Patents Act 1977 **Opinion Number** **07/17**

OPINION UNDER SECTION 74A

Patent	EP (UK) 2308855
Proprietor(s)	Novartis AG
Requester	Urquhart-Dykes & Lord LLP
Observer(s)	Novartis AG
Date Opinion issued	21 July 2017

The request

1. The comptroller has been requested to issue an opinion as to the validity of EP (UK) 2308855 B1, (hereafter referred to as "the patent") filed on 14 March 2003 with an earliest priority date of 15 March 2002 as a divisional application of EP 1487805 also published as WO 03/078404 (hereafter referred to as "the parent") and granted on 17 October 2012, the patent is currently in force, and in the normal course of events it will expire on 13 March 2023.

2. The request is made under s74A of the Patents Act 1977 (hereafter The Act) for me to consider if the patent is invalid in the following respects:

   i) All 8 claims comprise added matter i.e. having regard to section 72(d) of The Act;

   ii) Claims 1, 3, 5 and 8 are not novel and claims 1-8 are not inventive having regard to section 72(a) of The Act; and

   iii) Claims 7 and 8 are insufficient i.e. having regard to section 72(c) of The Act.

3. The request dated 19 April 2017 relies on the following documents:

   D1 WO 01/60816
   D2 WO 97/19065
   D3 WO 01/64654
   D4 WO 01/64656
   D5 WO 00/39101

   Observations have been received from the proprietor dated 23 May 2017, these include reference to a response (dated 7 March 2014) to opposition proceedings initiated centrally against the patent. I note that the opposition was withdrawn before

the EPO ruled in this matter. Therefore the arguments concerning the opposition have not been tested. I have therefore considered the response dated 7 March 2014 in full. I have also considered the observations in reply submitted by the proprietor with their email of 7 June 2017.

Section 74A(3)(b) - has this matter been considered before

4. Section 74A(3) of the Patents Act 1977 states:

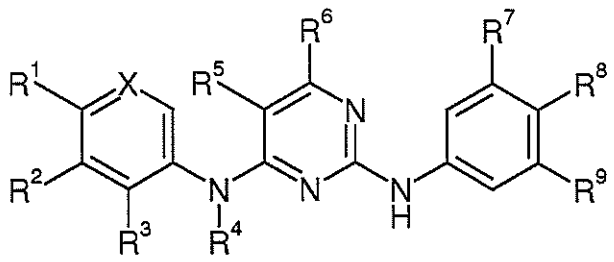
> *The comptroller shall issue an opinion if requested to do so under subsection (1) above, but shall not do so –*
> *(a) in such circumstances as may be prescribed, or*
> *(b) if for any reason he considers it inappropriate in all the circumstances to do so.*

5. Documents D1, D2 and D5 above were also cited on the search report on the parent dated 18 June 2003 and considered in an EPO examiner's opinion dated 3 March 2011. Grant of amended claims having regard to the applicant's submission dated 11 July 2011 may be considered to demonstrate that some aspects of the request have already been considered by the EPO and that as such I should not give my opinion in these aspects having regard to section 74A(3)(b). Accordingly, I have considered if I should refuse to issue an opinion insofar as it is inappropriate to do so, this matter having already been considered. However as the requester has raised some new documents which could cast the state of the art in a different light, I consider it is justified to reappraise all of the arguments and documents in full.

The patent

6. 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, as follows:

1. A compound of formula I



(I)

wherein

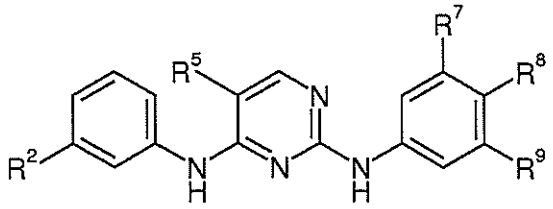
X is $=CR^0$-;
R^0 is hydrogen;
R^2 is $-SO_2N(R^{10})R^{11}$;
each of R^1 and R^3 independently is hydrogen; hydroxy; C_1-C_8alkyl; C_2-C_8alkenyl; C_3-C_8cycloalkyl; C_3-C_8cycloalkyl-C_1-C_8alkyl; hydroxyC_1-C_8alkyl; C_1-C_8alkoxyC_1-C_8alkyl; hydroxyC_1-C_8alkoxyC_1-C_8alkyl; arylC_1-C_8alkyl which optionally may be substituted on the ring by hydroxy, C_1-C_8alkoxy, carboxy or C_1-C_8alkoxycarbonyl;
or each of R^1 and and R^3, independently, is halogen; halo-C_1-C_8alkyl; C_1-C_8alkoxy; halo-C_1-C_8alkoxy; hydroxyC_1-C_8alkoxy; C_1-C_8alkoxyC_1-C_8alkoxy; aryl; arylC_1-C_8alkoxy; heteroaryl; heteroaryl-C_1-C_4alkyl; 5 to 10 membered heterocyclic ring; nitro; carboxy; C_2-C_8alkoxycarbonyl; C_2-C_8alkylcarbonyl; $-N(C_1$-C_8alkyl)C(O) C_1-C_8alkyl; $-N(R^{10})R^{11}$; $-CON(R^{10})R^{11}$; or $-C_1$-C_4-alkylene-$SO_2N(R^{10})R^{11}$;
wherein each of R^{10} and R^{11} independently is hydrogen; hydroxy; C_1-C_8alkyl; C_2-C_8alkenyl; C_3-C_8cycloalkyl; C_3-C_8cycloalkyl-C_1-C_8alkyl; C_1-C_8alkoxyC_1-C_8alkyl; hydroxyC_1-C_8alkoxyC_1-C_8alkyl; hydroxyC_1-C_8alkyl; (C_1-C_8alkyl)-carbonyl; arylC_1-C_8alkyl which optionally may be substituted on the ring by hydroxy, C_1-C_8alkoxy, carboxy or C_2-C_8alkoxycarbonyl; or 5 to 10 membered heterocyclic ring;
R^4 is hydrogen;
R^5 is hydrogen; halogen; C_{1-4}alkyl; or CF3;
R^6 is hydrogen;
each of R^7, R^8 and R^9 is independently hydrogen; hydroxy; C_1-C_8alkyl; C_2-C_8alkenyl; halo-C_1-C_8alkyl; C_1-C_8alkoxy; C_3-C_8cycloalkyl; C_3-C_8cycloalkylC_1-C_8alkyl; arylC_1-C_8alkyl; -Y-R^{12} wherein Y is a direct bond or O and R^{12} is a substituted or unsubstituted 5, 6 or 7 membered heterocyclic ring comprising 1, 2 or 3 heteroatoms selected from N, O and S; carboxy; (C_1-C_8alkoxy)-carbonyl; $-N(C_{1-8}$alkyl)-CO-$NR^{10}R^{11}$; $-CONR^{10}R^{11}$; $-N(R^{10})$ (R^{11}); -SO2N(R^{10})R^{11}; R^7 and R^8 or R^8 and R^9, respectively form together with the carbon atoms to which they are attached, a 5 or 6 membered heteroaryl comprising 1, 2 or 3 heteroatoms selected from N, O and S; or a 5 or 6 membered carbocyclic ring;
wherein any alkyl, alkoxy, alkenyl, cycloalkyl, heterocyclic ring, aryl or heteroaryl may be unsubstituted or substituted by one or more substituents selected from halogen; OH; C_1-C_8alkyl; C_1-C_8alkoxy; nitro; cyano; COOH; carbamoyl; $C(NH_2)$=NOH; $-N(R^{10})R^{11}$; C_3-C_6cycloalkyl; 3 to 7 membered heterocyclic ring; phenyl;

phenyl-C_{1-4}alkyl; 5 or 6 membered heteroaryl;

in free form or salt form.

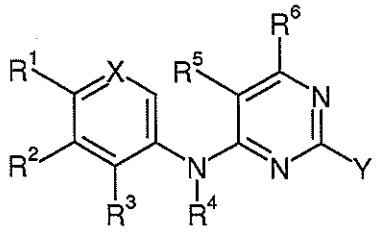
2. A compound according to claim 1 wherein at most one of R^1 or R^3 is $-CON(R^{10})R^{11}$.

3. A compound according to claim 1 which is a compound of formula X_4



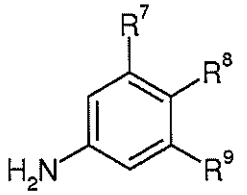
wherein R^2, R^5, R^7, R^8 and R^9 are as defined in claim 1.

4. A process for the production of a compound of formula I according to claims 1 to 3, comprising the steps of reacting a compound of formula II



(II)

wherein R^1, R^2, R^3, R^4, R^5, R^6 and X are as defined in claim 1, and Y is a leaving group;
with a compound of formula III



(III)

wherein R^7, R^8 and R^9 are as defined in claim 1;
and recovering the resulting compound of formula I in free form or in salt form, and, where required, converting the compound of formula I obtained in free form into the desired salt form, or vice versa.

5. A compound according to claims 1 to 3 in free form or in pharmaceutically acceptable salt form, for use as a pharmaceutical.

6. A pharmaceutical composition comprising a compound of formula I according to claims 1 to 3 or a pharmaceutically acceptable salt thereof, together with one or more pharmaceutically acceptable carriers or diluents therefor.

7. A compound of formula I according to claims 1 to 3 in free form or in pharmaceutically acceptable salt form, as a

pharmaceutical for use in the treatment or prevention of a disease or condition in which ZAP-70, FAK and/or Syk tyrosine kinase activation plays a role or is implicated.

8. A combination which comprises (a) a therapeutically effective amount of a compound of formula I according to claims 1 to 3 as a ZAP-70, FAK and/or Syk inhibitor and (b) a second drug substance.

Added matter by intermediate generalization

7. The requester considers that claim 1 comprises added matter at least by way of the definition of $R^2 = SO_2N(R^{10})R^{11}$ finding that the compounds having this substituent are not "singled out" in the parent. The requester considers the basis for the compounds having this substituent "represents a mosaicking of undisclosed combinations of selections from a number of lists of constituents, as well as undisclosed individual selections", see page 7 line 17-19 of the opinion request.

8. I have considered the precedent in this regard and consider Pumfrey J's observations as the guiding precedent when he described intermediate generalisation in *Palmaz's European Patents [1999] RPC 47* (at page 71) as follows:

> *If the specification discloses distinct sub-classes of the overall inventive concept, then it should be possible to amend down to one or other of those sub-classes, whether or not they are presented as inventively distinct in the specification before amendment. The difficulty comes when it is sought to take features which are only disclosed in a particular context and which are not disclosed as having any inventive significance and introduce them into the claim deprived of that context. This is a process sometimes called 'intermediate generalisation.*

9. Having regard to Pumfry J's comments I consider that the disclosure on pages 1 line 1 - page 2 line 10 of the parent encompasses the compounds of the present claims, therefore, I consider added matter may only arise having regard to intermediate generalisation. The passage on page 2, line 11 - page 3, line 13, of the parent comprises generalised statements clarifying the nature of the substituents of formula (I) and indicating which compounds are preferred. These passages place no particular context relevant to the basis for claim 1 and, in particular, place no particular context on the basis for $R^2 = SO_2N(R^{10})R^{11}$. I note the passage on page 3, lines 12-13, of the patent which states "preferably at most one of R^1, R^2 or R^3 is $CON(R^{10})R^{11}$ or $SO_2N(R^{10})R^{11}$, more preferably $SO_2N(R^{10})R^{11}$ ". Without any limiting context provided for the specified nature of R^2, I find that the context provided by page 1 line 1 – page 2, line 10, is the broadest in the description and that this passage provides an unambiguous basis for the subclasses of the patent. I consider the basis does not rely on a contextual mosaic of combinations of subclasses, or on selection from a number of separate lists.

10. Furthermore, the requester proposes that the passage on page 3, lines 12-13 of the patent, does not disclose the selection. However, taking the application as a whole, I note that table 4 of the parent as well as the patent at issue both disclose compounds of formula (I) that satisfy claims 1 and 3 including in relation to the provision that R^2, and only R^2, of $R^{1-3} = SO_2N(R^{10})R^{11}$. I consider the skilled person

finding these compounds so disclosed would be reassured that the scope of the invention, correctly construed, encompasses these compounds. As a consequence, I am of the view that claim 1 is not an intermediate generalisation over the disclosure in the parent and, as such, I do not consider that claim 1 comprises added matter.

11. As regards the other claims of the patent, I consider claim 2 finds basis in the passages on page 3 line 12-13 particularly when considered in light of the entire description. The skilled person would be reassured that the scope of the invention, if correctly construed encompasses these compounds on finding a compound that satisfies claim 2 as defined in the parent application and the patent (example 54). Claim 4 finds basis in page 5 line 1-6. Having found basis for the compounds of the present invention the use of these compounds is disclosed in the description page 26 line 20-page 29 line 23. Accordingly none of the claims of the patent are considered to comprise added matter.

Novelty

12. To justify a finding that the claims of the patent lack novelty I consider I must find, not only a description of the compound in the prior art, but additionally that the disclosure is "enabled" such as by some indication of how the compound is prepared. Particularly having regard to the anticipation of Markush claims, I am assisted by LJ Jacob's comments in *Dr Reddy's Laboratories (UK) Ltd v Eli Lilly & Co. Ltd* when he said *"logic dictates rejection of the argument that a disclosure of a large class is a disclosure of each and every member of it"* and that *"only a technical teaching of this kind can be prejudicial to novelty, If any such teaching is to apply in the case of a chemical substance, an individualised description is needed"*. I can find no individualised description of a compound in the prior art, and means to prepare it, that falls within the scope of the patent, therefore as regards claims 1, 3, 5 and 8. I do not consider there is a novelty destroying disclosure as I would interpret it having regard to LJ Jacob's comments above.

13. The observer proposes that the documents of the prior art anticipate the patent in a different way, insofar as they define Markush formulae that overlap with the Markush formulae defined in the claims of the patent - such a situation is sometimes referred to as "generic overlap". The observer disagrees that this would amount to a novelty destroying disclosure when they say, "However ... the applicant for the opinion has not stated which example [from the prior art document] may take novelty of the instant patent claims", page 3-4 of the letter in response to the request dated 23 May 2017. I agree with the observer that the Markush formulae of the prior art overlap with those of the patent, but need to consider how relevant this is to a consideration of novelty. Whereas the EPO would consider the degree of generic overlap to be a matter of assistance in determining anticipation, it is a matter of practice at this office to consider generic overlap of claims with regard to inventiveness rather than novelty. See "Examining patent applications relating to chemical inventions" June 2017 paragraph 90.This approach arises from LJ Jacob's comments that I have indicated above, without an enabled individualised description of a compound of the present claims novelty is not considered relevant in this jurisdiction. I will however proceed to consider this further under inventive step.

Inventive step

14. In the statement dated 19 April 2017 the requester makes separate attacks on the inventive step of claim 1 having regard to Windsurfing Pozzoli (pages 17-page 18 line 29 with reference to D1-D4 and with regard to D5 on page 19 line 6-page 20 line 8).

15. To determine whether or not an invention defined in a particular claim is inventive over the prior art, I will rely on the principles established in *Pozzoli SPA v BDMO SA [2007] EWCA Civ 588*, in which the well known Windsurfing steps were reformulated:

> *(1)(a) Identify the notional "person skilled in the art";*
> *(1)(b) Identify the relevant common general knowledge of that person;*
> *(2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;*
> *(3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;*
> *(4) Viewed without any knowledge of the alleged invention as claimed, determine whether those differences constitute steps which would have been obvious to the person skilled in the art.*

Step 1a - identify the skilled person

16. The requester has determined the skilled person to be "skilled in the selecting and producing [of] pharmaceutical compounds and compositions, particularly compounds and compositions that modulate kinases such as tyrosine kinases", the observer has made no comment on this choice, and I consider this to be a fair assessment of the nature of the person skilled in the art.

Step 1b – what is their common general knowledge

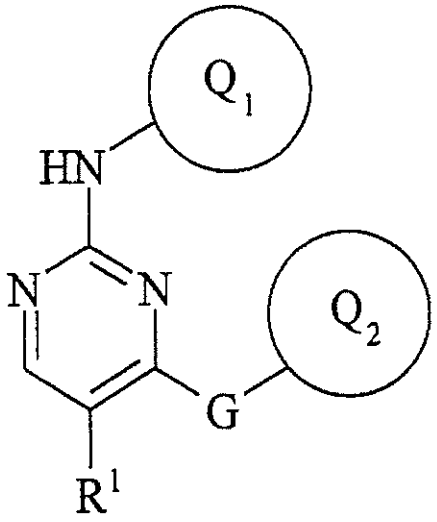
17. As regards common general knowledge the requester has characterised the skilled person to be "familiar with selecting and producing known pharmaceutical compounds and compositions, and would be able to modify such compounds and compositions with the aim of achieving a pharmaceutical effect. They would be familiar with the chemical, physical and pharmacological characteristics of such known pharmaceutical compounds and compositions". I consider this reasonable as far as it goes but would add that the skilled person would understand the common general knowledge would include the fact that structural modifications could provide benefits as regards enhanced activity *in vivo* and that the skilled person would be aware of *in vitro* tests that would facilitate determining which compounds would be likely targets.

Step 2 – identifying the inventive concept or construing the claim

18. Construing the main claim of the patent is relatively easy, the compounds encompassed albeit large in number are clearly set out in claim 1.

Step 3 – what differences exist between the state of the art and the inventive concept

19. Turning first to documents D1-D4, I consider that they differ from the claimed compounds of the patent in that they do not share the same core of the Markush Formula , however the Markush formulae of documents D1-D4 overlap considerably with the present claims. I will illustrate this with D3. Claim 1 of D3 defines certain pyrimidines based on the formula:



D3 overlaps with the present claims as regards the substituents at position R^2 of the patent in that Q_1 and Q_2 are independently selected from aryl... ; and one of Q_1 and Q_2 or both Q_1 and Q_2 is substituted on a ring carbon by one group selected from sulphamoyl, N-(C_{1-4}alkyl)sulphamoyl (optionally ...) N,N-di-(C_{1-4} alkyl)sulphamoyl..." so whereas D3 defines a large number of compounds these include compounds within the scope of the patent.

20. As regards D5, I have been directed by the observer to consider the compound of example 74, where $R_1 = SO_2NH_2$, this is within the scope of $SO_2N(R^{10})R^{11}$ as defined in the present invention, but example 74 is substituted at position R^2 of formula (I) rather than at position R^1. Thus the difference between the prior art and the inventive concept is the provision of compounds of formula (I) wherein the sulphonamide group is at position R^2 (meta) rather than R^1 (para).

Step 4 – Are the differences obvious?

21. Having regard to D1-D4, I consider that the compounds of the patent are not inventive *per se* insofar as compounds of the patent are encompassed by the prior art. However given that the inventions of D1-D4 propose a vast number of compounds and that invention may lie in the selection of the compounds of the patent, I will go on to consider if the selection itself is inventive (see below).

22. As regards D5, I have not been supplied with any specific evidence that would lead the skilled person to choose the para to meta substitution or anything to provide any

particular expectation that making such a change to Example 74 would be favourable, and as such, I do not find Example 74 of D5 to show that the present claim 1 is obvious. Nonetheless D5, like D1-D4, shows considerable generic overlap with the claims of the patent, thus I consider there is *prima facie* obviousness and will include it in my consideration as to whether or not the selection of the compounds of the patent are inventive.

Selection Invention

23. Having found *prima facie* obviousness with respect to any of the documents D1-D5, I will now consider if the selection of the compounds of claim 1 itself represents an inventive step. In doing so I have considered the available case law that can guide me. In this regard, *Dr Reddy's Laboratories (UK) v Eli Lilly & Co Ltd [2010] RPC 9* requires that I consider whether the selection makes a hitherto unknown technical contribution or is merely arbitrary. Further assistance is provided in *Generics [UK] Ltd v Yeda Research and Development Co. Ltd [2013] EWCA Civ 925* which sets out certain factors that are helpful in deciding this question (I have added the text in square brackets):

> *i) Article 56 of the EPC [concerning inventive step] is in part based on the underlying principle that the scope of the patent monopoly must be justified by the patentee's contribution to the art;*
> *ii) If the alleged contribution is a technical effect which is not common to substantially everything covered by a claim, it cannot be used to formulate the question for the purposes of judging obviousness;*
> *iii) In such circumstances the claim must either be restricted to the subject matter which makes good the technical contribution, or a different technical solution common to the whole claim must be found;*
> *iv) A selection from the prior art which is purely arbitrary and cannot be justified by some useful technical property is likely to be held to be obvious because it does not make a real technical advance;*
> *v) A technical effect which is not rendered plausible by the patent specification may not be taken into account in assessing inventive step;*
> *vi) Later evidence may be adduced to support a technical effect made plausible by the specification;*
> *vii) Provided the technical effect is made plausible, no further proof of the existence of the effect is to be demanded of the specification before judging obviousness by reference to the technical effect propounded.*

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.

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.

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.

28. Having found that the invention of claim 1 is obvious by the same reasoning any of the claims 2-8 appended thereto are also not inventive.

Insufficiency

29. The requester proposes that claims 7 and 8 are insufficient "for lack of an adequate definition of a medical indication..." specifically that "the skilled person would incur *prima facie* undue burden to work the claimed invention as this would require the skilled person to derive which indications, known and not-yet known, fall within the full scope of the claim" see page 10 of the original request.

30. The observer counters this view by pointing out the tests indicated in the description show "target related support of pharmacological efficacy" and additional support for example on page 26/27 [of the patent], where indications pertaining to ZAP-70 inhibition or Syk inhibition are tested"

31. I have considered the application as filed and note that the description indeed provides methods showing how a target compound may be identified as inhibiting ZAP-70 (beginning at the foot of page 21), FAK (beginning at the foot of page 24) and/or Syk protein tyrosine kinase (beginning second paragraph on page 22), and that particular conditions "where ZAP-70 inhibition and/or Syk inhibition play a role" on page 26 (see third paragraph) or "conditions connected with FAK" are listed on page 27, second paragraph.

32. I must determine if these disclosures, and anything else in the description as filed, disclose the inventions of claims 7 and 8 clearly and completely enough for it to be performed by the person skilled in the art. To assist in this I have considered the relevant case law and found that I am assisted in reaching a conclusion having regard to two pieces of case law, *T241/95 (Eli Lilly and Company)* and *Kirin-Amgen Inc. and Ors. v Hoechst Marion Roussel Ltd & Ors. [2005] RPC 9* "hereafter Kirin-Amgen" to be relevant. I will consider the relevance of these in turn.

33. The patent considered in T241/95 and the present patent share claims that rely on a mechanism for the definition of conditions to be treated, wherein those conditions limit the scope of the claim. In particular in the case of T241/95 "R-fluoxetine... for the preparation of a medicament for treating a mammal suffering from, or susceptible to a condition which is capable of being improved or prevented by selective occupation of the 5-HITC receptor". This I find comparable to the present claim 7, "A compound of formula I ...as a pharmaceutical for use in the treatment or prevention of a disease or condition in which ZAP-70, FAK and/or Syk tyrosine kinase activation plays a role or is implicated."

34. The decision makes clear that reciting conditions that respond to R-fluoxetine does not itself render the claims clear and sufficient.

> *"due to the functional definition of the claimed subject-matter, the scope of claim 1 is not limited to the treatment of said specified conditions but, by contrast, embraces an undefined number of other conditions all allegedly capable of being improved or prevented by the selective occupation of the 5HTIC receptor. Under these circumstances, the independent claim can only be regarded as clear if means are available to the skilled person for assessing whether or not an additional condition, not expressly cited in the application, but nevertheless affected by the administration of (R)-fluoxetine is comprised in the scope of claim 1."*

35. Therefore, applying this reasoning to the present application, I need to determine if the tests provided in the application and/or the common general knowledge enables the skilled person to determine in which diseases or conditions, ZAP-70, FAK and/or Syk tyrosine kinase activation plays a role or is implicated. The observer has not provided any evidence in this regard but, whereas the tests indicated propose how to select compounds that show pharmacological efficacy, I do not consider the tests provided enable conclusions to be drawn of the relevance of the respective kinases to particular diseases/conditions. I have considered the admitted art and similarly find no overarching test by which the relevance of a kinase to a disease state can be determined, therefore, I do not find the invention of claim 7 to be disclosed clearly and completely enough for it to be performed by the skilled person. As a result, I

consider that claim 7 is invalid having regard to section 14(3) of The Act.

36. Claim 8 relates to a combination of a ZAP-70, FAK and/or syk inhibitor with a second drug. Insofar as it additionally requires a therapeutically effective amount to be derived, it implicitly requires a condition/disease to be identified, and, as a consequence, it suffers from the same deficiency as claim 7.

37. As regards Kirin-Amgen, I find further support for my conclusion that claims 7 and 8 are insufficient. In this judgment Lord Hoffman provided an example of how a lack of clarity can in the most egregious examples amount to insufficiency

> *"If the claim says that you must use an acid, and there is nothing in the specification or context to tell you which acid, and the invention will work with some acids but not with others but finding out which ones work will need extensive experiments, then that in my opinion is not merely lack of clarity; it is insufficiency. The lack of clarity does not merely create a fuzzy boundary between that which will work and that which will not. It makes it impossible to work the invention at all until one has found out what ingredient is needed."*

38. I consider the present patent analogous to this example in Kirin-Amgen. In the absence of a test to determine in which diseases or conditions ZAP-70, FAK and/or Syk tyrosine kinase activation plays a role or is implicated, the addressee is left in irresolvable doubt as to which diseases or conditions are in scope. The fact that some diseases and conditions are stated to be in scope does not, in my opinion, overcome the insufficiency across the entire scope of claims 7 and 8. Accordingly, I consider claims 7 and 8 are invalid having regard to section 14(3) of the Act in that they are insufficient due to ambiguity.

39. I have not specifically been asked by the requester to provide an opinion on the sufficiency of claims 1-6, however under the heading of inventive step the initial observations (at page 18 line 31-page 19 line 2) is the comment, "separately it is not credible that the inventive concept has been solved over the entire scope of claim 1, which relates to an incredibly large number of compounds". This statement leaves me in some doubt as to what the requester intends that I consider. In the context of inventive step this comment may be considered to allude to "AgrEvo obviousness" In *AgrEvo/Triazole sulphonamides, T 939/92 [1996] EPOR 171*, hereafter "AgrEvo", it was held that a patent specification must include credible or plausible basis for the technical contribution in an entire class of compounds claimed. However given that I have not been explicitly asked to consider AgrEvo obviousness and because this case law is entirely founded on the problem solution approach, which is not the conventional test for examining obviousness in the UK, I am not minded to consider the question in this way. As an alternative I will consider the question as to whether or not it is credible that the invention is sufficiently disclosed to enable it to be worked across its entire scope. I have reformulated the question arising from the request in this way to limit the scope of this question to sufficiency and to not stray into considerations of obviousness which I have already considered.

40. I have considered the vast range of compounds defined in the patent claims and consider that the task of their preparation is one that the skilled addressee could (if given enough time) conduct on the basis of their common general knowledge in preparative chemical techniques. Therefore I do not consider that the claims 1-6 are

insufficient.

Opinion

41. In summary, I consider that claims 1, 3, 5 and 8 of the patent are novel and none of the claims comprise added matter. However, I consider that all the claims are obvious. I also consider that claims 7 and 8 are invalid in that they are not disclosed clearly and completely enough to be performed by the skilled person in the art.

Application for review

42. Under section 74B and rule 98, the proprietor may, within three months of the date of issue of this opinion, apply to the comptroller for a review of the opinion.

Jason Bellia
Examiner

NOTE

This opinion is not based on the outcome of fully litigated proceedings. Rather, it is based on whatever material the persons requesting the opinion and filing observations have chosen to put before the Office.