (upheld at appeal, though this was solely concerned with the construction of the claim¹⁷²), a claim to "the use of maltotriitol to modify or control the form of maltitol crystals", was held to lack novelty over a number of prior art documents which disclosed crystallisation of maltitol in the presence of maltotriitol at levels at which it would control crystal formation, even though this effect was not recognised (see MoPP 2.14-2.14.1). Our practice based on this case law is therefore that a newly-discovered technical effect cannot on its own confer novelty to a second medical use claim.
- 173. Notwithstanding the decision in T 290/86³⁸, there are a number of EPO Board of Appeal decisions which establish that merely specifying a new mechanism of action is not enough to provide novelty if it does not lead to a genuinely new therapeutic use. In T 254/93¹⁷³ the EPO Technical Board of Appeal held that a newly discovered mechanism (in this case, how a dermatological composition with reduced side-effects achieved this effect) could not confer novelty; the claimed "technical effect" related merely to an explanation of the mechanism behind the treatment.

"The Board considers that the mere explanation of an effect obtained when using a compound in a known composition...cannot confer novelty on a known process if the skilled person was already aware of the occurrence of the desired effect when applying the known process"

T 254/93 ORTHO PHARMACEUTICAL/Prevention of skin atrophy OJEPO 1998, 285

- 174. This was reinforced by the EPO Board of Appeal in T 486/01¹⁷⁴, which held that the discovery of an additional mechanism of action of the protein IGF-1 in treating neurological diseases did not give rise to any new use over the prior art.
- 168 El-Tawil's Application [2012] EWHC 185
- 169 Actavis v Janssen Pharmaceutica [2008] FSR 35
- 170 G 02/88 MOBIL/Friction reducing additive III OJEPO 1990, 93
- 171 Tate & Lyle Technology v Roquette Frères [2010] FSR 1
- 172 Tate & Lyle Technology v Roquette Frères [2010] EWCA Civ 1049
- 173 T 254/93 ORTHO PHARMACEUTICAL/Prevention of skin atrophy OJEPO 1998, 285
- 174 T 486/01 GENENTECH

"For a medicinal application to be construed as a 'further medical use' this new technical effect would have to lead to a truly new therapeutic application, such as the healing of a different pathology or the treatment of the same disease with the same compound, however, when carried out on a new group of subjects distinguishable from the previously suggested subjects for such treatment..."

T 486/01 GENENTECH

Similarly, in T 406/06¹⁷⁵, the "stimulation of beta cell proliferation" was considered to merely an explanation of the known anti-diabetic effects of GLP-1.

- 175. However, in other EPO decisions, claims defining the use of an agent to treat the same disease as the prior art but defined in terms of a specific effect have been allowed. For example, in T 509/04¹⁷⁶, a claim relating to the use of botulinum toxin to promote normal muscle growth in juvenile cerebral palsy patients was held to be novel over the previous successful use of the toxin to treat the same disease, in the same patient group. The prior art document did not suggest any activity in promoting muscle growth - it was instead known to act as a muscle relaxant - but the Opposition Division considered that the muscle promotion activity was inherent in the prior art treatment. Nonetheless, the claim was considered to be both new and inventive on the basis that the claimed technical effect (promoting muscle growth) was not disclosed or suggested in the prior art. In T 836/01¹⁷⁷, the use of a medicament to directly restrict the growth of tumour cells was held to be novel over its previous use in immunotherapy for cancer. In a similar case, the use of an agent to treat cancer by restricting the growth of new blood vessels was held to be novel over its previous use as a direct anti-tumour effect¹⁷⁸, and a treatment of bacterial infection by killing the bacteria as opposed to merely neutralising their toxins was also allowed¹⁷⁹. In these latter three cases it was held that the new technical effect either led to a different category of patients who would be suitable for treatment, and/or a treatment of a different clinical situation. As discussed above in paragraphs 166-169, claims defined by a new and inventive patient group or the administration to patients in different clinical circumstances can be allowed in situations where this is not encompassed by the prior art treatment. A newly-discovered technical effect may therefore lead to a new and inventive claim defined in part by the patient group, the clinical circumstances, the dosage or some other feature of the treatment which is clearly distinguishable from the prior art.
- 176. In *G W Pharma's Application*¹⁸⁰, a claim solely distinguished on mechanistic grounds from the prior art was refused by the Hearing Officer under s.1(2) as being a discovery, rather than on grounds of novelty, and the non-medical use claim in *Tate & Lyle Technology v Roquette Frères*¹⁷¹ was also held to be a discovery in addition to lacking novelty. However, recent case law has confirmed that EPC 2000 second medical use claims (which are now the only allowable form) are construed as products, limited by their purpose, and so this objection should not be raised to claims in this format if the only new feature is the discovery of the mechanism then the claim should be objected as lacking novelty and any objection under s.1(2) would in any case be superfluous.

v) New advantage to known use

177. The discovery of an unexpected advantage in a known treatment does not constitute a new therapeutic use, although it may form the basis of such a use. In the *Taxol*^{118 167} case, the claim was based partly on the unexpected discovery that a shorter infusion time for a chemotherapeutic agent led to a lessening of the harmful reduction in white blood cells (neutropenia). However, the shorter infusion time had already been disclosed - this was merely an additional piece of information about a known treatment.

"...there is a big difference between new information that a prior proposal previously thought unworkable in fact works and new information to the effect that a prior proposal has an additional advantage."

Jacob J, Bristol-Myers Squibb v Baker Norton Pharmaceuticals [1999] RPC 253

Similarly, the identification of symptoms which are alleviated by a known treatment does not in itself confer novelty¹⁶⁸.

vi) Level of efficacy of treatment

178. In general, a claim solely distinguished by an improved level of efficacy over an existing treatment would not be regarded as a new therapeutic application, and may also lack clarity as being defined by desired result. For example the "hastened onset" of pain relief was not considered to be a new medical use when the substance in question was already known as an analgesic¹⁸¹. However, in Hospira v Genentech (2015)¹²⁶, the patent in dispute claimed the use of an antibody to treat breast cancer in combination with a taxoid (a class of anticancer compound) "to provide clinical benefit as measured by increased time to disease progression". "Time to progression" (TTP) is one of a number of measures of the efficacy of anti-cancer treatments. On the facts of the case, Arnold J held that this meant that the claim required that the treatment be capable of providing increased TTP compared to treatment with a taxoid alone, although in the event this feature was not critical for the establishment of novelty as it could not be established that this combination of drugs had been used to treat cancer in the prior art, and the patent was revoked on inventive step grounds. It was accepted that an actual measurement of TTP may not be needed if the increased TTP could be inferred from another measurement consistent with the finding in T 669/01¹⁸² that "a different test for the same medical condition cannot render a known process or use novel". It was also accepted that the claim did not require any specific level of increase. Nevertheless, in this case the achievement of a defined level of therapeutic efficacy was considered to be a functional technical feature of the claim. Of course, if a claim defines a certain level of efficacy and the prior art discloses actual treatment with the same agent for the same purpose in the same way, it would be reasonable to infer that the efficacy would be comparable in the absence of any contradictory evidence.

vii) Functional definition of the new medical use

179. Section 4A(4) allows the protection of a **specific** new and inventive therapeutic application of a substance or composition. The scope of the claimed use must be clear to the person skilled in the art. In cases where the disease or diseases to be treated are clearly defined in the claim, then this requirement is met. However, this may not be the case where the use is only defined in mechanistic terms; and so if the examiner is in any doubt that the skilled person would know what the claimed use means in terms of the treatment of specific conditions then an objection of lack of clarity should be raised. It is then for the applicant to show that the skilled person would be able to determine the scope of the claim without an undue burden of research. As held in T 241/95¹²⁷, a second medical use claim in which the new use is defined in functional terms can only be regarded as clear if means (in the form of experimental tests or other testable criteria) for assessing whether or not a condition falls within the scope of the claim are available to the skilled person from the specification or the common general knowledge. In this decision the Board of Appeal rejected on grounds of clarity a Swiss-type claim for the use of a compound in the treatment of "a condition which can be improved or prevented by selective occupation of the 5-HT_{ic} receptor".

"...the selective occupation' of a receptor, although being indisputably a pharmacological effect, cannot in itself be considered a therapeutic application. The discovery on which an invention is based, even if representing an important piece of scientific knowledge, still needs to find a practical application in the form of a defined, real treatment of any pathological condition in order to make a technical contribution to the art and be considered an invention eligible for patent protection."

T 241/95 ELI LILLY/Serotonin receptor OJEPO 2001, 103

Similarly, in *G W Pharma's Application*¹⁸⁰, it was held that the application did not teach how to determine whether or not a cancer fell within the mechanistic definition used in this application. Definitions of therapeutic uses based on molecular activities (such as inhibition of the activity of a receptor, as in T 241/95) may be particularly problematic from a clarity point of view. Although it may be relatively straightforward to determine whether an agent binds or inhibits a receptor, it is likely to be much more complex to definitively determine the role of the receptor in a given pathology.

180. Nevertheless, functional or mechanistic definitions of the therapeutic use are not necessarily unclear. In *Regeneron Pharmaceuticals v Genentech*¹²¹ the Patents Court considered whether a claimed use for the treatment of "a non-neoplastic disease or disorder characterised by undesirable excessive neovascularisation" was so ambiguous and unclear as to be insufficient. Floyd J rejected this allegation:

"There was no evidence that the skilled addressee would have any difficulty in determining whether a given disease would fall within the terms of the claim as I have construed them."

Floyd J, Regeneron Pharmaceuticals v Genentech [2012] EWHC 657

Although (being a post-grant revocation case) Floyd J was addressing sufficiency (s.14(3)) rather than clarity (s.14(5)(b)), this decision (upheld at appeal¹²³) does show that mechanistically-defined uses are not considered to be inherently so unclear as to be insufficient by the UK courts.

181. In addition to considering clarity, the examiner should also consider whether a functional or mechanistic definition is merely the identification of a mechanism or additional advantage of a known treatment (see above, paragraphs 170-177). A novelty objection should be raised if the functional definition includes diseases which have already been treated by the drug in question in the prior art. A common mechanistic feature, if new and inventive, may nevertheless provide the common subject matter between second medical use claims for different diseases (see below, paragraph 191).

viii) Use in association with another agent

- 182. Second medical use claims to the use of a composition comprising two or more agents together for the treatment of a disease are allowable providing the combination has not previously been used for the specified purpose. The inventiveness of claims of this type needs to be scrutinised carefully, to determine whether the claim represents a mere collocation of known elements see paragraphs 227-230 below. A claim to the use of an agent for the manufacture of a medicament to reduce the side effects¹⁷³, or to potentiate the effects¹⁶⁹, of another agent in the treatment of a disease will not be considered novel if the two agents have been used together before for the treatment of that disease and these effects can be inferred. It is irrelevant whether the prior art discloses the specific effect that the agent has this is merely the discovery of an additional advantage to a known treatment. For example, in *Actavis v Janssen Pharmaceutica*¹⁶⁹, the use of one stereoisomer to potentiate the blood-pressure reducing effects of other agents including one of the other stereoisomers was held to be anticipated by the use of a racemic mixture of the isomers for the treatment of hypertension. The fact that the synergistic effect of the isomers was not recognised in the prior art did not render the claim novel.
- 183. The absence of a synergistic effect between the two agents is likely to lead to an inventiveness objection, but providing some efficacy in the claimed treatment is shown then a lack of synergistic effect does not give rise to an objection on grounds of sufficiency or support¹⁸³. However, if as in T 677/11¹⁸⁴ the claim actually defines the synergistic effect as an essential feature, then the absence of any evidence in the application showing such synergy could lead to such an objection.
- 184. In T 1075/09¹⁶¹, a claim relating to the combined use of two hormones was worded in such a way that it was construed as being a second medical use claim to one, and a method of treatment claim to the other, as discussed above in paragraph 164. The wording of claims relating to combined treatments therefore needs to be checked to ensure that they do not define a method of treatment by therapy, separate from the definition of the new use.

ix) Use in treatments performed outside the body

- 185. As discussed in paragraph 41, therapeutic treatments such as dialysis where blood or tissue is treated outside of the body and returned to the patient are considered to be methods of treatment by therapy and so are unpatentable under s.4A(1). It therefore follows that an invention relating to the use of a known substance or composition for such an *ex vivo* treatment method could be protected using a second medical use claim. This practice accords with the decision of the EPO in T 2003/08⁵², where a second medical use claim to the use of an agent for the treatment of a condition by removing immunoglobulins from plasma *ex vivo* before reinfusing the blood was allowed. This reversed the EPO practice established in T 138/02¹⁸⁵, where it was held that Swiss-type claims could only protect the use of the substance or compound as a "medicament" (based on the wording of the decision in G 05/83⁹), and it was an essential feature of a medicament that it was administered to the body. (NB s.4A(4) make no reference to "medicaments", and so the reasoning in T 138/02 would not in any case appear to apply to EPC 2000 claims.) In view of T 2003/08, and the UK case law^{4 50} which establishes that such methods are excluded under s.4A(1), we would allow second medical use claims for new and inventive uses of substances in *ex vivo* treatments.
- 186. As discussed in paragraph 41, this applies only to treatments where the blood or tissue is returned to the patient treatment of stored blood is not regarded as therapy and so could not be protected by a second medical use claim.

Second medical use claims - the substance or composition

- 187. In determining the scope of the claimed substance or composition in a medical use claim, the established principles of claim construction (as set out in MoPP 2.11-2.17, 14.111-14.120 and 125.01 - 125.24) should be be followed. The Court of Appeal applied these principles to a second medical use claim in American Home Products v Novartis¹⁸⁶, concerning Swiss-type claims for the use of a known antibiotic (rapamycin) for inhibiting organ or tissue transplant rejection. The Court of Appeal held that the claim did not cover derivatives of rapamycin - thus finding the claim not infringed by the use of a rapamycin derivative as an immunosuppressant. On the other hand, in Regeneron v Genentech¹²¹ (upheld at appeal¹²³), it was held, on interpreting the claims in light of the description, that the term "isolated hVEGF receptor" included fragments and variants of the naturallyoccurring receptor which were capable of binding hVEGF and inhibiting its activity. In American Home Products v Novartis also it was held that the presence of the compound in question as an impurity in a medicament does not fall within the scope of a second medical use claim. In Actavis v Eli Lilly (2014)¹⁸⁷ the Patent's Court applied the "Protocol" questions to determine the scope of a second medical use claim to the use of "pemetrexed disodium" and concluded that it could not extend to other salts or the acid of pemetrexed, even though the choice of counter-ion made no difference physiologically. The Court of Appeal¹⁸⁸ agreed on this point, but held that the claim did encompass a solution comprising at least twice as many sodium ions as pemetrexed ions. This decision has been appealed further to the Supreme Court.
- 188. Claims are often made for the second medical use of a group of compounds defined functionally; for example, antagonists of a particular receptor. This type of claim was at issue in *Pfizer's Patent*¹²⁰, which included claims to the second medical use of phosphodiesterase inhibitors. Such claims are not inherently objectionable, and in this case there was no suggestion that this form of claim was unduly broad and speculative. However, the support for such claims must be considered this is considered further in paragraphs 196-209 below. Clearly, the mere fact that a member of a functional class of compounds can be used to treat a disease does not mean that all such compounds will, particularly if there is no evidence that the treatment is related to that specific activity. It was established in *Pfizer's Patent*¹²⁰ that a second medical use claim relating to, for example, the use of an inhibitor of A for the treatment of disease X, is anticipated by any disclosure of the use in treating disease X of a compound which is capable of inhibiting A, regardless of whether the treatment is explicitly stated as being caused by the inhibition of A.

- 189. Claims of this type may give particular problems when searching. It is not feasible or economic for the examiner to identify all such agents and searching should be directed to the specific examples of the agents given in the application since finding these would produce the most relevant citations. In addition, keywords based on the functional class defined in the claim should be searched. An appropriate comment should be added to the search letter to indicate the extent to which the invention has been searched.
- 190. A prior art citation showing the use of a substance produced by a chemical reaction from the compound in question does not anticipate a second medical use claim (though it may be relevant for inventiveness). This question was particularly relevant to Swiss-type claims: the wording of Swiss-type claims (but not the new form of second medical use claims) could suggest that they encompass derivatives produced from the substance in question. The Court of Appeal in Monsanto v Merck¹⁸⁹ considered whether a claim to "the use of compound X in the manufacture of a medicament for the treatment of disease Y" encompassed the use of X as a chemical intermediate in the production of the active agent in the medicament. It was held that it was at least arguable that it could, although it did not come to a final conclusion on the matter. However, the Court of Appeal in American Home Products v Novartis¹⁸⁶ decided that if this was the case this would require a wide construction of the term "medicament" in the claim (that is, to mean a medicament not restricted to one comprising compound X), and this would leave the claim hopelessly broad. This question was also addressed in relation to infringement in Ranbaxy v AstraZeneca¹⁹⁰. In this instance the Patents Court also held that a Swiss-type claim would be construed as being restricted to the use of the substance as a medicament, rather than as an intermediate in the production of a medicament, though Kitchin J emphasised that he had interpreted with reference to the description in this patent, rather than providing an absolute rule of construction of Swiss claims. The patent in guestion included both Swiss-type medical use claims and second medical use claims in the form "Substance X for use in the treatment of disease Y". It was accepted by all parties that the latter claim clearly does not encompass any derivative produced from substance X, and so this ambiguity does not arise with the new format of second medical use claim. As we no longer allow Swiss-type claims, this issue of construction no longer arises in pre-grant patent applications at the Office.

Plurality

191. Where the substance is known to have a medical use, second medical use claims directed to a variety of different diseases may give rise to a plurality objection. A plurality objection may be avoided if the conditions are related (and unrelated to the known conditions), or if there is a common mechanism linking the treatments (see paragraph 181).

Second medical use, apparatus and devices

192. Second medical use claims, like first medical use claims, can only be used in relation to substances or compositions. Claims to a new use of surgical apparatus framed in the Swiss format were disallowed by the EPO in T 775/97⁸⁹ and T 227/91⁸⁸, and by the Hearing Officer in *National Research & Development Corporation's Application*⁸⁷. Similarly, a purpose-limited product (EPC 2000) claim to a known device "for use in" a method of treating substance addiction was held to lack novelty over the previous disclosure of the device used for a different purpose in T 2369/10⁹², and claims in both forms to the new use of a known implanted device for preventing incontinence were refused in T 1099/09⁹¹.

- 193. On the other hand, the EPO have allowed Swiss-type claims to the use of a substance in the manufacture of a "device" for intrapulmonary administration¹⁹¹ and the use a substance in the manufacture of a "column" for removing immunoglobulins from the blood *ex vivo* before re-infusing the blood to the patient⁵². The Swiss-type format used in these claims is no longer allowable, but these decisions raise the question of whether a second medical use claims to the use of a known substance or composition can be defined in part by the device or apparatus used to deliver the agent to the body (or to the bodily fluids as in T 2003/08⁵²). As discussed above at paragraphs 151-165, second medical use claims may be distinguished from the prior art by the method used to administer the agent, and so in principle this may extend to the delivery device used. However, as discussed in paragraph 119, the decision in T 1278/12¹¹⁶ established that second medical use claims cannot be defined solely in terms of method of administration they must define an actual therapeutic use. The claim at issue in T 138/95¹⁹¹, which defined the use as being simply "intrapulmonary administration" by a particular device, would not seem to meet this criterion. Moreover, in general where a drug is known to be used in therapy by administration through a particular route (e.g. intra-pulmonary or intravenous) then the selection of a known device for administration of agents by that route would not be considered inventive in the absence of any strong reasons pointing away from its use.
- 194. In addition, in both T 1099/09⁹¹ and T 2003/08⁵² it was held that second medical use claims can only be used to protect the use of a known substance or composition as an active agent. In the former case, Swiss-type second medical use claims to the use of a "biocompatible material" in the manufacture of a device were refused as the therapeutic effect of treating incontinence did not result from the nature of the "biocompatible material"; instead it depended on the shape and dimensions of the implant. This indicates that a new method of using a known medical device cannot be protected merely by defining it as "material X for use in a method of treating disease Y by means of [device Z]", wherein the material is not itself pharmacologically active and is merely a constituent of the device.

Second medical use claims: sufficiency, support, priority and industrial application

195. There is now a considerable body of case law (from the UK Courts, EPO Boards of Appeal and IPO Hearing Officers) concerning the related questions of sufficiency (under s.14(3)/Art.83 EPC) and support for the claims (s.14(5)(c)) for inventions relating to second medical uses, as discussed below. There is also case law concerning the requirements for entitlement to priority under s.5. In *Biogen v Medeva*¹⁹² (which did not concern medical use claims) Lord Hoffmann said that the requirements for sufficiency in s.14(3), for support in s.14(5)(b) and for entitlement to priority under s.5(2)(a) all related to the requirement for an enabling disclosure, and so case law in relation to sufficiency is persuasive (where relevant) on questions of support or entitlement to priority and vice versa. Lack of sufficiency – but not lack of support – is a grounds for revocation under s.72(1)(c), and so all of the post-grant case law in this area relates to sufficiency. In rare instances, an insufficient application relating to medical uses may also be considered to lack industrial applicability under s.4 as discussed below.

i) Sufficiency

- 196. As with inventions in all fields of technology, the application must disclose the invention in a manner which is clear enough and complete enough to be performed by the person skilled in the art. As discussed at greater length in MoPP 14.58-14.104, there are three types of insufficiency objection that have been established in the case law: "classical" insufficiency, insufficiency by excessive claim breadth and insufficiency by ambiguity, and there is case law relating to second medical use inventions for all of these objections.
- 197. "Classical" insufficiency relates to a lack of a disclosure which would enable the skilled person to perform the invention without exercising inventiveness or an undue burden of research. In the case of invention relating to the medical use of a known substance or composition, the agent in question can generally be produced and formulated in a composition suitable for administration to the patient without undue burden or inventiveness. However, this is not the end of the story, as the UK Courts have followed the EPO Technical Board of Appeal's decision in T 609/02¹²² in holding that the claimed medical use is a "functional technical feature" of the claim. This means, firstly, that if the agent is not effective for the treatment of the disease, then the application or patent is insufficient. In *Eli Lilly v Janssen Alzheimer Immunotherapy*¹²⁴, evidence obtained after the filing date (the failure of subsequent clinical trials) was held to show that the teaching of the patent was insufficient.

198. Moreover, the Board of Appeal in T 609/02¹²² held that the specification must disclose the suitability of the agent for the claimed therapeutic application. Absolute proof of efficacy, or clinical trials, was not necessary, but a simple assertion was not enough. *In vitro* tests could suffice if the skilled person would know from the prior art, or the specification demonstrates, that the *in vitro* effect shown has a direct bearing on the disease in question. In T 1685/10¹⁹³ it was held that *in vitro* test conditions should be carefully selected and should correspond as closely as possible to *in vivo* conditions; in this case it was held that it did not, in particular through the selection of an inappropriate cell type. It was emphasised in T 609/02 that post-filed evidence could only be used to back up the findings provided in the patent application, and not in itself to establish sufficiency of disclosure.

"If the description of the patent specification, like in the present case, provides no more than a vague indication of a possible medical use for a chemical compound yet to be identified, later more detailed evidence cannot be used to remedy the fundamental insufficiency of such subject matter."

T 609/02 SALK INSTITUTE

199. The approach taken in T 609/02¹²² was followed by the Patents Court¹²¹ and the Court of Appeal¹²³ in *Regeneron Pharmaceuticals v Genentech*. The Court of Appeal in this case held that the specification must make it "plausible" that the invention would work (i.e. be effective to treat the disease) across the claimed scope. This concept was summarised by Birss J in *Hospira v Genentech (2014)*¹²⁵:

"...a rule which demanded clinical results could cause real difficulties. On the other hand, if all the patent contains is a mere proposal, then it has not made a contribution to the art in this example ... Moreover it would be a recipe for abuse if all that was required in order to obtain a patent in this field was a proposal, without any basis, to use drug A to treat disease B. Patent law seeks to address these factors balancing the requirements for sufficiency of disclosure against the rules of novelty and inventive step. But the conventional sufficiency test of asking whether the claimed invention works, does not help. The treatment does work but what if the patent does not say so? For these reasons the idea of "plausibility" as part of the law of sufficiency of disclosure has been developed ... The term "plausibility" has been coined to characterise what it is that a patent specification must provide in order to be sufficient, short of full clinical proof of efficacy."

Hospira v Genentech [2014] EWHC 1094

200. In Merck Sharp Dohme v Ono¹²⁹ it was emphasised that there is no standard test for plausibility and it must be determined on the facts of the case. As "plausible" is not a term used in either the Patents Act or the EPC 2000 there is no law of plausibility as such. In Generics v Warner-Lambert¹¹⁰ Arnold J held (at 344) that data which merely made it "obvious to try" to use the agent for the condition in question was not enough for sufficiency. On the other hand, in Actavis v Eli Lilly (2015)137, Carr J held that the standard for plausibility was lower than the "reasonable expectation of success" test in the context of obviousness (see paragraph 143 above). He also held that there was no absolute requirement for experimental evidence to be provided in the specification for plausibility to be established - on the facts of the case it was held that a proposed mechanism based on prior art findings concerning the active agent rendered the claimed use plausible. In both Merck Sharp Dohme v Ono¹²⁹ and Eli Lilly v Janssen Alzheimer Immunotherapy¹²⁴ a claim was held to be plausible even though the active agent was not actually tested - in both cases, experimental evidence relating to active immunisation by a protein or peptide was held to render plausible a second medical use claim relating to an antibody against that protein or peptide for passive immunisation. In Epshtein's Applications¹⁹⁴ (a case involving both applications with per se composition claims and with second medical use claims), there was experimental evidence (both in vitro and in vivo) provided in the applications, but the claimed effects were considered by the Hearing Officer to be inherently implausible according to the conventional scientific view of therapeutic mechanisms, as a dose of any of the compositions would be statistically unlikely to contain any active agent due to the extremely low dilutions used. It was considered that a higher burden of proof was needed in such a case to show that the conventional view should be ignored, and the applications were held to be insufficient - this decision is currently under appeal.

- 201. Insufficiency by excessive claim breadth has been considered by the Courts in terms of both the breadth of the class of agents, and the range of conditions to be treated. The agent in second medical use claims may be broadly defined structurally (for example, by Markush formula for chemical compositions, or by reference to a defined level of sequence identity for proteins or nucleic acids) or defined in functional terms. The Court of Appeal in *American Home Products v Novartis*¹⁸⁶ (see above, paragraph 187) concluded that, had the claim in question been construed as covering derivatives of rapamycin (or presumably, worded as covering derivatives), the patent would have been insufficient because there was no disclosure in the description enabling the skilled person to decide which of the many possible derivatives would have worked. Although there was a strong possibility that some of the large number of derivatives would work in the same way as rapamycin itself, it was impossible to say which would so work, unless the skilled person undertook the "vast and correspondingly burdensome" research task necessary.
- 202. However, if the specification discloses a general principle capable of general application, a claim in correspondingly general terms may be acceptable in *Regeneron Pharmaceuticals v Genentech*¹²¹ (upheld at appeal¹²³), this test was applied and the claim to the use of antagonists of a particular receptor was considered to be a fair generalisation. In this case it was pointed out that in the pharmaceutical industry a period of trial and error, sometimes extending over months or even years, is entirely normal, and so the need for such experimentation does not render the claim insufficient. There is no need to show proof of its application in every individual possible instance which could fall within the scope of the claim. This principle is, of course, applicable to more than just second medical use claims, but is particularly important for such claims as they are defined by the purpose of the product.

"Thus if the patentee has hit upon a new product which has a beneficial effect but cannot demonstrate that there is a common principle by which that effect will be shared by other products in that class, he will be entitled to a patent for that product but not for the class, even though some may subsequently turn out to have the same beneficial effect... On the other hand, if he has disclosed a beneficial property which is common to the class, he will be entitled to a patent for all products of that class (assuming them to be new) even though he has not himself made more than one or two of them."

Aldous LJ, American Home Products v Novartis [2001] RPC 8

- 203. On the other hand, in *Eli Lilly v Janssen Alzheimer Immunotherapy*¹²⁴, a claim to the use of "antibodies against beta-amyloid peptide" for treating Alzheimer's disease was not considered to be enabled across its full scope, in part because it was not considered plausible that antibodies targeting the mid-region or C-terminus of the peptide would have the desired effect.
- 204. In Regeneron Pharmaceuticals v Genentech^{121 123} it was also argued that the claim was not sufficient due to the breadth of the conditions to be treated a "non-neoplastic disease or disorder characterised by undesirable excessive neovascularisation". Both the Patents Court and Court of Appeal considered that it was a fair prediction that an anti-angiogenic effect demonstrated in the specification in tumours would also extend to non-neoplastic diseases characterised by excessive angiogenesis (growth of new blood vessels into a tissue), due to the common underlying mechanism. Similarly, in *Merck Sharp Dohme v Ono*¹²⁹, a broad claim to the "treatment of cancer" was considered to be a soundly based and reasonable prediction given the evidence provided in the patent this did not mean that the invention would necessarily treat all cancers, but it was plausible that it treated a wide range of them and this was borne out by the evidence after the filing date. On the other hand, in *Generics v Warner-Lambert*¹¹⁰ Arnold J held that there was no common underlying mechanism which would allow extrapolation from an animal model of inflammatory pain to other types of pain.
- 205. In *Regeneron Pharmaceuticals v Genentech*¹²¹ the Patents Court also considered whether the claimed use was insufficient due to ambiguity. It was concluded that the skilled person would not have any difficulty determining whether a disease fell within the scope of "a non-neoplastic disease or disorder characterised by undesirable excessive neovascularisation", and so rejected this attack on the patent.

ii) Support

206. There is a body of UK case law which has consistently held that second medical use claims to the further medical use of a substance or composition must be supported by evidence in the specification that the agent is (or at least is likely to be) effective for the specified use. The absence of any such evidence in a patent application leads to an objection under s.14(5)(c) that the claims are not supported by the description. The Hearing Officer rejected second medical use claims for this reason in *Hoerrmann's Application*¹⁹⁵ and *McManus's Application*¹⁹⁶.

"...unless there is some indication in the description of applications of this type of tests, however rudimentary, demonstrating that the invention has been carried out in an effective manner then the application must fail for lack of support for the invention claimed."

Hoerrmann's Application [1996] RPC 341

In *Consultant Suppliers' Application*¹⁹⁷ it was emphasised that mere assertion that tests had been carried out was not sufficient. The decision of the Patents Court in *Prendergast's Applications*¹⁰³ confirmed that speculative second medical use claims are not allowable. It was emphasised that full clinical trials on humans are **not** needed to satisfy the requirements of section 14(5)(c), but there must be some evidence.

"...where you have a claim for the use of a known active ingredient in the preparation of a medicament for the treatment of a particular condition, the specification must provide, by way of description, enough material to enable the relevantly skilled man to say this medicament does treat the condition alleged...pure assertion is insufficient."

Prendergast's Applications [2000] RPC 446

It was clearly stated that this support must be found in the **specification**, implying that late-filed evidence cannot overcome the absence of any such support in the application as filed. The decision of the Patents Court in *Prendergast's Applications* was acknowledged with approval by the House of Lords in *Conor v Angiotech*¹³⁸, and the requirement for some evidence in the application to support second medical use claims was confirmed by the Patents Court decision in *El-Tawil's Application*¹⁶⁸.

- 207. The judgement in *Prendergast's Applications*¹⁰³ has been applied in a number of subsequent IPO hearing decisions. It was held in *Advanced Biofactures of Curacao's Application*¹⁵¹ that the evidence provided does not need to meet the standard required of, for example, a peer-reviewed journal. Furthermore, in *F. Hoffmann La Roche's Application*¹⁰⁴ the Hearing Officer held that the claimed use could be supported by *in silico* modelling or as in the case in question through sequence homology comparisons. In this case, the evidence was only considered to support some of the claimed diseases or substances, and similarly in *Commonwealth Scientific & Industrial Research Organization's Application*¹⁸ the application was not considered to provide support for the full range of claimed conditions.
- 208. However, if the evidence in the application shows an effect on a common underlying mechanism behind a broader class of diseases, then a correspondingly broad claim may be considered supported. In *Agency for Science, Technology and Research's Application*¹⁹⁸ the Hearing Officer applied the case law on sufficiency from *Regeneron Pharmaceuticals v Genentech*¹²¹¹²³ and T 609/02¹²² to the question of support, using Lord Hoffmann's remarks in *Biogen v Medeva*¹⁹² (see paragraph 195 above) as basis for doing so. He held that experiments performed solely on breast cancer cells made it plausible that the claimed agents could treat any cancer characterised by the over-expression of a particular protein. In this case he also made it clear that support must be ascertained from the point of view of the skilled person at the priority date. In *G W Pharma's Application*¹⁸⁰ on the other hand, there was considered to be no disclosure in the application that the *in vitro* evidence provided in the application that the agent blocked a particular receptor related to a mechanism underlying prostate cancer (the claimed use), and the evidence from other sources available at the priority date did not clearly show such a link either.
- 195 Hoerrmann's Application [1996] RPC 341
- 196 McManus's Application [1994] FSR 558
- 197 Consultant Suppliers' Application [1996] RPC 348
- 198 Agency for Science, Technology and Research's Application BL O/221/13

209. All the case law relating to support under s.14(5)(c) relates to pre-grant hearings and appeals from Office decisions, as this is not a grounds for revocation of a granted patent. In addition, EPO practice (eg in T 939/92¹⁴³) has generally been to consider issues of plausibility and claim breadth under either Art. 56 (inventive step) or Art. 83 (sufficiency) rather than Art. 84 EPC (the equivalent of s.14(5)). Nonetheless *Prendergast's Applications*¹⁰³ and other UK court decisions concerning support remain binding on our practice and should be followed.

iii) Priority

210. In order for a patent application for an invention relating to a medical use to validly claim priority from an earlier application, the earlier application must itself make the claimed use plausible – a mere assertion unsupported by any evidence is not enough. This was established by the Patents Court decision in *Hospira v Genentech* (2014)¹²⁵:

"The establishment of priority includes a requirement for an enabling disclosure. In order to make an enabling disclosure of an invention it must be possible to make a reasonable prediction that the invention will work. In the context of an invention which includes the achievement of a therapeutic effect as one of its features, absolute proof is not required but the patentee must show that the therapeutic effect is plausible. It seems to me that this logic applies just as much to priority as it does to sufficiency of disclosure ... I find that in law the test for priority includes the requirement for plausibility in a case like this one."

Hospira v Genentech [2014] EWHC 1094

This principle was subsequently applied by the Patents Court in Merck Sharp Dohme v Ono¹²⁹.

iv) Industrial application

211. In *Epshtein's Applications*¹⁹⁴, the Hearing Officer considered a group of applications relating to compositions comprising ultra-low doses of antibodies, diluted such that statistically a single dose would be unlikely to contain any molecules of the antibody itself – the applications included both *per se* composition claims and second medical use claims. On the facts of the case, the Hearing Officer held that it was implausible that the compositions could have any therapeutic effect, and so refused the applications on grounds of industrial applicability as well sufficiency – this decision is currently under appeal. An objection of lack of industrial applicability in relation to medical use claims should only be made where (as was held to be the case in this instance) it is considered implausible that the substance or composition could have **any** useful activity of any kind, or where the invention is otherwise considered contrary to established physical, chemical or biological principles.

v) Search and examination practice

212. Second medical use claims must be supported by some evidence in the description of the likely efficacy of the substance or composition for the claimed medical use. The specification should therefore provide, in the description as filed, an indication that *in vivo* or *in vitro* tests have been conducted and that positive or encouraging results ensued (not necessarily quantified). Clinical or animal model data is not necessarily required, but if *in vitro* data is relied on then its relevance to the disease in question should either be known to the skilled person or demonstrated in the specification (as held in T 609/02¹²²). It may also be possible for the application to rely on, for example, *in silico* modelling, or sequence homology¹⁰⁴, if this is considered to provide a credible level of support (although if the new use is based solely on, for example, sequence homology with a known useful protein or nucleic acid then the inventiveness of the claim will clearly need to be considered carefully). Lack of any data, even rudimentary, in the description of an application which relates to a second medical use should be objected to under section 14(5)(c) as lacking support.

- 213. In addition, if the specification is not considered to render the claimed medical use plausible, an objection of lack of sufficiency under s.14(3) may also be raised. It should be made clear in the examination report whether the objection (under either s.14(5)(c) or s.14(3)) relates to the entire scope of the claimed invention or only to some of the claimed agents and/or uses. In the former case, the objection is likely to be fatal to the application. There is established case law that "classical" insufficiency cannot be overcome by amendment, and the judgement in *Prendergast's Applications*¹⁰³ clearly stated that the **specification** must provide support for the claimed use. This objection cannot therefore be overcome by subsequent filing of evidence which supports the claim the evidence must be provided in the application as filed. This objection is therefore fatal if the application relates solely to a further medical use of a known substance or composition. A warning, e.g. in the form of an examination opinion, should therefore be provided at the search stage if the main claims relate to a second medical use, and no or inadequate data is provided to support this use.
- 214. Moreover, if the application claims priority from an earlier application which discloses the claimed use but does not provide evidence to render it plausible, then it should be assumed at search and examination stage that the medical use claims in question are **not** entitled to a priority date based on the earlier application.
- 215. It is common for second medical use claims to be included as subsidiary claims to a main claim or claims relating to a new compound. In such cases, if the substance or composition claim is new, inventive and supported by the description, further consideration of support for the medical use claim(s) may not be necessary as a matter of practicality. Of course attention should be paid to any claims which were filed later than the application to check that they are supported by the description (see <u>MoPP 18.43</u>).
- 216. If the examiner considers that it is implausible that the substance or composition of the claims could have **any** therapeutic effect, then an objection under s.4 of lack of industrial applicability may be raised, in addition to an objection of lack of sufficiency.

CLAIMS TO PHARMACEUTICAL COMPOSITIONS

Compositions adapted to a particular use

217. The previous two sections have detailed the ways in which known substances can be protected for the first or subsequent medical uses, by the use of purpose-limited first or second medical use claims. In addition, known substances may be protected by per se product claims to pharmaceutical compositions containing them, if the composition is in a form which is novel and inventive over any known products. In particular, a claim may be made to a medicament having a form of administration which is novel and distinct from the previous use, where this implies a difference in the chemical or physical composition. For example, an anti-eczema ointment containing X would be regarded as clearly distinct from a tablet containing X for controlling blood pressure. The ointment is new because X has never been formulated in this form before, and it would be inventive if the previous use of X would not suggest its use in topical form. In general, the term "adapted to" is construed as being the same as "suitable for", as held by the Patents Court in a non-medical case, Brundle v Perry¹⁹⁹. However, it was stated in this case that this was not an absolute rule of claim construction, and a contrary view was taken on the facts of the case by the Technical Board of Appeal in in T 289/84²⁰⁰. In this case, the Board of Appeal held that there was a difference in meaning between a claim to composition adapted for topical use, as opposed to one **suitable** for such a use. Both eye drops and injectable formulations typically consist of sterile aqueous solutions, so either might be "suitable" for the other use. However, an eye-drop formulation was not "adapted" for use as an injectable solution or vice versa - injectable solutions had to both be sterile and pyrogen-free, whereas eye-drops do not need to be pyrogen-free but have a very narrow range of acceptable pH. However, a claim to a composition "adapted to" a specific use should be objected to on clarity grounds as being defined by its intended result, unless it would be clear to the person skilled in the art as to what is meant.

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- 218. In two cases where the main claims related to a contraceptive composition comprising compounds that were already known as pharmaceuticals, the EPO Technical Board of Appeal, in decisions T 303/90²⁰¹ and T 401/90²⁰², was of the opinion that the words "contraceptive composition" was not sufficient to distinguish the claim from known pharmaceutical compositions. In these cases the claims were amended to Swiss-type second medical use claims, although this would not normally be appropriate for methods of contraception as they are not excluded under Section 4A(1).
- 219. Claims to compositions with a novel physical characteristic, such as shaped forms or tablets with particular surface features, may be acceptable providing the feature relates to a genuine technical effect. For example, a claim to a tablet of a particular shape or structure would be acceptable if this resulted in a particularly favourable release profile for the active agent. However, if the new shape or form is merely presentational or conveys information (for example, by allowing blind patients to distinguish different types of pill), then it represents either an aesthetic creation or a mere presentation of information. As aesthetic creations and the presentation of information are not in themselves patentable, these features cannot impart novelty to the claim.

Clarity of composition claims

- 220. Composition claims of the form "a pharmaceutical composition containing compound X together with a diluent, excipient or carrier" are considered to be clear; X being a medically active compound which characterises the composition, and the diluent, excipient or carrier being any material suitable for the purpose and being selectable by knowledge of the art or by non-inventive experiment. There is no requirement for the diluent, excipient or carrier to be further characterised. However, a claim to the active ingredient "with an auxillary substance or substances", was considered (in T 80/96²⁰³) to be so broad as to be meaningless, and this could not distinguish the claim from the prior art. In addition, a claim to a solution of the compound, where the compound was known to be water soluble, could not make a claim novel²⁰³.
- 221. Terms such as "therapeutically effective amount" of an active ingredient are generally considered to be clear. However, if such a term is used to distinguish the composition from the prior art, then this is open to objection unless the specification teaches how this is tested, or there is a standard test in the art²⁰⁴. The purity of a product cannot be defined merely by defining the substance "as a pharmaceutical product"²⁰⁵. The Board of Appeal in T 1635/09⁴⁶ held that if a composition claim is defined in terms of parameters which require testing to determine its scope, then it may be objectionable on grounds of clarity if it could be defined without the need for such tests, particularly where the tests may be burdensome and/or ethically questionable.

Composition claims: support, sufficiency and industrial application

222. A *per se* claim to a pharmaceutical composition does not need to be supported by evidence of its suitability for its intended medical use in the same way as a medical use claim. In T 1616/09¹⁸³ it was held that the requirements for sufficiency for a pharmaceutical composition claim were that the specification enables the skilled person to produce the composition, and there are no substantial doubts that it could be used in therapy; this was contrasted with the requirement for second medical use claims that the agent's suitability for the claimed treatment is plausibly disclosed. On the other hand, if it is considered implausible that the composition could possibly have any therapeutic benefit (either because of toxicity or lack of any plausible activity) then an objection of insufficiency may arise, and if it is considered inherently implausible that it could have any useful properties at all then it may also be objected to under s.4 as lacking industrial applicability. In *Epshtein's Applications*¹⁹⁴, the Hearing Officer refused a group of applications relating to compositions comprising ultra-low doses of antibodies on grounds of both sufficiency and industrial applicability, as it was considered implausible that the compositions (in which a single dose would be statistically unlikely to contain any antibody molecules) could have any therapeutic effect – this decision is currently under appeal.

Compositions with a new non-medical purpose or property

223. Compositions which are allegedly distinguished from the same compositions in the prior art by the discovery of a new **non-therapeutic** property in one of the ingredients are not considered to be novel. This follows the general principle of novelty in UK law that once a substance or composition is known for whatever purpose then it cannot be patented again for another purpose - first and second medical use claims are the only accepted exception to this rule. Claims to the use of the agent in its non-therapeutic role are also not novel if the overall composition has previously been used in the same manner and the newly discovered property already put into effect, albeit unknowingly. Toothpastes with sodium bicarbonate as a cleaning/tingling agent are known, and so a claim to the use of sodium bicarbonate as a masking agent for bitter ingredients present in the known toothpaste formulations would not be novel. In this respect, the Intellectual Property Office has not followed the decision of the EPO Enlarged Board of Appeal in G 02/88¹⁷⁰, where it was held that novelty could be derived from a new technical effect (see <u>MoPP 2.14-2.14.1</u>).

Claims to unit dosage forms

- 224. A unit dosage form consists of a tablet, suppository, ampoule or other device, containing a definite amount of a drug, the whole of which is intended to be administered as a single dose. It is thus distinguished from a supply of an indefinite amount of a medicament, eg a bottle of medicine, from which a dose has to be measured out.
- 225. It may be possible in cases where the required dosage for a new medical use is **markedly** different from that for the known use, to allow a claim to a unit dosage form containing the known active ingredient in such an amount that the unit dosage form is novel and not obvious to have been made up in that amount for the prior art use. Thus if the new medical use requires a dose of, for example, ten times (or one tenth) that for the prior art use, then a claim to a unit dosage form might be judged to be novel and inventive and allowable. In assessing the inventiveness of such claims it should be remembered that dosages required are usually related to body weight so that children's doses are smaller than those for adults. It is also well known in medicine for patients to be asked to take more than one tablet at a time and it is known for half tablets to be taken.
- 226. Claims to unit dosage forms must clearly define a specific amount of medicament. A claim specifying an amount of medicament per unit body weight of patient is unclear in scope. Moreover there must be clear support in the description for a unit dosage form containing a specific amount of active ingredient. Claims derived from dosages of x mg/kg bodyweight by calculations using an average patient's body weight have been rejected as lacking in support, as have claims derived from the amounts of active ingredient fed to experimental animals.

Combined preparations and packs of medicaments

- 227. It is common in the pharmaceutical field for inventions to relate to the combined use of two or more known medicaments. Such claims may be in the form of per se composition claims or first or second medical use claims, and may also define a kit of parts for simultaneous or sequential administration. Following the practice established by the House of Lords in *SABAF v MFI Furniture Centres*²⁰⁶ the first question that must be addressed is whether for the purpose of assessing inventive step the claim in question relates to a single invention or plural inventions. If the two (or more) ingredients simply perform their usual function in the body, and there is no synergy between them, then the claim relates to two separate inventions, and there is no inventiveness in combining them. The Hearing Officer in *Lalvani et al's Applications*¹⁰⁵ applied this practice to dietary supplement compositions with multiple ingredients, with no evidence in the application of any synergy between them. On the facts of the case, he considered that each of the ingredients was either a known or obvious ingredient of compositions intended for the uses in question, and so the applications were refused on grounds of lack of an inventive step.
- 228. Moreover, synergistic effects between the components must be identified **in the specification**²⁰⁷. Evidence of synergy provided after the filing date cannot be used to demonstrate inventiveness, if there is no indication of such synergy in the specification as filed²⁰⁸.

"If a synergistic effect is to be relied on, it must be possessed by everything covered by the claim, and it must be described in the specification. No effect is described in the present specification that is not the natural prediction from the properties of the two components of the combination."

Glaxo Group's Patent [2004] RPC 43

- 229. Moreover, evidence of unexpected synergy between the two components does not render a combination inventive if the combination would in any case be obvious to the skilled person. In particular, if it is known to combine two categories of active agent (such as an analgesic and a decongestant), it is unlikely to be inventive to merely substitute a newer, more effective agent of one or other category in the combined preparation the patents in question in both *Glaxo Group's Patent*²⁰⁷ and *Richardson-Vicks' Patent*²⁰⁸ were revoked on these grounds. If the synergy demonstrated by the new combination is no greater than the equivalent prior art combination, then it does not provide evidence of inventiveness²⁰⁹. Although lack of evidence of synergy in a combined composition may give rise to an obviousness objection, it does not render the application insufficient¹⁸³.
- 230. In *Richardson-Vicks' Patent*²⁰⁸ the argument was made that combined preparations faced particular difficulties in obtaining regulatory approval, and this would constitute a prejudice away from a new combination. This was rejected by the judge any perceived regulatory difficulty is considered irrelevant for inventiveness. On the other hand, if there is a **technical** prejudice that would point away from the combination in question, then inventiveness may be acknowledged, even if the combination is superficially obvious²¹⁰.
- 231. Pack or "kit of parts" claims are sometimes used where the invention comprises the administration of two or more different drug compositions at particular time intervals, or merely simultaneously or sequentially. A claim of this form was considered by the EPO Board of Appeal in T 09/81⁹⁵. It was held in this case that the combination was novel and inventive, but needed to be "purpose limited" ie in the first or second medical use format to distinguish it from a medical kit, collection or package containing the two agents together for their known independent uses. This is in line with the practice of the Intellectual Property Office that such claims are allowable provided that the pack is stated to be for the method in which the invention really resides, and that the pack is novel and not obvious for any other application. In addition there must be clear support in the description for such a pack, and a claim for a kit or pack for carrying out a method must define all the essential elements for carrying out the method.
- 232. Claims to a pack or container containing a known substance with instructions for the new use should be rejected on the grounds that the only novel feature the instructions is merely a presentation of information and thus not a patentable invention under Section 1(2)(d)²¹¹. However, the acceptance of second medical use claims has now made such claims redundant in the medical fields.
- 233. However, a new package may be new and inventive if there is some physical relationship between the new and inventive method and the package, which goes beyond merely presenting instructions for the new use. In *Organon's Application*²¹², a claim was allowed under the 1949 Act to a pack containing two types of known contraceptive pill arranged in the order in which they were to be taken, the arrangement being novel and not obvious from the art. This was despite the fact that packs containing contraceptive pills in a given order were known the particular order defined in this case was not obvious as it was based on a new and inventive method of contraception.

- 210 Norbrook Laboratories' Patent [2006] FSR 18
- 211 Bayer's (Meyer's) Application [1984] RPC 11
- 212 Organon's Application [1970] RPC 235

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