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## DECISION of 16 March 2006

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Case Number:	T 0604/04 - 3.3.0
Application Number:	92910478.4
Publication Number:	0577752
IPC:	C12N 15/12

Language of the proceedings: EN

Title of invention: Human PF4A receptors and their use

**Patentee:** GENENTECH, INC.

**Opponent:** SmithKline Beecham plc

Headword: PF4A receptors/GENENTECH

Relevant legal provisions:

EPC Art. 56, 57, 83

Keyword:
"Main request - claims 21 and 22 - sufficiency of disclosure no"
"Auxiliary request I - inventive step - yes"
"Auxiliary request I - industrial applicability - yes"

Decisions cited: T 0338/00, T 0870/04, T 1329/04, G 0009/92

Catchword:

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Boards of Appeal

Chambres de recours

**Case Number:** T 0604/04 - 3.3.08

### D E C I S I O N of the Technical Board of Appeal 3.3.08 of 16 March 2006

<b>Appellant:</b> (Proprietor of the patent)	GENENTECH, INC. 460 Point San Bruno Boulevard South San Francisco California 94080 (US)
Representative:	Armitage, Ian Michael Mewburn Ellis LLP York House 23 Kingsway London WC2B 6HP (GB)
<b>Respondent:</b> (Opponent)	SmithKline Beecham plc 2 New Horizons Court Great West Road Brentford, Middx TW9 9EP (GB)

Representative:	Easeman, Richard, L. Dr. GlaxoSmithKline	
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Decision under appeal: Interlocutory decision of the Opposition Division of the European Patent Office posted 26 February 2004 concerning maintenance of European patent No. 0577752 in amended form.

Composition of the Board:

Chairman:	L.	Galligani
Members:	F.	Davison-Brunel
	s.	Perrvman

#### Summary of Facts and Submissions

I. European patent No. 0 577 752 with the title "Human PF4A receptors and their use" was granted on the basis of the European patent application No. 92 910 478.4 published as WO 92/17497, with 22 claims for all Designated Contracting States except ES and GR and 30 claims for the Designated Contracting States ES and GR.

Claims 1 to 3, 17, 21 and 22 (for all non-ES, non-GR States) read as follows:

"1. An isolated platelet factor 4 superfamily receptor (PF4AR) polypeptide having at least an 85% amino acid sequence homology with the translated amino acid sequence of figures 2, 4 or 5.

2. An isolated PF4AR polypeptide wherein the nucleic acid encoding the PF4AR polypeptide hybridises with the complement of the nucleic acid encoding the polypeptide of figures 4 or 5 under high stringency conditions.

3. An isolated PF4AR polypeptide comprising an amino acid sequence that is at least 10 residues in length and is contained in an extracellular region of the polypeptide of figure 4 or 5 and is capable of raising an antibody that will cross-react with the polypeptide of figure 4 or 5.

17. A monoclonal antibody that is capable of specifically binding the PF4AR polypeptide according to any one of claims 1 to 5.

21. A composition comprising the monoclonal antibody of any one of claims 17 to 20 and a pharmaceutically acceptable carrier.

22. A monoclonal antibody of any one of claims 17 to 20 for use in therapy or diagnosis."

Dependent claims 4 to 9 related to further features of the polypeptide of respectively claim 3, 1 to 4, 1 and of any one of the preceding claims. Claims 10 to 12 and 13 respectively related to nucleic acids and an expression vector encoding /comprising the sequence of the PF4AR polypeptide of any one of the preceding claims. Claims 14, 15 and 16 respectively related to a host cell transformed with the expression vector of claim 13 and to methods of using a nucleic acid sequence encoding the PF4AR polypeptide of any one of the preceding claims. Claims 18 to 20 related to monoclonal antibodies capable of binding the PF4AR polypeptide of Figure 2, 4 or 5 or to fragments thereof.

Corresponding claims were granted for the Designated Contracting States ES and GR.

II. An opposition was filed under Article 100(a) to (c) EPC for reasons of lack of novelty, lack of inventive step, insufficiency of disclosure, added subject-matter and non-compliance with Articles 52(2) and 57 EPC.

> The opposition division maintained the patent in amended form on the basis of the second auxiliary request then on file comprising 17 claims corresponding to granted claims 1, 6 to 19, 21 and 22 insofar as they

directly or indirectly related to the translated amino acid of Figure 2. The corresponding claims were maintained for the Designated Contracting States ES and GR.

- III. The opposition division rejected all claims directly or indirectly relating to the translated amino acid sequences of Figure 4 or 5 for lack of inventive step and lack of industrial applicability. In its opinion, cloning the DNA encoding these polypeptides was an obvious task and the polypeptides themselves had not been characterised as having technically useful properties, or a credible function. In this respect, reference was made to Rule 23e(3) EPC and Recital 23 of the EU Directive 98/44/EC of 6 July 1998.
- IV. The appellant (patentee) filed an appeal and submitted a statement of grounds of appeal together with seven new documents.
- V. The board sent a communication pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal identifying the issues to be discussed at oral proceedings and stating its preliminary non-binding opinion.
- VI. Observations were received by a third party under Article 115 EPC on 8 December 2005.
- VII. The respondent (opponent) who had not hitherto made any submissions during the appeal proceedings advised the board by its letter dated 11 January 2006 that it would not attend the oral proceedings.

- VIII. In answer to the board's communication, the appellant filed a further submission together with four auxiliary requests and six new documents.
- IX. Oral proceedings took place on 16 March 2006. The four auxiliary requests were abandoned and a new auxiliary request I was filed.

Auxiliary request I for all designated contracting states except Spain and Greece comprised 32 claims. Claims 1 to 17 were the claims accepted by the opposition division, namely granted claims 1, 6 to 19, 21 and 22 directly or indirectly relating to the translated amino acid sequence of Figure 2. Claims 18 to 32 were the granted claims 1 to 4, 7, 10 to 17, 19 and 20 directly or indirectly relating to the translated amino acid sequence of Figure 4 or 5. Claims 18 and 30 read as follows:

"18. An isolated platelet factor 4 superfamily receptor (PF4AR) polypeptide having at least an 85% amino acid sequence homology with the translated amino acid sequence of figure 4 or figure 5.

30. A monoclonal antibody that is capable of specifically binding the PF4AR polypeptide according to any one of claims 18 to 21."

The request did not comprise claims corresponding to granted claims 21 and 22 (section I, supra).

The corresponding claims were filed for Spain and Greece.

- X. The following documents are mentioned in the present decision:
  - (1) : Grob, P. M. et al., The Journal of Biological Chemistry, Vol. 265, No. 14, pages 8311 to 8316, May 1990;
  - (2) : Holmes, W. E. et al., Science, Vol. 25, pages 1278 to 1280, September 1991;
  - (22) : Stoeckle, M. Y. and K. A. Barker, The New Biologist, Vol. 2, No. 4, pages 313 to 323, April 1990.
- XI. The appellant's arguments in writing and during oral proceedings which are relevant for the present decision may be summarised as follows:

Main request, claim 1 relating to an isolated PF4AR polypeptide with the translated amino acid sequence of Figure 4 or 5.

Article 56 EPC; inventive step

Document (2) embarked on characterising the receptors for known cytokines beginning with the IL-8 receptor resulting in the cloning of the sequence of Figure 2. So one could postulate a future extension of the work in document (2) looking for the receptors to the other known cytokines of that family. If one were to go down that route, one might follow an expression cloning route as was done for the Fig. 2 receptor but one would not naturally follow a route of hybridisation screening using the Fig. 2 sequence since one would not know the extent of homology with the Fig. 2 sequence and therefore not know what conditions to use.

The remarkable thing about the work that led to the Fig. 4 and Fig. 5 sequences was that they were in fact found by hybridisation screening. Since their ligands were not known, there was no reason to suppose that they even existed. And the very fact that these turned out to be receptors whose ligands were not known meant that they could not have been found by the ligand screening method used for the sequence of Fig. 2.

Para. [0164] of the printed patent was not reflecting any doubt that the polypeptides of Figures 4 and 5 were members of a family of receptors: they had structural and homology features that rendered it plausible to hold that belief. The fact that they resembled the IL-8 receptor more than any other receptors added confidence to the belief that they belonged to the PF4AR family of receptors. The fact that they did not bind to the other known ligands so far tested did not mean that they should not be regarded as part of that family, since they may bind to other PF4A ligands that had not yet been discovered or tested.

In summary, the inventive step comprised the following contributory elements: (a) uncertainty as to whether there was anything there to find, (b) uncertainty as to the experimental methodology appropriate to find them (if they existed), and (c) the difficulty in deploying what turned out to be the appropriate methodology.

#### Article 57 EPC; industrial applicability

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The prior art itself recognised the therapeutic potential surrounding the chemokines and their receptors in connection with inflammation and wound healing in particular, so the common general knowledge appreciated those important practical aspects that would flow from the identification of chemokines and their receptors.

The very fact that much about the particular biology of these molecules remained to be elucidated made it important to have research tools for that purpose. One of the most important research tools in that connection would be antibodies, particularly monoclonal antibodies. The antibody research tools resulting from the invention did not require knowledge of the ligands and indeed were probably important in identifying them. But beyond that, an antibody that blocked the receptor and thereby produced a useful physiological effect of therapeutic potential did not require that one knew the identity of the ligand. Diagnostic use of the DNA, protein and antibodies to PF4A receptors was mentioned on pages 20 to 22 of the patent in suit, in a variety of contexts.

Right from the outset, if new PF4A receptors were found, there was obviously going to be a demand for the proteins themselves and antibodies to the proteins, if only for the purpose of finding more about them. So at the very least a claim to antibodies to the proteins of Figures 4 or 5 should certainly be regarded as capable of industrial application. This was also true for the receptors themselves which were being used in the industry that commercially made the antibodies.

The situation was different from the situation described in T 870/04 of 11 May 2005 for BDP1 which suggested a role in complex cellular signal transduction or cellular housekeeping but without identifying any therapeutic use whereas the present patent clearly and unequivocally identified a role for antibodies to the receptors of Fig. 4 and 5 in antiinflammatory treatment [par.0151].

In the case dealt with in decision T 338/00 of 6 November 2002, the description contained references to the possible relevance of the disclosed heterodimers in several physiological processes. The board concluded on this basis that the products disclosed in the application were aimed at a direct technical result that may clearly be applied in an industrial activity and, in consequence, held that the claimed subjectmatter fulfilled the requirements of Article 57 EPC. It was very much the case with the present invention also. This family of chemokines were of intense interest because of their already known activities. Therefore the identification of their receptors and consequent derivation of antagonizing molecules such as antibodies to the receptors had obvious practical implications which justified acknowledgment of industrial applicability.

Claims 21 and 22 relating to a composition comprising a monoclonal antibody against either of the polypeptides of Figure 4 or 5 and to a monoclonal antibody against said polypeptides for use in therapy and diagnosis. Article 83 EPC; sufficiency of disclosure

A monoclonal antibody that is capable of specifically binding the PF4AR polypeptide of Figure 4 or 5 was a monoclonal antibody directed against the receptor of a member of the PF4A family of chemokines. These chemokines were known to mediate inflammation. By providing the monoclonal antibody, the appellant provided for the first time a means to fight inflammation. Accordingly, claims to a pharmaceutical composition or to a first medical indication should be allowed.

XII. The third party's submissions under Article 115 EPC insofar as relevant to the present decision may be summarised as follows:

Main request; claim 1 relating to an isolated PF4AR polypeptide with the translated amino acid sequence of Figure 4 or 5.

Article 56 EPC; inventive step

The closest prior art was document (2) and the objective problem to be solved could be formulated as the provision of receptors for further members of the IL-8 family of cytokines. This aim was already mentioned in said document and, thus, the criterion "obvious to try" was satisfied.

The criterion "reasonable expectation of success" was also answered in the affirmative as the positive clones comprising the DNA encoding the polypeptides of Figure 4 or 5 were identified without any difficulties by the classical method of DNA hybridisation to a known probe. In addition, the patent in suit did not provide any data that the alleged receptors bound ligands, in fact no effect was associated with them. Thus, inventive step could not be acknowledged on the basis of the properties of the newly isolated molecules, either. For these reasons, the requirements of Article 56 EPC were not fulfilled.

## Article 57 EPC; industrial applicability

The standards to be fulfilled for industrial applicability to be acknowledged were clearly identified in the earlier decision T 870/04 (Headnote; supra). The patent in suit did not identify the ligands to the claimed receptors, only hypothesizing that once they were identified, then they could be used for diagnosis. The claimed polypeptides were only "believed" to represent receptors for different and as yet undetermined members of the PF4 superfamily. The indication that the DNA of Figures 4 and 5 would be useful for diagnosis was highly speculative. These mere assumptions did not fulfil the above mentioned standards. The requirements of Article 57 EPC were not fulfilled.

XIII. The appellant requested that the decision under appeal be set aside and that the patent be maintained as granted as main request or on the basis of auxiliary request I filed at the oral proceedings on 16 March 2006. In its submission dated 11 January 2006, the respondent requested that the decision of the opposition division be maintained.

## Reasons for the decision

1. The patent proprietor is the sole appellant against the interlocutory decision maintaining the patent in amended form on the basis of the second auxiliary request only comprising claims directly or indirectly relating to the translated amino acid sequence of Figure 2. In accordance with the Enlarged Board of Appeal's decision G 9/92 (OJ EPO 1994, 875), the maintenance of the patent on the basis of this set of claims cannot be challenged. The appeal is, thus, confined to assessing the validity of the decision of the first instance concerning the claimed subjectmatter defined in relation to the translated amino acid sequences of Figure 4 or 5.

Main request for all designated contracting states except Spain and Greece Claim 1 to an isolated PF4AR polypeptide having at least an 85% sequence homology with the translated amino acid sequence of Figure 4 or 5.

Article 56 EPC; inventive step

2. The patent in suit claims priority from the two priority documents US 677 211 and US 810 782 respectively filed on 29 March 1991 and 19 December 1991. There is no disclosure of the polypeptides having the amino acid sequences of Figure 4 or 5 in the first of these priority documents. Claim 1 is, thus, not

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entitled to the first priority date. Consequently, document (2) which was published in September 1991 is part of the state of the art and may be considered when evaluating inventive step. In fact, it is the closest prior art.

3. Document (2) describes the structure and functional expression of a human interleukin-8 receptor. On page 1278, IL-8 is defined as a chemoattractant for neutrophils which belongs to the superfamily of proinflammatory cytokines (also known in the art as the PF4A superfamily). In the passage bridging the first and second column, it is mentioned that:

> "In order to better understand the range of activities exhibited by this family of cytokines, we have begun to characterize the family of receptors with which they interact, beginning with the IL-8 receptor".

> The cloning of the DNA encoding the IL-8 receptor is achieved using a strategy involving the expression of the receptor in the positive recombinant clones which are accordingly identified by their ability to bind to <sup>125</sup>I-labeled IL-8, ie the screening of the positive clones involves the use of the receptor's specific ligand. On the basis of a comparison between the IL-8 receptor sequence and those of two other neutrophil chemoattractants, it is suggested that the IL-8 receptor belongs to the subfamily of related G proteincoupled receptors that transduce signals for the IL-8 family of pro-inflammatory cytokines (page 1280, lefthand column).

4. Starting from the closest prior art, the problem to be solved may be defined as pursuing the characterisation of receptors interacting with members of the PF4A family of cytokines.

5. The solution provided is the two polypeptides of Figures 4 and 5. The first question which arises is whether or not these are bona fide solutions to the above defined problem. In accordance with the case law (T 1329/04 of 28 June 2005),

> "the definition of an invention as being a contribution to the art, i.e. as solving a technical problem and not merely putting forward one requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem it purports to solve."

- 6. The patent in suit discloses in section [0164] with reference to the polypeptides of Figures 4 and 5 that: "Like the IL-8 receptor of Fig. 2 they are members of the G-protein-coupled superfamily" and also in section [0169], that the amino acid sequences of Figures 4 and 5 respectively share 34% and 38% identity with the IL-8 receptor. The ligands of these polypeptides are not identified. For this reason, there is no absolute certainty that the polypeptides of Figures 4 and 5 are receptors for members of the PF4A family of cytokines to which IL-8 belongs -. Yet, in the board's judgment, the above mentioned structural features make it plausible that this is indeed the case.
- 7. In this context, it is worth noticing that the situation is different from that encountered in the

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decision T 1329/04 (supra) where it was not accepted that the polypeptide SEQ ID No. 3 then claimed was a member of the TGF- $\beta$  superfamily. In this earlier case, in addition to the fact that the polypeptide had not been shown to have any function, its structure did not conform to that expected from members of this family and the expected sequence homology to previous members of the family was not present.

- 8. Having concluded in the affirmative as regard the plausibility that the molecules of Figures 4 and 5 are receptors for members of the IL-8 family of cytokines, the second question to be answered is whether or not they may be considered inventive.
- 9. Document (2) discloses a straightforward and successful method for the isolation of the IL-8 receptor, namely by using an expression cloning strategy (point 3, supra). Document (22), a review reflecting the common general knowledge on chemokines at the filing date teaches that numerous such molecules had already been identified (see in particular Table 1). The obvious way for the skilled person to solve the above mentioned problem of finding the receptors for chemokines would, thus, have been to proceed as in document (2), using radiolabelled derivatives of the chemokine of interest to identify which recombinant clones would bind to it, ie which recombinant clones expressed the corresponding receptor. The appellant chose to proceed differently; it used IL-8 cDNA for probing under low stringency conditions cDNA libraries made from cells for which IL-8 was a chemoattractant (HL-60, document (1), abstract; lymphocytes, document (22), Table 3). In doing so, it provided the possibility of isolating

receptors irrespective of the proteins they were receptor for. This course of action was undoubtedly unexpected and, beside, it was fraught with uncertainties given that low stringency conditions of hybridisation might result in the isolation of cDNA artefacts. Had this different method not been chosen instead of the expression cloning strategy, the two molecules of Figures 4 and 5 would not have been isolated. Thus, inventive skills were exercised when isolating the claimed polypeptides which imply that they are patentable providing that they fulfil the further requirements for patentability.

- 10. Of course, claim 1 is not restricted to the polypeptides of Figures 4 and 5 but is rather directed to PF4AR receptor polypeptides having at least 85% homology with the amino acid of Figures 4 or 5. In the board's judgment, this does not alter the findings on inventive step insofar as firstly, the claimed "85% homologous" polypeptides have to belong to the PF4AR family of receptors and secondly, inventive step was acknowledged on the basis of the method of isolation of the relevant clones being unexpected.
- 11. All further claims which are within the scope of the appeal (see point 1, supra) directly or indirectly relate to the translated amino acid sequences of Figures 4 and 5. Consequently, they fulfil the requirements of Article 56 EPC.

Article 57 EPC; industrial applicability

12. The technical information in the patent in suit relating to the polypeptides of Figures 4 and 5 is

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found in sections [0164], [0168] and [0169], with a short reference to the probe used for the isolation of the corresponding cDNAs on page 6, lines 37 to 39. Section [0168] describes the relevant cloning method. In section [0169], it is disclosed that the polypeptides themselves are respectively 34% and 36% identical to the IL-8 receptor. In section [0164], the polypeptides of Figure 4 or Figure 5 are identified as members of the G-protein-coupled superfamily of receptors and it is observed that they bear greater similarity to the IL-8 receptor than other receptors. The recombinant cells bearing them are said not to respond to the specific chemokines of the PF4A family which had been tested, whether they be from the CXC subfamily (IL-8 itself, MGSA) or from the CC subfamily (Rantes, MCP1). It can be inferred from the remainder of the description that, like the IL-8 receptor, the polypeptides of Figures 4 and 5 could be used, in particular, to isolate monoclonal antibodies (Mab) which, in turn, may be suitable to inhibit the inflammatory response due to the natural chemokine ligand (eg sections [0146] and [0147]).

13. In summary, the patent in suit identifies applications for the claimed polypeptides which may ultimately lead to some profitable use. It provides a structural characterisation which enables their assignment to the category of receptors which bind members of the PF4A family of chemokines and, insofar, indicates what their function might be. Yet, in the absence of any characterisation of their ligands, this function remains at best incompletely understood. 14. The earlier decision T 870/04 (supra) identified a number of criteria which had to be fulfilled for industrial applicability to be acknowledged. In particular, it is stated in point 6 of the "Reasons for

the Decision" that:

"(3) In cases where a substance, naturally occurring in the human body, is identified, and possibly also structurally characterised and made available through some method, but either its function is not known or it is complex and incompletely understood, and no disease or condition has yet been identified as being attributable to an excess or deficiency of the substance, and no other practical use is suggested for the substance, then industrial applicability cannot be acknowledged."

- 15. The board agrees with the criteria defined in T 870/04 and observes that, taken in isolation, the technical data provided in respect of the polypeptides of Figures 4 and 5 fall somewhat short of fulfilling them insofar as, as already above mentioned, there is no evidence available as to which ligands these polypeptides bind to. Yet, of course, each case has to be considered on its own merit (see eg. T 338/00 of 6 November 2002) and it is important here to take into account the common general knowledge at the priority date as well as the then prevalent attitude of the person skilled in the art as it may be inferred from the documents illustrating this common general knowledge.
- 16. In 1991, chemokines were already known as mediators of the inflammatory response, a role which most of them were thought to play, in particular, through being

chemoattractants (document (22), page 313, left-hand column and Table 3). Chemoattraction implies a biological interaction of the chemokines with the cells which they attract which involves binding to the receptors present on the cell surface. Thus, the skilled person would understand that any role of a given chemokine was reflected in its receptor.

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17. It is striking that at that date, there seems to have been a wider acceptance of the practical importance of chemokines than that to be attributed to specific members of the family. Indeed, it is mentioned on page 320 of document (22):

> "The PF4-related proteins comprise two families of small secreted peptides... These proteins function as chemoattractants, activating agents, and mitogens for specific types of cells that are involved in the inflammatory response. One of the major challenges is to determine the biological activities of each of these closely related peptides....Other important areas for investigation are to unravel the pathways of signal transduction that lead to induction of these genes and to identify the receptors and signal transduction pathways that are activated by these proteins. Finally, the PF4-related proteins are attractive targets for the development of new therapeutic agents. Inhibition of their activity may be an effective anti-inflammatory strategy and promoting that activity might enhance wound healing and tissue repair." (emphasis added by the board).

18. It is clear from this statement that chemokines as a family were considered not only to be interesting in

fundamental research but also as important for the pharmaceutical industry **irrespective** of whether or not their role had been clearly defined. It follows that their receptors must have been considered equally important since the mode of action of chemokines is through their receptors. It is, thus, reasonable to conclude that the polypeptides of Figures 4 and 5 which exhibit the characteristics of receptors of members of the PF4A family of cytokines would have been regarded as important to the pharmaceutical industry, ie that industrial applicability may be acknowledged.

19. As all further claims on appeal directly or indirectly relate to the polypeptides of Figures 4 and 5 (DNA encoding them, method of production, monoclonal antibody there against), they fulfil the requirements of Article 57 EPC.

Article 83 EPC; sufficiency of disclosure

- 20. Sufficiency of disclosure was also cited as a ground of opposition. In the decision of the first instance, it was not assessed in respect of the claimed subjectmatter now on appeal since this was rejected under Articles 56 and 57 EPC. Taking into account the length of the proceedings, the board decides to make use of the provisions of Article 111 EPC to exercise the power of the opposition division to evaluate whether or not the claimed invention is sufficiently disclosed.
- 21. At the first instance, the respondent only gave very short reasons for its opinion on sufficiency of disclosure (point 3.2 of the grounds of opposition), namely that

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- the patent in suit did not disclose the ligands for the receptors of Figures 4 and 5, and that

- it did not disclose "a utility in respect of association of the receptor with a diseased state".

- 22. The first of these arguments does not appear to be relevant to sufficiency of disclosure insofar as the identity of the ligands has no bearing on the isolation of the polypeptides of Figures 4 and 5 (see point 9, supra). In the board's judgment, and in the absence of any evidence to the contrary, the patent specification provides adequate experimental instructions for the skilled person to be able to reproduce without undue burden the polypeptides of Figures 4 and 5 and also polypeptides which would 85% homologous therewith.
- 23. The second argument is somewhat unclear. The board interprets it as meaning that the patent in suit did not adequately disclose any involvement of the receptor in a disease state and that, consequently, it did not disclose any therapeutic use directly or indirectly involving the receptor. A therapeutic use/a pharmaceutical composition indirectly involving the polypeptides of Figures 4 and 5 are, in fact, claimed in the form of monoclonal antibodies raised against them for these purposes. Accordingly, what is at stake is sufficiency of disclosure in respect of the subjectmatter of claims 21 and 22.
- 24. The patent in suit provides no evidence at all that an antibody blocking the receptor would thereby produce a useful physiological effect of therapeutic potential.

25. Document (22) (page 320, right-hand column) teaches that the PF4-related proteins are mediators of the inflammatory response which have some activities that are overlapping; for example, Table 3 shows that the ability of being a chemoattractant for neutrophils which is associated with the inflammatory response is shared by many chemokines (IL-8,  $\beta$ TG, PF4). Thus, unless experimentally demonstrated, it is not evident that the blocking of the receptor for any one specific chemokine with monoclonal antibodies would, on its own, necessarily result in a therapeutic effect. Consequently, the mere disclosure of a monoclonal antibody against the polypeptides of Figure 4 or 5 without identifying a diseased state caused by the "misfunctioning" of these polypeptides is not sufficient to acknowledge a use in therapy for the monoclonal antibody. For these reasons, it is concluded that the requirements of Article 83 EPC are not fulfilled in respect of the subject-matter of claims 21 and 22.

- 26. At oral proceedings, the appellant remarked that it would somehow be odd if industrial applicability was to be acknowledged to the polypeptides of Figures 4 and 5 on the basis of them being receptors of members of a family of proteins involved in the inflammatory response while sufficiency of disclosure would be denied in respect of monoclonal antibodies against these polypeptides for use in therapy.
- 27. However, the board's decision to accept industrial applicability was not made on the above mentioned basis but on the basis that at the priority date, the person skilled in the art perceived chemokines and any

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molecules capable of interfering with their activity as of great interest to the pharmaceutical industry if only to investigate their potential as targets for drug development, irrespective of what the end result might be (see the last two sentences in the passage of document (22) cited point 17, supra). The conclusion cannot be drawn from this reasoning that monoclonal antibodies to the polypeptides of Figures 4 or 5 could necessarily be of use in therapy or as a pharmaceutical composition.

28. The main request is rejected for lack of sufficient disclosure in respect of the subject-matter of claims 21 and 22.

Auxiliary request I for all Designated Contracting States except Spain and Greece

29. Claims 1 to 17 of this request are not the subjectmatter of the appeal. Claims 18 to 32 correspond to granted claims 1 to 4, 7, 10 to 17, 19 and 20 of the main request directly or indirectly relating to the amino acid sequence of Figures 4 and 5 - the introduced amendments simply reflecting the necessity for renumbering. They fulfil the requirements of inventive step, industrial applicability and sufficiency of disclosure for the same reasons as given for the granted claims. The claim request does not contain any claims corresponding to the claims 21 and 22 of the main request which caused the request as a whole to be refused (points 19 to 28). The auxiliary request, thus, fulfils the requirements for patentability. Auxiliary request I for Spain and Greece

30. Claims 1 to 23 of this request are not the subjectmatter of the appeal. The conclusions as regard patentability of claims 18 to 32 of auxiliary request I for all Designated Contracting States except Spain and Greece apply to claims 24 to 42 of these requests for the reasons given in points 2 to 28.

# Order:

## For these reasons, it is decided that:

- 1. The decision under appeal is set aside.
- 2. The case is remitted to the first instance with the order to maintain the patent on the basis of auxiliary request I filed at the oral proceedings on 16 March 2006 and a description to be adapted thereto, if necessary.

The Registrar

The Chairman

A. Wolinski

L. Galligani