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Datasheet for the decision of 11 December 2014

Case Number: T 1902/11 - 3.3.08

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Language of the proceedings: EN

Title of invention:
MAMMALIAN INTERLEUKIN-12 P40 AND INTERLEUKIN B30. COMBINATIONS THEREOF. ANTIBODIES. USES IN PHARMACEUTICAL COMPOSITIONS

Patent Proprietor:
Merck Sharp & Dohme Corp.

Opponent:
Janssen Biotech, Inc.

Headword:
Human IL-23/MERCK SHARP & DOHME

Relevant legal provisions:
EPC Art. 54, 56, 83, 84, 123(2)

Keyword:
Main request - requirements of the EPC met (yes)

Decisions cited:

Catchword:

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Case Number: T 1902/11 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 11 December 2014

Appellant: (Patent Proprietor)	Merck Sharp & Dohme Corp. 126 East Lincoln Avenue Rahway, NJ 07065-0907 (US)
Representative:	Evenson, Jane Harriet Zvesper, Thomas Mathys & Squire LLP The Shard 32 London Bridge Street London SE1 9SG (GB)
Appellant: (Opponent)	Janssen Biotech, Inc. 800/850 Ridgeview Drive Horsham PA 19044 (US)
Representative:	Wise, Daniel Joseph Mr. Duffield Mr. Verhage Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 20 June 2011 concerning maintenance of the European Patent No. 1210434 in amended form.**

Composition of the Board:

Chairman	M. Wieser
Members:	B. Stolz
	C. Heath

Summary of Facts and Submissions

I. The patent proprietor (appellant I) and the opponent (appellant II) each filed an appeal against the decision of the opposition division dated 20 June 2011, whereby European patent No. 1 210 434 was maintained in amended form on the basis of auxiliary request III filed on 6 May 2011.

II. The opposition division decided that the main request (the patent as granted) lacked novelty (Article 54 EPC), that auxiliary request I did not meet the requirements of Article 123(2) EPC, and that auxiliary request II did not meet the requirements of Article 56 EPC.

III. With its statement of grounds of appeal appellant I filed new documents D24 to D27, maintained its main request and filed new auxiliary requests 1 to 3. Appellant II filed new documents D19 to D23 with its statement of grounds of appeal.

IV. Both parties made further submissions in reply to the other party's statement of grounds of appeal. Appellant II submitted further documents D28 and D29. Appellant I replaced auxiliary requests 1 to 3 filed with its grounds of appeal by auxiliary requests 1 to 16 and 1A to 16A and submitted further documents D30 and D31.

V. The parties were summoned to oral proceedings. A communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed to the summons, informed them of the preliminary non-binding opinion of the board on some of the issues of the appeal proceedings.

VI. In response to the board's communication, both parties submitted additional arguments. Appellant I filed 90 auxiliary requests, replacing the auxiliary requests previously on file.

VII. Oral proceedings were held on 11 December 2014. Appellant I withdrew the main request and made auxiliary request 26 its new main request.

VIII. Claims 1 to 3 of the main request read as follows:

1. A composition comprising a complex of:

i) a substantially pure mature human IL-12 p40 polypeptide; and
ii) a substantially pure mature polypeptide of SEQ ID NO: 2.

2. An antibody or binding fragment thereof that specifically binds to a complex of:

i) a substantially pure mature human IL-12 p40 polypeptide; and
ii) a substantially pure mature polypeptide of SEQ ID NO: 2

but not to a mature human IL-12 p40 polypeptide or a mature polypeptide of SEQ ID NO: 2 alone.

3. The use of a complex of:

i) a substantially pure mature human IL-12 p40 polypeptide; and
ii) a substantially pure mature polypeptide of SEQ ID NO: 2

in the manufacture of a medicament for modulating an inflammatory response.

IX. The following documents are cited in this decision:

D1: WO 99/05280

D4: US 5.851,523

D5: EP 0 960 622 A2

D12: Oppmann et al. (2000) Immunity 13:715-725

D13: Declaration of Mark Cunningham

D14: WO 2007/005955

D15: WO 2007/076524

D16: Declaration of Robert Kastelein

D18: Extract from Alberts et al. (1994) Molecular Biology of the Cell, page G-6

D25: Belladonna et al. (2002) J Immunol. 168(11): 5448-54

D26: Gerosa et al. (2008) J Exp Med. 205(6): 1447-61.

D30: WO 2012/009760

D31: Declaration of Tatyana Churakova

D32: Supplementary declaration of Tatyana Churakova

D33: Extract from Recombinant Gene Expression Protocols (1997)

D34: Carter et al. 2010. Protein Science 19:357-362

D35: Examples of common general knowledge: textbooks that lack a discussion of Ig constant domain fusions, in particular relating to solving expression problems

X. The arguments of appellant I, as far as relevant for the present decision, can be summarized as follows:

Article 123(2) EPC

Claims 1 to 3 corresponded to claims 1, 7 and 10 of auxiliary request 2 underlying the decision under appeal. Basis for the subject matter of claim 1 could be found on page 3, lines 13 to 17, page 8, lines 30 to 34, and page 13, lines 37 to 38. The invention was a novel cytokine made up of the mature forms of human IL-12p40 and human IL-B30. The subject matter of claim 2 was disclosed on pages 13, 19 ,34 and 36.

Article 84 EPC

The meaning of the term "antibody that specifically binds to a complex of i) and ii)" in claim 2 implied that the antibody had to recognize a complex consisting of i) and ii). All other objections concerned features already present in claim 7 as granted which were not open to an objection under Article 84 EPC. Moreover, the skilled person knew how to establish whether an antibody specifically bound to the complex of i) and ii).

Article 83 EPC

The patent referred to document D1 which disclosed IL-B30 and ways of producing it. The declarations D13 and D16 both provided evidence that IL-B30 could be expressed. The fact that the protein was not secreted did not affect its suitability for the performance of antibody binding assays. The additional evidence provided by appellant II did not prove the contrary. Document D12, the scientific publication describing the claimed invention, was published one year after the filing date without placing any emphasis on the fact that IL-B30 was expressed as a fusion protein. This was clear evidence that the expression of IL-B30 as a fusion protein belonged to the general knowledge of the skilled person. In conclusion, appellant II had not discharged its burden of proof.

Article 54 EPC

The subject matter of claim 2 was limited to antibodies binding to a complex consisting of i) and ii) but not to the individual subunits alone. This was the minimal requirement of the claimed antibody irrespective of whether the composition of claim 1 comprised further peptides. Such antibodies were not disclosed in the prior art documents on file.

Article 56 EPC

Starting from document D1, disclosing IL-B30, the technical problem consisted in the provision of a novel biologically active molecule. The claimed complex of IL-12p40 and IL-B30 was not obvious in view of the cited prior art. Documents D4 and D5 merely disclosed compositions comprising IL-6 and IL-12, and even if the

skilled person would have combined IL-12 and IL-B30 in a composition, no complex would have formed between IL-12p40 and IL-B30.

The antibody of claim 2 was specific for the claimed complex and would not bind to IL-12. This represented a significant difference and such an antibody could not be produced in the absence of the novel complex. The antibody of claim 2 was therefore not obvious.

XI. The arguments of appellant II, as far as relevant for the present decision, can be summarized as follows:

Article 123(2) EPC

The patent application did not provide a basis for the compositions of claim 1 comprising the specified complex of substantially pure mature human IL12p40 peptide and substantially pure mature polypeptide of Seq ID NO: 2. The feature 'mature' was only mentioned in the context of biologically active fusion polypeptides. The features 'substantially pure' and 'human' were only mentioned in the context of broader definitions.

The patent application did not provide a basis for the disclaimer of claim 2 excluding antibodies that also bound the individual subunits of the complex from the scope of the claim.

The specific medical use of the complex according to claim 3 was not disclosed in the patent application.

Article 84 EPC

The meaning of the term "complex of i) and ii)" in claim 2 was open to interpretation because it was not clear whether the term was limited to complexes of the two subunits only. Furthermore, the complexes disclosed in the patent were disulfide linked, but this was not necessarily a feature encompassed by the term. Commonly, the term had to be interpreted as "complex comprising i) and ii)". It was also open whether the term encompassed covalently linked subunits or not. Furthermore, the term 'specifically binds' in claim 2 was ambiguous because no assay conditions or thresholds were specified.

Article 83 EPC

The patent did not provide a single example of an antibody according to claim 2. It was crucial that the skilled person was in a position to readily produce the individual subunits alone in order to produce the antibodies according to the claim. As described in [0166] of the patent, IL-B30 (the protein of Seq ID NO: 2) was difficult to express and was not secreted from 293T cells. Moreover, if expressed alone, IL-B30 was complexed with endogenous IL12p40 as declared in document D13. The patent proprietor's own expert (document D31) had to express IL-B30 as an Fc fusion protein. Such fusion constructs were however not routinely used for the expression of proteins in eukaryotic cells. Appellant II had searched the literature for evidence that such fusion constructs were routinely used but could not find any. Document D34 provided some evidence that IL-B30 was still hard to express a long time after the filing date of the patent at issue. Appellant II's expert only obtained

inclusion bodies but no properly folded protein. As explained in decision T 63/06 of 24 June 2008, the opponent discharged his burden of proof by plausibly arguing that common general knowledge would not enable the skilled person to put the invention into practice if the patent did not give any information of how a feature of the invention could be put into practice.

Article 54 EPC

As mentioned in relation to clarity of the term "complex of i) and ii)", the term was not limited to complexes consisting of i) and ii) only but encompassed also complexes comprising for instance a FLAG tagged IL-B30. Antibodies against the FLAG tag were commercially available and fell within the scope of protection of claim 1. Support for this interpretation could be found in [0051, 0054 and 0171] of the patent.

Article 56 EPC

Document D1, disclosing IL-B30, represented the closest prior art. The term "complex" used in claim 1 was not limited to functional complexes but included complexes with denatured subunits without biological functions. The technical problem solved by the patent consisted in providing a combination of IL-B30 with another modulator. The claimed solution was obvious in view of D1 disclosing combinations of IL-B30 with other unspecified modulators, the similarities between IL-6 and IL-B30, and documents D4 or D5, disclosing combinations of IL-6 and IL-12.

Document D12, disclosing an antibody recognizing IL-12 as well as the protein complex of the patent at issue, represented the closest prior art for the antibody of

claim 2. Since the claimed antibody had the same properties as the antibody of document D12, no new technical effect was apparent. The technical problem consisted merely in providing an alternative antibody to the one disclosed in document D12. This required no inventive skills.

XII. Appellant I requested that the decision under appeal be set aside and the patent be maintained based on the Main Request filed at the oral proceedings.

XIII. Appellant II requested that the decision under appeal be set aside and the European patent be revoked.

Reasons for the Decision

1. The main request, filed on the day of the oral proceedings, is based on auxiliary request 2 underlying the decision under appeal. Claims 1 to 3 of the main request correspond to claims 1, 7 and 10 of auxiliary request 2, respectively. Appellant II did not raise an objection against its admissibility. Since the amendments are the result of the deletion of claims 2 to 6, 8, 9, and 11 to 27 of auxiliary request 2 underlying the decision under appeal, no new issues arise, and the board decided to admit the main request.

2. The parties had no objections against the admission of documents D19 to D31 filed in the appeal procedure. The board, therefore, had no reason not to admit them.

Article 123(2) and 123(3) EPC

3. Appellant II raised an objection that the specific combination of features of claim 1, in particular a

complex of substantially **pure mature human** IL-12 p40 and substantially **pure mature** polypeptide of SEQ ID NO: 2 was not directly and unambiguously derivable from the published international patent application WO 01/18051 (the patent application).

4. According to the description of the patent application, the present invention *"provides description and teaching of pairing of mammalian proteins to make a soluble cytokine which can mediate a signal"* (page 8, lines 31-33), and embodiments of the invention include those *"comprising both a substantially pure IL-12p40 polypeptide and a substantially pure IL-B30 polypeptide"* (page 4, lines 1-2). *"Preferred embodiments would be from human"* (page 12, line 27). It is furthermore disclosed that upon coexpression, the hIL-12p40 and the hIL-B30 proteins are secreted from eukaryotic cells and form a complex (Example VI, page 42).

5. The parties did not dispute that the term "mature polypeptide" refers to a protein having its signal sequence removed. Since the signal sequence is removed upon secretion of proteins from eukaryotic cells, it is implicit that the proteins constituting the secreted complex disclosed in Example VI are in their mature form.

6. The subject matter of claim 1 is therefore directly and unambiguously derivable from the patent application.

7. Appellant II submitted that claim 2 did not comply with the requirements of Article 123(2) EPC because the patent application only referred to binding compounds (page 5) or binding components (page 13) but not to antibodies or fragments thereof. Moreover, it argued

that there was no basis for the exclusion of antibodies which recognized the individual polypeptides only from the scope of the claim.

8. The board takes the view that the definition of binding compounds as compounds comprising an antigen binding site from an antibody (page 5, line 15) implicitly discloses antibodies as a prominent subgroup of binding compounds. This interpretation is consistent with the reference on page 13 to *"binding components, e.g. antibodies* [which] *typically bind the IL-12p40/IL-B30 complex with high affinity"*. The skilled person would not read a different meaning into this statement because it refers to components instead of compounds as on page 5. This interpretation is further supported by the statement on page 14, lines 12 to 14, that *"binding composition refers to molecules that bind with specificity to the IL-12p40/IL-B30 complex, e.g. in an antibody-antigen interaction, but not to the individual components alone".*

9. As for *"binding fragments thereof"*, the general description of antibodies refers to *"antibodies , including binding fragments"* which can be raised against predetermined fragments of the antigens or which can be used as potent antagonists (page 22, lines 3 and 22).

10. The subject matter of claim 2 is therefore directly and unambiguously derivable from the patent application.

11. Appellant II submitted that claim 3 related to a medicament for modulating an inflammatory response, whereas the description only disclosed the use of the claimed complex for the treatment of inflammatory conditions. *"Modulating"* was broader than *"treatment"*

and encompassed also maintaining or increasing an inflammatory condition.

12. The subject matter of claim 3 is disclosed on page 30 of the patent application. The reagents of the invention, which according to line 22 encompass the IL-12p40/IL-B30 complex, "*will be useful in the treatment of conditions associated with abnormal physiology, including inflammatory conditions*" (lines 28 to 29). Both, the term 'modulating' and the term 'treating an inflammatory condition', refer to 'acting on' an inflammatory condition and neither of them is limited to 'eliminating' an inflammatory condition. Should it be necessary for medical reasons to maintain an inflammation, this would also be encompassed by the term 'treating' (or 'modulating') an inflammatory condition.

13. The subject matter of claim 3 is therefore directly and unambiguously derivable from the patent application.

14. The main request meets the requirements of Article 123(2) EPC.

15. No objection was raised under the provisions of Article 123(3) EPC, and the board has no reason to raise any of its own motion.

Article 84 EPC

16. Appellant II submitted that the amendment rendered claim 2 unclear. It was not clear whether the term 'complex of (i) and (ii)' encompassed complexes consisting of the two subunits only or whether it included the covalently linked complexes disclosed in the patent, and whether fusion proteins were included.

Furthermore, the term 'specifically binding' in claim 2 was ambiguous because no assay conditions or thresholds were specified.

17. According to a textbook definition, a 'complex' is an assembly of molecules held together by non-covalent interactions (e.g. document D18), in the present case, an assembly of IL-12p40 and IL-B30. This assembly comprises the two polypeptides in mature properly folded form. According to expert declaration D16, protein complexes comprise two or more proteins held together by covalent and/or non-covalent interactions.

18. In its broadest sense, the term refers to a complex comprising IL-12p40 and IL-B30, which may or may not be held together by disulfide linkages, and which includes fusion proteins.

19. Appellant II submitted that the term complex encompassed also complexes comprising denatured proteins. The board does not agree as denatured proteins tend to form unspecific aggregates but not complexes within the general meaning of the term.

20. Appellant II also submitted that the term "complex of (i) and (ii)" encompassed complexes comprising (i) and (ii) and other unspecified compounds, and that antibodies recognizing such further compounds fell within the scope of claim 2.

21. The board disagrees. The second half-sentence of claim 2 sets a limit to the meaning of the first half sentence. The term 'an antibody binding to a complex of proteins (i) and (ii) but not to proteins (i) or (ii) alone' clearly refers to antibodies binding to a complex consisting of proteins a and b.

22. As for the meaning of the term "antibody that specifically binds to a complex of (i) and (ii)" but not its individual constituents, the bord refers to the established jurisprudence of the Boards of Appeal, saying that the skilled person when considering a claim should try to arrive at an interpretation of the claim which is technically sensible and takes into account the whole disclosure of the patent. In the absence of a definition of a particular term in the specification, terms should be given their normal meaning in the relevant art (see Case Law of the Boards of Appeal of the European Patent Office, 7th edition 2013, sections II.A.6.1 and II.A.6.3.3).

23. The term "specifically binds to" designates the degree to which an antibody discriminates between antigenic variants. No antibody has absolute specificity, in the sense that it will react with only one epitope, whatever the conditions; if present, an antibody can always react to some extent with chemically similar epitopes. However, the affinity of a monoclonal antibody for its proper epitope is significantly greater than its affinity for closely related epitopes. This difference in affinity is used to establish assay conditions, under which an antibody binds almost exclusively to a specific epitope.

In other words, an antibody within the scope of claim 2 has to bind the complex of the two polypeptides either exclusively or significantly better than its individual constituents in isolated form under the same appropriate assay conditions.

24. Appellant II submitted that Figure 1 of post-published document D30 disclosed an antibody binding to the

hIL12p40/hILB30 complex under certain conditions, which antibody also bound to isolated hILB30 under other conditions. It was therefore not possible to determine whether the antibody fell within the scope of the claim. The board is not convinced by this argument because the data in Figure 1 clearly show that in order to detect binding of the antibody to the isolated hILB30, the antibody concentration had to be increased at least 100fold compared to the antibody concentration needed to detect the complex. The antibody binds the protein complex significantly better than one of its individual constituents and is therefore regarded as specifically binding to it.

25. The board is therefore convinced that the skilled person knows how to establish whether an antibody specifically binds to the complex of (i) and (ii) but not to its individual constituents.

26. In view of the above considerations, the board decides that the main request meets the requirements of Article 84 EPC.

Article 83 EPC

27. Claim 2 requires that the antibodies do not recognize mature human IL-12p40 or mature human IL-B30 alone. This wording implies that the antibodies do not recognize native, properly folded IL-B30 alone and possibly also denatured or misfolded protein alone (cf. [0081] of the patent). In any case, antibodies recognizing properly folded IL-B30 alone, i.e. antibodies recognizing (conformational) epitopes on IL-B30 alone, are excluded from the scope of claim 2.

28. Appellant II objected that the patent did not disclose a single antibody according to claim 2 and that it was impossible to express a mature polypeptide of Seq ID No.: 2 (IL-B30) alone in order to select appropriate antibodies. It referred to the patent itself and to documents D12 and D13.

29. Appellant I submitted document WO 2012/009760 (D30), to demonstrate successful production of antibodies according to claim 2. This document, however, is of little relevance because it was published about 12 years after the filing date of the present patent.

30. Appellant I also submitted expert declarations D31 and D32, as evidence for the successful expression of hILB-30. Appellant I's expert expressed the protein as a fusion construct with a human Ig constant domain, and this fusion construct was used to raise antibodies. According to the expert, the human Ig constant domain was routinely used to express proteins.

31. The patent itself, in the context of raising antibodies, does however not suggest the expression of the hIL-B30 protein fused to anything but to marker molecules or to hIL-12p40. Therefore the question arose whether the skilled person would have routinely considered to express the protein fused to an Ig constant domain.

32. Appellant II submitted extracts from textbooks (D33, D35) and a scientific publication (D34) as evidence that the use of human Ig constant domain fusions for the expression of IL-B30 went beyond the general knowledge.

33. Indeed, documents D33 and D35 (D35 is in fact a collection of indexes from several textbooks) do not provide any evidence that fusions with a human Ig constant domain were used to improve protein expression.

34. Document D34, published 10 years after the filing the of the patent in suit discusses the use of fusion partners to increase expression of recombinant interleukins. In relation to IL-B30 (p19), the authors state that attempts to express this protein on its own had been fruitless. Fusion to an Fc part of a human antibody provided the highest expression levels, fusion to HSA provided some expression.

35. To sum it up, the various pieces of evidence provided by appellant I and appellant II, regarding the question whether the expression of hILB-30 as an Fc fusion protein belonged to the general knowledge, are contradictory.

36. Referring to decisions **T 491/08** of 21 October 2010, and **T 63/06** of 24 June 2008, appellant II submitted that it had discharged its burden of proof.

37. Decision **T 63/06** relates to the technical area of combustion engines and to the creation of flame kernels of a specific size in such an engine. The competent board assessed whether the skilled person, in the absence of any specific teaching, was in a position to readily produce the required flame kernels. The board decided that the patent specification did not contain detailed information of how to put the invention into practice, and that, under the circumstances, it was sufficient to raise serious doubts by comprehensible and plausible arguments.

Decision **T 491/08** concerned a medical use claim. The claim was directed to a prime/boost vaccination regime in order to potentiate an immune response to HIV-1. In this case sufficiency of disclosure depended on the technical information provided by the patent because an effect of the vaccination regime on metabolic mechanisms involved in HIV-1 infection did not belong to the general knowledge (point 8). The patent underlying the decision did however not provide sufficient information.

38. The situation in the present case is different because there is further evidence in the patent and in appellant II's expert declarations that the protein is expressed in E. coli and in eukaryotic cells.

39. Contrary to appellant II's submissions, the paragraphs recited from the patent and the corresponding paragraphs in document D12 do not state that it was impossible to express IL-B30 in the absence of IL-12p40. Rather, it is stated, that *"no soluble protein was detected in the cell supernatant"* and that *"transfection with the FLAG-IL-B30 construct resulted in no significant soluble protein"* (patent, [0166, 0167]). Document D12 (page 716), published shortly after the present filing date and disclosing the invention, reports that only a small amount of mouse protein but not the human protein could be immuno-precipitated from the cell supernatant and that *"both proteins could be detected in the cellular lysates of transfected cells, indicating inefficient secretion"*.

Appellant II's expert declared that free IL-B30 was not secreted from mammalian cells and that attempts were made to express the protein in E. coli and cell free

systems but that it could not be purified to homogeneity. This implies that the protein was expressed in E. coli. Finally, the expert stated that there was no evidence that p19 alone could be secreted as a properly folded protein such that it could be used for the identification of neutralizing antibodies.

Appellant I's expert stated in declaration D16 (cf. point 9), that purified protein was not needed to perform binding assays with IL-B30.

40. To sum it up, the available evidence shows that IL-B30 protein can indeed be expressed in the absence of IL-12p40 (both, in prokaryotic and eukaryotic cells), but that it is only secreted from eukaryotic cells if co-expressed with IL-12p40.

41. The board is not convinced by the evidence on file that properly folded IL-B30 protein alone can only be produced with undue burden. No attempts have been made to demonstrate that protein which is not secreted by mammalian cells or which is produced in E. coli is unsuitable, or that an undue amount of work would be required to bring it into a suitable form, for the performance of binding assays in order to select antibodies according to claim 2.

Appellant II has therefore not discharged its burden of proof.

42. The board decides that the main request meets the requirements of Article 83 EPC.

Article 54 EPC

43. The complex of claim 1 has not been described in the prior art and is therefore novel. Since the complex is novel, antibodies according to claim 2 and the medical use of the complex according to claim 3 are also novel.

Article 56 EPC

44. The closest prior art, document D1, discloses the gene encoding human IL-B30, gene expression patterns, and the protein. IL-B30 is described as an interleukin.

45. Starting from document D1, the technical problem underlying the present invention consists in providing a new interleukin.

46. As a solution to this problem, the patent proposes the complex of claim 1.

47. According to items VIII A, B, and D (pages 43 to 45 of the patent application), a complex formed by a fusion protein of hIL-12p40 with hIL-B30 indeed affects the proliferation and differentiation of T cells and IFN-gamma production by human PHA blasts.

The board is therefore satisfied that the technical problem is solved.

48. Appellant II submitted that claim 1 encompassed non-working embodiments. According to document D12, the complex had to be disulfide linked in order to be functional. The claim was however not limited to disulfide linked complexes.

49. The board does not agree to appellant II's interpretation of document D12 which merely describes that the two proteins are disulfide linked upon expression in eukaryotic cells and only secreted when co-expressed. There is no evidence on file that a complex (or a dimer) of hIL-12p40 and hIL-B30 has to be disulfide linked in order to be stable and functional.

50. It remains to be established whether the claimed solution involves an inventive step.

51. Document D1 contains no incentive to provide a complex comprising IL-B30 as one of its constituents.

52. Appellant II submitted that document D1 (page 12, line 36) described IL-B30 as a long chain cytokine exhibiting sequence similarity to IL-6 and G-CSF. Since it had similarity with IL-6, the skilled person would turn to documents describing the use of IL-6, such as document D4, disclosing the use of combinations, or mixtures, of IL-6 and IL-12 to activate T cells (e.g. column 12, lines 35-37). Therefore, also the use of combinations of IL-B30 and IL-12 was obvious. Such a combination would fall within the scope of claim 1.

53. Document D1 does not mention or even point to the use of combinations of IL-B30 and IL-12. It refers to fusion polypeptides of IL-B30 with other peptides (page 20, lines 9 to 24) in general terms but does not suggest IL-12, let alone IL-12p40, as a fusion partner. Document D4, on the other hand, discloses combinations, i.e. mixtures, of IL-6 and IL-12 but suggests no alternatives to these combinations. Thus, the skilled person, had no incentive to combine document D1 with document D4.

54. Furthermore, as mentioned in point 17 above, a complex is an assembly of molecules held together by non-covalent and/or covalent interactions. A complex comprising two peptides is fundamentally different from a combination, e.g. a solution, comprising two non-complexed peptides.

IL-12 itself is a complex consisting of two peptides, IL-12p40 and IL-12p35, held together by non-covalent interactions. Simply combining IL-6 and IL-12 does therefore not result in the formation of a new complex consisting of IL-6 and IL-12p40.

Thus, even if the skilled person, for whatever reason could have turned to document D4, and could have tried to replace IL-6 by IL-B30 and combine it with IL-12, it would not have arrived at the complex of claim 1.

55. The subject matter of claim 1 is therefore based on an inventive step.

56. Since the protein complex of claim 1 is not obvious, an antibody according to claim 2, specifically recognizing such a complex but not the individual proteins alone, is also not obvious. The skilled person had no motivation and no means to look for antibodies specifically binding to the previously unknown protein complex. Likewise, the medical use of claim 3 is not obvious.

57. The main request meets the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent based on claims 1 to 3 of the Main Request filed at the oral proceedings, and a description to be adapted thereto.

The Registrar: The Chairman:

T. Buschek M. Wieser

Decision electronically authenticated