

## Dosage regimen patent claims in Europe

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Maximum patent term protection is key to maintaining market exclusivity for important commercial products. Typical vehicles for achieving this are second (and subsequent) medical use patent claims, supplementary protection certificates (SPCs), orphan drug provisions, and data & marketing exclusivity provisions. In this review, we look at the relevant European case law relating to second medical use claims and, in particular, to a subset of this claim category known as dosage regimen claims. The latter have attracted considerable interest and are the subject of a pending referral to the Enlarged Board of Appeal of the European Patent Office (EPO) - G2/08, which is expected to be published this summer.

### Second medical use claims - overview

Second medical use claims were first held permissible by the EPO a quarter century ago (G5/83 - *Eisa*). Despite this, however, for much of the last 25 years the EPO has generally refused to grant dosage regimen claims on the basis that any perceived technical contribution constitutes nothing more than a method of medical treatment, which falls within the excluded subject-matter provisions of Article 53(c) EPC1 and is thus unpatentable.

More recently, with *Genentech* (T1020/03) providing the catalyst, we believe there has been a general trend towards a more favourable assessment by the EPO of dosage regimen claims. This pro-patent approach has been mirrored by the UK Court of Appeal in *Actavis v. Merck* ([2008] EWCA Civ 444), which confirmed explicit approval of *Genentech*.

### Second medical use claims - history

Patents have long been granted by the EPO for a new use of a known substance. Within the pharmaceutical and biotech fields, however, there lies an additional problem, as a new use when couched as a "use of substance X for treating disease Y", falls foul of the Article 53(c) EPC. The solution to this, of course, is use of a "Swiss" style claim format (G5/83) – "use of substance X for the manufacture of a medicament for use in the treatment of disease Y". Thus, by claiming the manufacture of a medicament, no method of treatment is claimed as such.

The Swiss claim format has allowed applicants to obtain patent protection for a new medical use of a substance, provided, of course, that said new use is both novel and inventive.

However, in the case of dosage regimen claims the general position of the EPO (prior to *Genentech*) was that, since any perceived technical contribution must lie in a method step that would be performed by a physician, any corresponding patent claim characterised by said technical contribution must relate to subject-matter excluded from patentability under Article 53(c) EPC1.

### *Genentech* (T1020/03)

*Genentech* had applied for patent protection for a new way of using Insulin-like Growth Factor-1 (IGF-1). The claims at issue were drafted in the correct "Swiss" format for second medical use claims. IGF-1 was to be given discontinuously in a cyclic "on/off" fashion, wherein IGF-1 was administered for a given period of time before administration was discontinued for a further period of time, whereupon the cycle repeated.

*Genentech*'s application was initially rejected during prosecution, with the Examining Division taking the view that the pattern of administration of IGF-1 was something for a medical professional to decide and was therefore disallowed under Article 53(c) EPC1. Upon appeal, the Technical Board of Appeal ruled in *Genentech*'s favour.

### Interpreting *Genentech*

*Genentech* was in many ways a landmark decision and notable for the lengths the Technical Board went to in order to explain and justify their decision. In refusing to follow earlier EPO Decisions, which had ruled that dosage claims were impermissible, the Board in *Genentech* asserted that G5/83 should apply equally to dosage claims: if a dosage regimen patent claim is presented in a Swiss claim format, the claim (by definition) must relate to the use of a compound for the manufacture of a medicament, which is not a method of treatment excluded by Article 53(c) EPC1.

### Obtaining patent protection for dosage regimens

Thus, following *Genentech*, the first hurdle is that of claim language, namely use of the correct format for a second medical use claim. *Genentech* confirms that by using the correct second medical use format, said claims will automatically avoid the prohibition of Article 53(c) EPC1. Thereafter, any further consideration of a claim's allowability under Article 53(c) EPC1 is unnecessary and superfluous – the requirements are met and the claim should be examined on grounds of novelty and inventive step as per any other type of claim.

It is worth noting, however, that the claimed subject-matter must relate to a method of treatment excluded by Article 53(c) EPC1, and that mere recitation of the approved second medical use wording does not negate this requirement. Referring to T292/04, a claim was rejected because, although drafted in the correct second medical use format, it was held that the claim embraced subject-matter (use as a sterilising agent for contact lens) falling outside of Article 53(c) EPC1.

### EPO decisions post-*Genentech*

EPO Boards of Appeal are not bound by rules of precedent in the way that English Courts are. Despite this, a number of Decisions since *Genentech* have indicated approval of the conclusions reached in *Genentech*.

In assessing a claim for an anti-tumour medicament, in which novelty was derived from the order in which a DNA-damaging agent and a

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p53 protein or gene were administered, the Board of Appeal in T36/04 referred to both G5/83 and *Genentech* and again held that if a claim was in the approved "Swiss" form then it automatically fell outside the prohibition on claims to methods of medical treatment – "The decisive question to be answered in accordance with decision G5/83 is ... whether the intended method of treatment for which the medicament was manufactured was novel and inventive, and not any further considerations under [Article 53(c) EPC1]" [see para 3].

In T230/01, decided some six months after *Genentech*, the second medical use claims at issue were to the treatment of allergic rhinitis in humans. The Board held the claim novel on account of both the selection of allergic rhinitis (over the prior art disclosure of allergies) and a dosage regimen reciting a recommended daily dose of 0.2 mg to 1 mg [of the drug in question] [see para 10].

## The importance of inventive step

Correct drafting of claims is only the first step. For a dosage regimen claim to succeed, it must truly be novel and be supported by an inventive step.

*Genentech* noted that if a claim is to be regarded as novel, it can not merely be directed to a use of a physiological or pharmacological mechanism or effect underlying a previous therapeutic use, which had not been identified at the time [see para 8]. Another way of viewing this is that an inherent mechanism of action or effect cannot be relied on to confer novelty – see the established EPO case law on this point [e.g. T254/93 & T241/95].

Inventive step for a dosage claim is likely to represent a slightly higher than normal hurdle for an applicant to clear, with evidence (or a strong teaching-away) almost certainly being required in order to demonstrate a surprising technical effect.

In T230/01 (noted above), the claimed dosage regimen of "a daily dose of 0.2 mg to 1 mg" of DCL for the treatment of allergic rhinitis was held inventive as it was so much lower than the prior art teachings of a daily dose of 10-20 mg. There was no teaching that would suggest to a skilled person that a dose of DCL some 50 times lower than that in the prior art would be of any use in the treatment of any allergic condition [see para 11].

T230/01 decision should perhaps be viewed with some caution, as it might be argued that a skilled person would always seek to achieve use of a lower dosage, as was noted in [UK Court decision] This potential difficulty in demonstrating the inventive nature of a novel dosage regimen has been recognised by the UK Court of Appeal in *Actavis v. Merck* "... on the contrary, nearly always such [novel] dosage regimes will be obvious – it is standard practice to investigate appropriate dosage regimes. Only in an unusual case ... could specifying a dosage regime as part of the therapeutic use confer validity on an otherwise invalid claim." [32]

In T36/04 (noted above), the Board held that the order in which a DNA-damaging agent and a p53 protein or gene were administered not only provided novelty but was also inventive, as a skilled person would not have been able to arrive at this claimed method of killing tumour cells from the prior art disclosure [para 20].

Dosage regimen claims might be considered akin to "selection" inventions. These arise when an unexpected technical effect is associated with a specific compound (a "species") that is a member of a larger "genus" of (typically) structurally-related compounds. While it may be relatively easy (at least under EPO practice) to achieve novelty for such a selection, demonstrating inventive step will nearly always require experimental data to confirm that the unexpected technical effect is not common across the genus.

## Re-evaluating pre-*Genentech* cases

It is difficult to be certain whether EPO decisions relating to dosage claims pre- *Genentech* would have succeeded in the post-*Genentech* legal climate, as many were ultimately decided on grounds other than patentability under Article 53(c) EPC1.

One example of a pre-*Genentech* case is T56/97, which featured second medical use claims to the use of a thiazide diuretic for manufacture of an anti-hypertensive and non-diuretic composition. Novelty was alleged to reside in a claimed dosage regimen.

There was concern on the part of the Board in T56/97 that acknowledging the novelty of such claims would lead to the patenting of a new therapeutic application; in addition, it was felt that dosage would be something decided by a physician. These arguments would not have arisen post- *Genentech* (and indeed *Genentech* criticised T56/97), although it should be noted that the patent separately failed on novelty and was therefore revoked.

In another pre-*Genentech* case, T584/97, the issue of what was permissible as a second medical use claim caused difficulties. In this case, the Board refused to acknowledge specific claim wording that related to a separate or sequential administration of increasing doses of nicotine. The claim was then held to lack novelty. In its reasoning, the Board held that a specific drug regimen could not be seen as an acceptable second medical use following G5/83 [see para 2.6]. This position is at odds with the interpretation of G5/83 as later taken in *Genentech*, and was heavily criticised by the Board in *Genentech*. Post-*Genentech*, we believe the outcome of this case might have been different. At the very least, a more complete claim interpretation would have been followed, leading to an acknowledgement of novelty. Thereafter, the remaining issue would have been that of inventive step, which was not assessed in T584/97.

## Referral of dosage claims to the Enlarged Board of Appeal

In Decision T1319/04, the issue of dosage claims was again considered. The claims at issue were drafted in the "Swiss" form and related to the use of nicotinic acid for the treatment of hyperlipidaemia. Novelty of the claim was alleged to lie in a dosage regimen – in this case the medicine was to be given once per day before the patient went to sleep. The patent application had been refused by the Examining Division on the grounds that "once per day prior to sleep" was a medical activity excluded under Article 53(c) EPC1, and that the use of nicotinic acid for the treatment of hyperlipidaemia *per se* was disclosed by the prior art.

Central to this case and its referral to the Enlarged Board of Appeal as G2/08 is the Technical Board's conclusion that the case should be decided under EPC 2000, which explicitly permits second medical use claims when couched in terms of "Compound X for use in ..." and thereby negates the need for "Swiss" format claim language.

Thus, a key question under EPC 2000 is whether a claimed dosage regimen feature will be recognised under Article 54(5) EPC 2000 as a specific use in a method referred to in Article 53(c) – if yes, this feature will be considered for the assessment of novelty and inventive step in a dosage regimen second medical use claim.

## G2/08 and the position under EPC 2000

We believe it is highly unlikely that G2/08 will reach a decision at odds with *Genentech*. Our view is that the Enlarged Board will rule that dosage claims are permitted under the second medical use provisions of EPC 2000, subject to compliance with the separate patentability requirements of novelty and inventive step.

As discussed by the Board in T1319/04, a refusal to allow dosage claims would require a very particular interpretation of "methods of treatment by therapy" for the purposes of Articles 53(c) and 54(5) EPC 2000, and there is no evidence that this was intended when drafting EPC 2000 [see para 5.1]. Preventing dosage regimen claims from being granted would also have the effect of denying patent protection where an applicant had exercised genuine skill in creating a novel and inventive dosage regimen for a given drug. Another way of arriving at said denial would necessitate the interpretation of a prior dosage regimen as disclosing all possible dosage regimens, which would be contrary to current EPO assessment of novelty.

## UK Court decisions

The UK Courts have recently overturned their previously negative approach to dosage claims. In *Actavis v. Merck* the Court of Appeal allowed a dosage claim in the "Swiss" form directed to the use of finasteride for the treatment of androgenic alopecia, stating:

"Research into new and better dosage regimes is clearly desirable, and there is simply no policy reason why, if a novel non-obvious regime is invented, there should not be an appropriate patent reward" [see para 29].

The Court of Appeal made it clear that it agreed with the position taken by the EPO in *Genentech*, and further that it felt it desirable that the UK Courts should align



themselves with the EPO on this issue, even if the UK Courts were not constitutionally bound to do so [48-49].

## Final conclusions

We feel that the legal environment at the EPO and in the English Courts is now generally in favour of the allowability of dosage claims, subject, of course, to novelty and inventive step compliance. In this regard, use of the approved second medical use claim format should be regarded as a formal requirement. Whilst the novelty of a dosage regimen might be established with relative ease, demonstrating that said regimen is inventive may prove more difficult.

As a final note, it is perhaps worth reflecting on the position in the United States, where there is no statutory bar to patenting methods of medical treatment. Given the complex legal manoeuvring that has been required in Europe in order to circumvent such prohibitions and rightly gain protection for dosage claims – which some have tried to portray as claims to methods of medical treatment – one cannot help but wonder if the position of the US might in some ways be better, something also pondered by Mr Justice Jacob in the case of *BMS v. Baker Norton*:

*"It is noteworthy that in the US any such exception [to methods of medical treatment] has gone, and yet no-one...suggests that its removal has caused any trouble". [see para 51 [1999] RPC 253].*

## Endnotes

- 1 Article 52(4) EPC 1973: *Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application.*  
  
has been replaced by  
  
Article 53(c) EPC 2000: *European patents shall not be granted in respect of:*  
(c) *methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body.*
- 2 *Actavis v. Merck* [2008] EWCA Civ 444
- 3 Art. 54(5) EPC 2000: *Paragraphs 2 and 3 shall also not exclude the patentability of any substance or composition referred to in paragraph 4 for any specific use in a method referred to in Article 53(c), provided that such use is not comprised in the state of the art.*