Intellectual Property Office

BL O/245/18

19 April 2018

PATENTS ACT 1977

BETWEEN

Novartis AG	Proprietor
and	
Urquhart-Dykes & Lord LLP	Opponent

PROCEEDINGS

Application under section 74B for a review of Opinion 07/17 in respect of EP(UK)2308855

HEARING OFFICER Phil Thorpe

DECISION

Introduction

1 Opinion 07/17 is concerned with the question of whether patent EP2308855 B1 is valid on the grounds that it comprises added matter, that it is lacking novelty or an inventive step and that it is insufficient. The opinion was issued on 21st July 2017 with the examiner stating his opinion that the patent is invalid because none of the claims involve an inventive step and that the invention in claims 7 and 8 is not disclosed clearly and completely enough for it to be performed by a person skilled in the art.

2 The proprietor has applied for a review of the opinion as provided by section 74B of the Act. The application for review was received within the three month period from the date of issue of the opinion and was accompanied by a statement setting out the proprietor's grounds for review. The requester of the original opinion (Urquhart-Dykes & Lord LLP and the opponent in these proceedings) contests the application for review and has filed timely observations on the grounds and the arguments presented.

3 Both sides have agreed that the review should be decided on the basis of the papers filed without the need for a hearing.

Grounds for review

4 The grounds for a review of an opinion are set out in rule 98(5) of the Patents Rules 2007:

> The application may be made on the following grounds only -
>
> > (a) that the opinion wrongly concluded that the patent in suit was invalid, or was invalid to a limited extent; or
> >
> > (b) that, by reason of its interpretation of the specification of the patent in suit, the opinion wrongly concluded that a particular act did not or would not constitute an infringement of the patent.

5 The nature of a review under section 74B was considered by the Patents Court in *DLP Limited*[1] in which Kitchen J said:

> In the case of an appeal under rule 77K, the decision the subject of the appeal is itself a review of the opinion of the examiner. More specifically, it is a decision by the Hearing Officer as to whether or not the opinion of the examiner was wrong. I believe that a Hearing Officer, on review, and this court, on appeal, should be sensitive to the nature of this starting point. It was only an expression of an opinion, and one almost certainly reached on incomplete information. Upon considering any particular request, two different examiners may quite reasonably have different opinions. So also, there well may be opinions with which a Hearing Officer or a court would not agree but which cannot be characterised as wrong. Such opinions merely represent different views within a range within which reasonable people can differ. For these reasons I believe a Hearing Officer should only decide an opinion was wrong if the examiner has made an error of principle or reached a conclusion that is clearly wrong. Likewise, on appeal, this court should only reverse a decision of a Hearing Officer if he failed to recognise such an error or wrong conclusion in the opinion and so declined to set it aside. Of course this court must give a reasoned decision in relation to the grounds of appeal but I think it is undesirable to go further. It is not the function of this court (nor is it that of the Hearing Officer) to express an opinion on the question the subject of the original request.

6 Hence a review is not intended to be a second opinion on the matters presented in the opinion. Whether I necessarily agree or disagree with the examiner's opinion is also not the matter at hand in this review. Furthermore, the matter is not whether any of the parties agrees or disagrees with the opinion. What matters is whether the examiner made an error of principle or reached a conclusion in their opinion which was clearly wrong.

7 In its request for the review the proprietor has requested that the opinion be set aside in its entirety and that the patent be found to have been validly granted. As the opponent rightly notes, it is not the purpose of a review to make any finding on the validity of the patent hence I shall limit myself to considering whether the opinion should be set aside.

The patent

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[1] *DLP Limited* [2007] EWHC 2669

8 The patent concerns 2, 4-Diaminopyrimidine derivatives, their preparation and their use (alone or in combination with existing drugs) as kinase inhibitors, particularly zeta chain-associated protein of 70kD (also known as ZAP-70), focal adhesion kinase (also known as FAK) and/or p72syk protein tyrosine kinase (also known as syk). The claimed compounds are defined by a Markush formulae in claim 1 of the patent. Further details of the claims can be found in the opinion.

Argument and analysis

Added Matter

9 In its observations, the opponent has suggested that should the review find that the opinion has reached a conclusion that is clearly wrong on the matter of inventive step, then consideration be given to the opinion's conclusion on added matter. More specifically the opponent is arguing that I should review the opinion examiner's conclusion that the patent does not add matter. It is however not within the scope of a review to reconsider those parts of an opinion that did not conclude that the patent was invalid.

Inventive Step

10 The opinion considers the question of whether the patent involves an inventive step in paragraphs 14-28 with the paragraphs up to paragraph 23 setting out the examiner's analysis based on the steps set out in *Pozzoli SPA v BDMO SA*[2]. The proprietor accepts that the approach adopted by the examiner is appropriate. Further the proprietor accepts that the examiner correctly identifies the skilled person in step 1a.

11 The proprietor however believes that the examiner erred in his assessment of the common general knowledge of the skilled person. More particularly it argues that the examiner was wrong to conclude that the common general knowledge includes knowledge that structural modifications of compounds and compositions could provide benefits as regards enhanced activity in vivo without also concluding that relatively small structural modifications can significantly reduce or remove the pharmacological effect of compounds.

12 The opponent contends that this further qualification is merely the inverse of what the examiner has already concluded and that, in effect, both the proprietor and examiner are in agreement that structural modifications of a compound affect its pharmacological activity.

13 On this point I am more with the opponent. The examiner in the opinion does refer explicitly just to the possible benefits from modifying the compounds however there is nothing to indicate that he would think that the skilled person would not also be aware that such modifications could have a negative effect. Furthermore the proprietor has not shown how even if this was not the case that this then led to the examiner reaching a conclusion that was clearly wrong.

[2] *Pozzoli SPA v BDMO SA* [2007] EWCA Civ 588 [2007] All ER (D) 275 (JUN)

14 For the next step the examiner considers the differences between the inventive concept and the prior art concluding that documents D1-D4 overlap considerably with the claims of the patent. He goes on to conclude that the compounds of the patent are not "inventive per se insofar as the compounds are encompassed by the prior art". No objection is made to this.

15 The examiner then goes on to consider whether the selection of the particular compounds of claim 1 represent an inventive step. The examiner refers to relevant case law that provides guidance on how this question should be answered. The proprietor does not suggest any error of principle by the examiner in this respect. Rather it is examiner's subsequent assessment that the selection is arbitrary which the proprietor argues is clearly wrong. The examiner's reasoning on this point is set out in paragraphs 24-27 of the opinion which read as follows:

> 24. To determine if the selection is arbitrary, I must first determine what the patent contributes to the art, in effect, what is the technical contribution? I consider this is the useful property that the compounds of the claims are put to, namely the use of the compounds to cure diseases or conditions where ZAP-70, FAK and/or Syk tyrosine kinase activation plays a role or is implicated. I do not consider the ability to inhibit these kinases is an end in itself that constitutes a contribution to the art but rather it is a proxy for determining which compounds may provide the required technical contribution. However the results of such inhibition tests may in my opinion make the technical effect plausible.
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> 25. Having considered the patent in light of my proposed technical effect, I consider that the selection is arbitrary because the patent does not show a real technical advance [item (iv) above] as there is no clear demonstration in the patent that the compounds of the invention have the desired effect of curing disease.
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> 26. I have also considered the alternative, wherein I give the proprietor the benefit of the doubt and find that the property of ZAP-70, FAK and/or Syk tyrosine kinase inhibition to be a technical contribution in itself. From this perspective I still find the selection is arbitrary. This is because the compounds indicated in the description which are subject to the inhibitor tests as defined on pages 19-21 of the patent are not compounds that fall within the scope of the invention, so it is not demonstrated that the compounds of the patent make the technical contribution and the selection would appear to be arbitrary.
>
> 27. To be certain I have also considered what would be my conclusion if I were to decide in the proprietors favour that the inhibitor tests as defined on pages 19-21 make the technical effect plausible. In this case I would go on to consider the post filed evidence supporting the technical effect (provided in Table 1 in the observations filed by the proprietor on 23 May 2017). From this perspective I am still unable to conclude that there is support for the technical effect. The evidence in Table 1 of the observations dated 23 May 2017 show comparative tests of inhibition in a ZAP-70 kinase assay for certain compounds bearing the sulphonamide group at R^1 (para), R^2 (meta), and R^3 (ortho). I consider this evidence shows that at least some compounds bearing the sulphonamide group at the R^2 (meta) position show the effect of ZAP-70 kinase inhibition. However I do not consider that, on the balance of probabilities, this evidence relating to a single compound justifies a finding that the technical effect is common to substantially everything covered by claim 1 of the patent [step (ii) above]. In particular, given the high degree of variation of compounds covered by the claim in respect of the substituents near R^2, i.e. R^1 and R^3 and the substituents that make up R^2 i.e. R^{10} and R^{11}, I do not consider that a single compound wherein R^1=R^3=R^{10}=R^{11}=H is sufficiently representative of all the compounds covered by claim 1 of the patent. Accordingly, I still consider that the selection is arbitrary and as the selection of the compounds of claim 1 is not inventive, I find this claim is obvious.

16 The proprietor contends that the contribution to the art is new compounds which act as inhibitors of specific kinases and that the examiner made an error of fact in

concluding that there is no demonstration in the specification that the claimed compounds have the stated activity ie. that they act as inhibitors of specific kinases.

17 The proprietor makes three points on this. Firstly it notes that the specification, in respect of the ZAP-70 Kinase assay, states that all of the compounds of the invention have an IC_{50} value in the range 10nM to 2µM. Accordingly the compounds exemplified in the specification which fall within the scope of the claims of the patent demonstrate inhibitory activity against the ZAP-70 kinase. The specification therefore makes plausible the claimed technical effect of the compounds defined in claim 1 in respect of this kinase.

18 Secondly, in relation to the Syk Kinase assay, the specification states that that all of the compounds of the invention have an IC_{50} value in the range 100nM to 10µM. Again this establishes that the compounds exemplified in the specification which fall within the scope of the claims of the patent demonstrate inhibitory activity against the Syk kinase. The skilled person would further understand that this is based upon the testing of the exemplified compounds.

19 The third point relates to the FAK assay. The proprietor argues that the specification states that the compounds of Formula I have an IC_{50} value of less than 1µM. This again establishes that the compounds exemplified in the specification which fall within the scope of the claims of the patent demonstrate inhibitory activity against the FAK kinase. The proprietor further argues that with regard to the data relating to the reduction of the phosphorylation levels of FAK in the specification, it was also found that the compounds of Formula I reduce phosphorylation at an IC_{50} value of less than 1µM. This it contends establishes again that the compounds exemplified in the specification which fall within the scope of the claims of the patent demonstrate inhibitory activity against the FAK kinase. The skilled person would further understand that this is based upon the testing of the exemplified compounds.

20 According to the proprietor all of this shows that the technical effect with respect to all three kinases has been made plausible by the specification and hence in accordance with established case law no further proof of the existence of the effect can be demanded before judging obviousness. Hence given that the technical effect is made plausible by the specification the opinion examiner should have concluded that the technical contribution to the art is not arbitrary. It concludes by arguing that the fact that compounds with a different substitution pattern are also active in relation to these specific kinases does not make the selection of the claimed compounds any less meaningful.

21 The opponent contends that the conclusions reached by the examiner on inventive step are entirely reasonably. It argues that the examiner was correct to conclude that the technical effect for the claimed compounds is not plausible from the application as filed. It highlights that the specific examples referred to in the specification as demonstrating the claimed technical effect and for which IC values are provided all fall outside the scope of the claims as granted. It adds that the disclosure of any technical effect in respect of the other compounds is mere speculation especially when this is considered with the proprietor's argument that small changes can change the functional properties of the compounds.

22 The opponent adds that in its view the examiner's precautionary assessment of the post-filed data as not being sufficient to demonstrate a technical effect across the range of compounds covered by claim 1 is reasonable.

23 I have carefully considered the arguments put forward by both parties. I have not however been able to find anything in the approach adopted by the examiner in respect of his assessment of inventive step that is clearly wrong. The examiner acted reasonably with respect to his consideration of the technical effect. He reasonably concluded that the assertions that all compounds falling within the claims have appropriate IC_{50} values was merely assertions. He recognised that the examples with specifically stated IC_{50} values all fall outside the scope of the granted claims. He reasonably dismissed them as not providing evidence for the compounds of claim 1. The examiner also considered the post filed evidence filed on 23rd May 2017. He noted only example 75 falls within the scope of the claim 1 and that claim 1 encompasses a large number of compounds. He reasonably noted that for selection to be used when assessing inventive step, the technical contribution must be common to substantially everything covered by the claim. His conclusion that a single example does not demonstrate that the effect is available to every compound within claim 1 is not wrong. Hence I believe that the conclusion he came to on inventive step is therefore within the bounds of being reasonable given the material before him.

Lack of sufficiency

24 The examiner's assessment of sufficiency is set out in paragraphs 29-40. In assessing whether claims 7 and 8 are sufficient, the examiner acknowledged that the patent does include methods for assessment of whether compounds inhibit ZAP-70, FAK or Syk, and that some conditions relevant thereto are noted. He sought guidance on whether this was sufficient disclosure to allow a third party to identify which disorders fall within the scope of the claims from T241/95 (Eli Lilly and Company) and *Kirin-Amgen Inc. & Ors. V Hoechst Marion Roussel Ltd & Ors*.[3]. The examiner found that although some disorders were listed in the patent, this only enabled a portion of claims 7 and 8 whereas to be sufficient, the whole scope of the claim needed to be enabled.

25 The proprietor argues that the examiner should have construed claim 7 as the treatment or prevention of a disease or condition in which ZAP 70, FAK or Syk tyrosine kinase is known to play a part or is implicated. Adopting this construction would mean that the skilled person is not required to determine the biological pathways involved in the disease state or condition. On claim 8 it notes that all that this claim requires is a combination of a therapeutically effective amount of a compound according to claim 1 and a second active ingredient. It contends that it would be a matter of routine drug titration to arrive at a therapeutically effective amount of the compound of claim 1.

26 The opponent argues that the proprietor's arguments do not really address the issue of whether the application as filed contains sufficient information to ascertain whether the inhibition of the recited kinases are relevant to the diseases described in the application as filed. It contends claims 7 and 8 are reach-through claims with no

[3] *Kirin-Amgen Inc. & Ors. V Hoechst Marion Roussel Ltd & Ors*. [2005] RPC9

disclosed technical basis to establish the purported indication. It concludes by noting the examiner's conclusion on sufficiency is reasonable.

27 I am of the view that in considering the question of sufficiency, the examiner did not make any error of principle nor did he reach a conclusion that is clearly wrong. Rather he reasonably found that the patent does not provide enabling disclosure to allow a third party to identify which disorders fall within the scope of the claims. Furthermore, in reference to *Kirin-Amgen Inc. & Ors. V Hoechst Marion Roussel Ltd & Ors. [2005] RPC9*, the examiner found that although some disorders were listed in the patent, this only enabled a portion of claims 7 and 8 whereas to be sufficient, the whole scope of the claim needed to be enabled.

Conclusion

28 For the reasons set out above I find no reason to set opinion 07/17 aside.

Costs

29 Neither side has sought costs so I make no award.

Appeal

30 Any appeal must be lodged within 28 days after the date of this decision.

Phil Thorpe