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**Datasheet for the decision
of 31 May 2007**

Case Number: T 1396/06 - 3.3.04

Application Number: 97916104.9

Publication Number: 0888120

IPC: A61K 38/00

Language of the proceedings: EN

Title of invention:

HLA binding peptides and their uses

Applicant:

Epimmune Inc.

Opponent:

-

Headword:

HLA Binding Peptides/EPIMMUNE

Relevant legal provisions:

EPC Art. 54, 56, 83, 123(2)

Keyword:

"Main request, first to fifth auxiliary request - inventive step (no)"

"Sixth auxiliary request - added subject-matter (no), novelty, inventive step, sufficiency of disclosure (yes)"

Decisions cited:

T 0386/89, T 0091/98, T 1045/98, T 0918/01, T 0609/02,
T 1329/04, T 1336/04

Catchword:

-



Case Number: T 1396/06 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 31 May 2007

Appellant: Epimmune Inc.
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 27 February 2006
refusing European Patent application
No. 97916104.9 pursuant to Article 97(1) EPC.

Composition of the Board:

Chair: U. Kinkeldey
Members: M. Wieser
R. Moufang

Summary of Facts and Submissions

I. The appeal was lodged by the Applicant (Appellant) against the decision of the Examining Division to refuse under Article 97(1) EPC the patent application EP 97 916 104.9 (published as WO 97/34 617), having the title: "HLA binding peptides and their uses".

II. The Examining Division decided that the subject-matter of the claims of the main request and of the first and second auxiliary request before them did not meet the requirements of Article 56 EPC as it did not involve an inventive step in the light of the disclosure in the following documents:

(1) WO 94/20 127

(4) Journal of Immunology, vol.152, 1994, pages 3913 to 3924

III. The Board expressed its preliminary opinion in a communication dated 6 December 2006.

Oral proceedings were held on 31 May 2007.

IV. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request or, in the alternative, of the first, second, third, fourth or fifth auxiliary request, all filed with the grounds of appeal, or of the sixth auxiliary request, filed at the oral proceedings.

The claims of the main request and of the first and second auxiliary request were identical to the claims before the Examining Division.

V. Claim 1 of the main request read:

"An immunogenic peptide of less than 15 amino acid residues, wherein the peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 57-60, 65-69, 71-74, 76-77, 88-104, 108 and 109."

Claim 1 of the first auxiliary request corresponded to claim 1 of the main request except that peptides comprising SEQ ID NOs 57, 77, 88, 92, and 95 had been removed.

Claim 1 of the second auxiliary request corresponded to claim 1 of the first auxiliary request except that peptides comprising SEQ ID NOs 65, 94, 96, 97, 99, 100 and 103 had been removed.

Claim 1 of the third auxiliary request corresponded to claim 1 of the main request except that peptides comprising SEQ ID NOs 1, 2, 57, 66, 68, 74, 76, 77, 88, 90, 92, 95, 96, 99, 100 and 103 had been removed.

Claim 1 of the fourth auxiliary request corresponded to claim 1 of the third auxiliary request except that peptides comprising SEQ ID NOs 65, 72, 73, 91, 93, 94, 97, 98, 102, 104 and 108 had been removed.

Claim 1 of the fifth auxiliary request read:

"An immunogenic peptide of less than 15 amino acid residues, wherein the peptide comprises the amino acid sequence of SEQ ID NO: 101."

VI. Claim 1 of the sixth auxiliary request read:

"An immunogenic peptide consisting of the amino acid sequence of SEQ ID NO 101."

Dependent claims 2 to 6 of this request referred to a composition comprising the peptide of claim 1. Claim 7 related to a vector comprising a nucleic acid encoding the peptide, claim 8 to the peptide or a composition comprising it for use in medicine and claims 9 and 10 to the use of the peptide or a composition comprising it in the preparation of a medicine for treating HIV infection.

VII. Besides those documents mentioned in section (II) above the present decision refers to the following document which was introduced into the proceedings by the Board:

(6) Journal of Immunology, vol.171, 2003, pages 5611 to 5623

and to

Annexes (1) to (4), submitted by the Appellant with the grounds of appeal.

VIII. The submissions made by the Appellant may be summarised as follows:

Document (1) related to the provision of peptides binding to HLA-A2.1 molecules, whereas the peptides of claim 1 of the main request referred to peptides capable of binding HLA-A3.2 molecules. A person skilled in the art, knowing that a binding motif for HLA-A.3 binding peptides was disclosed in document (4), had no reasonable expectation of success to find the specific peptides of claim 1 of the main request by applying the methods disclosed in document (1) to the peptide motif of document (4). Even if peptides complying with this motif were found on a viral protein, this was not indicative that these peptides would be effective, which means that they actually bound to a HLA-A.3 molecule and that they were immunogenic.

The peptides according to auxiliary requests one to four were additionally characterized by having either improved binding affinity for HLA-A.3 (auxiliary request one and two), or increased cross-reactivity with different HLA-A.3 haplotypes (auxiliary request three and four). A skilled person had no expectation to succeed in finding these specific peptides by combining the disclosure of prior art documents (1) and (4).

The claims of the fifth and sixth auxiliary request were restricted to peptides comprising, respectively consisting of, SEQ ID NO 101. This specific peptide, upon administration to Peripheral Blood Mononuclear Cells (PBMC) of HIV-infected patients, had been shown to give rise to an immune response. Data proving the vaccinating effect of a peptide having SEQ ID NO 101

had been provided in Annex (3), submitted with the grounds for appeal.

Reasons for the Decision

Main request

Inventive step - Article 56 EPC

1. Document (1) discloses peptides specifically binding to HLA-A2.1 and a process for their identification. The first step of this process consists of the isolation and purification of HLA-A2.1 from antigen presenting cells (APC), the isolation and sequencing of peptides naturally bound to it, the identification of an HLA-A2.1 specific motif and the definition of potential high-affinity peptides by using an algorithm to predict the peptides' affinity for HLA-A2.1 (see examples 1 to 8 and figure 1). Subsequently the cytotoxic activity of the identified peptides is determined by a standard ⁵¹Cr-release assay (see examples 9 and 10; especially page 73, lines 16 to 23 and page 76, lines 1 to 17). The results of these experiments indicate that peptides whose binding affinity goes beyond a defined threshold are immunogenic (see page 76, lines 31 to 33 and table 24). Finally, various viral and tumor-related proteins are screened for the presence of the identified peptide motifs by use of the computer program "FINDPATTERNS" and of the standard quantitative binding assay described in example 5 (see examples 11 and 12).

Furthermore, it is mentioned on page 8, lines 1 to 4 that HLA-A3.2 is one of the most frequently expressed HLA allele subtypes of the Caucasoid population.

Document (1) is considered to represent the closest state of the art. The technical problem underlying the invention according to the main request is the provision of immunogenic peptides specifically binding to HLA-A3.2.

This problem has been solved by providing peptides according to claim 1, which comprise an amino acid sequence selected from a group of thirty-six peptides with specific SEQ ID Nos, which are distinguished from those in document (1) in so far as they refer to peptides specifically binding to a different HLA allele, namely HLA-A3.2.

2. Document (4) discloses allele-specific motifs for the human MHC class I molecules HLA-A1, HLA-A3, HLA-A11 and HLA-A24 (see tables I, II and III). The motif identified to be specific for HLA-A3 is identical to the motif disclosed on page 3, lines 6 to 10 and in table V on page 34 of the present application. Document (4) envisages the potential use of these motifs to identify peptides of clinical relevance (see page 3914, left column, first full paragraph and page 3923, last sentence).

3. The Appellant argued that a skilled person applying the method described in document (1) to a peptide motif described in document (4) in order to find immunogenic viral peptides for use as vaccines which specifically bind to HLA-A3.2, will be confronted with different

areas of uncertainty, which deprives him of any reasonable expectation of success. He referred to Annex (4), submitted with the grounds of appeal, and argued that the screening of just one HIV strain resulted in the location of a total of 1240 peptides with the motif defined on page 3, lines 6 to 9 of the present application. Only some of them, which had to be determined by additional screening processes, were selected as being useful for the purpose of the present invention. Only peptides containing the desired motif, which are processed and presented to the MHC molecule in nature in the required form and which will actually bind to the MHC molecule are of interest. Even if these requirements are met the peptide will not elicit a Cytotoxic T-Cell (CTL) response, and thus not act as a vaccine, if no T-cells exist in the respective individual patient which are responsive to the peptide. Thus, according to the Appellant, a combination of the disclosure in documents (1) and (4) results in nothing more than an invitation to carry out a major research project.

4. Page 33, lines 7 to 11 of the present application read as follows:

"To identify peptides of the invention, class I antigen isolation, and isolation and sequencing of naturally processed peptides was carried out as described in the related applications. These peptides were then used to define specific binding motifs for each of the following alleles A3.2, A1, A11, and A24.1. These motifs are described in the related applications and summarized in Tables 5-8, below."

Page 36, lines 3 to 5 read:

"Using the motifs identified above for various MHC class I allele [sic] amino acid sequences from various viral and tumor-related proteins were analyzed for the presence of these motifs. Screening was carried out described in the related applications."

5. Document (1), although not explicitly mentioned, is a "related application" and, as shown in point (1) above, discloses the isolation-, sequencing- and screening-steps referred to in the cited passages. Document (4), co-authored by a group of thirteen persons, three thereof are designated as inventors of the present application, discloses the HLA-A3.2 specific peptide motif disclosed in table 5 of the present application.

6. To apply the method of document (1) in order to provide immunogenic peptides having the HLA-A3.2 motif disclosed in document (4) is not a task which, automatically and without requiring any effort, will allow the skilled practitioner to obtain the desired peptides. However, as isolation-, sequencing- and screening-steps are carried out following routine methods described in the document representing the closest state of the art, the provision of the peptides according to claim 1 of the main request, although undoubtedly requiring a high expenditure of work and time, is considered to fall within the normal routine capacity of the average person skilled in the art.

The Board agrees that a skilled person even when applying routine methods, such as those described in document (1), with the aim to solve a closely related

technical problem, namely the provision of peptides specifically binding to another HLA-allele, would not have absolute certainty to succeed.

7. However, certainty of success is not required according to the jurisprudence of the Boards of Appeal, which makes a clear distinction between reasonable expectation of success and certainty of success (cf. decision T 918/01 of 6 October 2004, point (9.1) of the reasons).

Rather, in spite of the understandable uncertainties which always characterize biological experiments, the skilled person would have had no reasons to adopt a sceptical attitude. He would have had either some expectations of success or, at worst, no particular expectations of any sort, but only a "try and see" attitude, which does not equate with an absence of a reasonable expectation of success (cf. decision T 91/98 of 29 May 2001, point (8) of the reasons for the decision and decision T 1045/98 of 22 October 2001; point (17) of the reasons for the decision).

8. For these reasons, the Board is convinced that a skilled person would arrive at the solution to the problem underlying the invention according to claim 1 of Appellant's main request in an obvious way, by combining the disclosures of documents (1) and (4). The main request does not involve an inventive step as required in Article 56 EPC and has therefore to be rejected.

First and second auxiliary request

Inventive step - Article 56 EPC

9. Claim 1 of the first auxiliary request is distinguished from claim 1 of the main request in so far as peptides comprising amino acid sequences of five SEQ ID NOs, disclosed in claim 1 of the main request, have been removed.

In claim 1 of the second auxiliary request peptides comprising sequences of seven additional SEQ ID NOs have been removed with regard to claim 1 of the main request.

10. The remaining immunogenic peptides claimed, which comprise an amino acid sequence selected from a group of thirty-one SEQ ID NOs (first auxiliary request), respectively twenty-four SEQ ID NOs (second auxiliary request), are said to have an improved, respectively a particularly high, binding affinity for the HLA-A3 allele.

This is substantiated by data provided in Annex (1) which discloses the results of a quantitative binding assay. The binding affinity of a peptide to a specific HLA allele is expressed therein by way of its IC₅₀ value expressed in nM, which is indicative of the specificity of binding (see document (1), example 4).

The data of Annex (1) show that the peptides of claim 1 of the first auxiliary request have an IC₅₀ of less than 500 nM; the peptides of claim 1 of the second auxiliary request have an IC₅₀ of less than 150 nM.

11. The technical problem underlying the invention according to the first and second auxiliary request is the provision of immunogenic peptides having improved (less than 500 nM), respectively particularly high (less than 150 nM), binding affinity for HLA-A3.

12. The binding capacity for HLA-A3 of two synthetic peptides, comprising nine, respectively ten, amino acids, is disclosed in document (4), table IV on page 3918. The peptides contain a Leucine residue at position two and a Lysine residue at the C-terminal end, thus they contain the HLA-A3.2 specific motif disclosed on page 3, line 6 to 10 of the present application, that is even less-well defined as the motif disclosed in table V of the present application. The IC₅₀ of the nonapeptide is indicated as being 85 nM, the IC₅₀ of the decapeptide is indicated as being 148 nM. Thus, both values lie below the threshold values of the peptides claimed in claim 1 of the first and of the second auxiliary request.

13. The reasons as given in points (1) to (8) above with regard to the main request apply mutatis mutandis here and therefore the Board arrives at the decision that a skilled person, upon combining the disclosure in documents (1) and (4), would arrive at the claimed solution to the posed problem according to the first and second auxiliary request in an obvious way. The first and second auxiliary request do not meet the requirements of Article 56 EPC as the subject-matter of claim 1 of both requests does not involve an inventive step and have therefore to be rejected as well.

Third and fourth auxiliary request

Inventive step - Article 56 EPC

14. Claim 1 of the third auxiliary request is distinguished from claim 1 of the main request in so far, as peptides comprising amino acid sequences of sixteen SEQ ID NOs, disclosed in claim 1 of the main request, have been removed.

In claim 1 of the fourth auxiliary request peptides comprising sequences of eleven additional SEQ ID NOs have been removed with regard to claim 1 of the main request.

15. The remaining immunogenic peptides claimed, which comprise an amino acid sequence selected from a group of twenty SEQ ID NOs (third auxiliary request), respectively nine SEQ ID NOs (fourth auxiliary request), are said to cross-react with at least two HLA-A3 haplotypes (third auxiliary request), respectively with at least three HLA-A3 haplotypes (fourth auxiliary request).

Data substantiating this feature has been provided in Annex (2), which discloses that binding affinity of the claimed peptides with different HLA-A3 haplotypes.

16. The Appellant considered the technical problem underlying the invention according to the third and fourth auxiliary request to be the provision of immunogenic peptides specifically binding to HLA-A3.2 which are effective in larger numbers of the population.

17. He argued that this re-formulation of the technical problem was allowable, as it could be deduced from the application as published. He referred in this respect to page 7, lines 18 to 26 and table I of the application. Moreover, he argued that the general knowledge of a skilled person would lead him to look for peptides being effective in large numbers of the population.
18. Page 7, lines 18 to 26 and table I of the application refer to the distribution of different MHC-alleles in the human population. It is said that the different alleles occur at different frequencies within different ethnic groups and that, for instance, the majority of the Caucasoid population can be covered by peptides which bind to four HLA-A allele subtypes, namely HLA-A2.2, HLA-A1, HLA-A3.2 and HLA-A24.1.
19. An **allele** is any one of a number of DNA codings, usually coding for a gene, that occupies a given locus (position) on a chromosome. An individual's genotype for that gene is the set of alleles it happens to possess. In a diploid organism, like a human, two alleles make up the individual's genotype.

A **haplotype** is the genetic constitution of an individual chromosome. In the case of diploid organisms a haplotype comprises one member of the pair of alleles for each locus (that is, half of a diploid genome). The term haplotype can be understood as "haploid genotype".

Thus the disclosure in the application as published that it is intended to concentrate on peptides specifically binding to HLA-**alleles** that are more

frequently expressed in a certain human population, expressed on page 7 of the application, does not allow to conclude that it was the intention of the application to identify peptides that cross-react with different HLA-A3 **haplotypes**.

20. The solution to the technical problem derivable from the application as filed, namely the provision of immunogenic peptides specifically binding to HLA-A3.2, is not associated with the technical effect subsequently invoked, i.e. effectiveness in larger numbers of the population. The alleged effect of a technical feature, in the present case cross-reactivity of the claimed peptides with different HLA-A3 haplotypes, cannot be taken into account when determining the problem underlying the invention for the purpose of inventive step, if it could not be deduced by a skilled person from the application as filed considered in relation to the closest prior art, on the grounds that to do so would alter the character of the invention (cf. decision T 386/89 of 24 March 1992, point (4.3) of the reasons).

21. The problem underlying the invention according to the third and fourth auxiliary request, as defined by the Appellant (see point (16) above), is therefore not acceptable, as the technical effect subsequently invoked is not to be taken into consideration.

As a consequence the problem underlying these auxiliary requests corresponds to the problem underlying the main request and the first and second auxiliary request. The board has already decided in points (1) to (13) above that the solutions to this problem according to claim 1

of the main request and to the first and second auxiliary request do not involve an inventive step.

The subject-matter of claim 1 of the third and fourth auxiliary request, when compared with the preceding requests, does not contain a technical feature causing an additional technical effect, which can be considered for the assessment of inventive step. Accordingly, also the claims of the third and fourth auxiliary request do not meet the requirements of Article 56 EPC, and the requests are rejected.

Fifth Auxiliary request

Inventive step - Article 56 EPC

22. Claim 1 refers to an immunogenic peptide of less than 15 amino acids **comprising** SEQ ID NO 101, which itself consists of ten amino acids.

The Appellant has submitted experimental data describing the results of trials with a peptide consisting of the ten amino acids of SEQ ID NO 101 (Annex (3)). An immunogenic effect was shown as well in splenocytes of transgenic mice as in PBMCs of HIV-infected patients expressing HLA-A3. Annex (3) contains a reference to document (6), which has been introduced into the procedure by the Board.

23. The problem underlying the invention according to the fifth auxiliary request is the provision of an immunogenic peptide with a high binding affinity for HLA-A3 for use as a vaccine to treat HIV infection.

Contrary to the situation with regard to the third and fourth auxiliary request (see points (14) to (21) above), this technical problem is derivable from the application as published (see page 20, lines 18 to 23 of the application as published).

24. However, the Board notes that Annex (3) as well as post-published document (6) (see tables II and III, page 5615 and figure 1) are concerned with a peptide designated "Pol 98" respectively "P98.A3" which **consists** of the ten amino acids of SEQ ID NO 101. Claim 1, however, due to its wording, refers to peptides having between ten and fifteen amino acids which **comprise** SEQ ID No 101.

No evidence has been provided that a peptide different from "Pol 98"/"P98.A3"/SEQ ID NO 101 and covered by the scope of claim 1 is effective as a vaccine to treat HIV infection.

25. Claim 1 covers embodiments for which not even in post-published document (6) a technical effect has been shown, that goes beyond the effects caused by the subject-matter of the preceding requests. As these requests have been decided by the Board to lack an inventive step contrary to the requirements of Article 56 EPC (see points (1) and (21) above), the same applies to the claims of the fifth auxiliary request.

This request is therefore rejected as well.

Sixth auxiliary request

26. Claim 1 is based on example 1, especially table 9 on page 39 of the application as published. Claim 2 finds a basis in claim 19, claim 3 in page 22, lines 7 to 9, claim 4 in page 24, line 15 and claim 5 in page 24, lines 3 to 5 of the application as published. The basis for claim 6 is found on page 22, line 24, for claim 7 on pages 25 to 26 and for claims 8 to 10 on page 20, lines 18 to 23 of the published application.

The application has not been amended in a way that it contains subject-matter which extends beyond the content of the application as filed. The requirements of Article 123(2) EPC are met.

27. The subject-matter of claims 1 to 10 is not disclosed in the prior art documents on file and is therefore novel within the meaning of Article 54 EPC.
28. The subject-matter of claim 1 is restricted to an immunogenic peptide **consisting of** the amino acid sequence of SEQ ID NO 101.

The application as published discloses that the claimed peptide has been isolated by screening HIV-1 POL65 "as described in the related applications" (table 9, page 39 and page 36, line 5). According to document (1), representing one of "the related applications", screening is carried out by searching the viral protein for the presence of a specific peptide motif, in the present case the motif for HLA-A3.2, shown in table 5 of the present application, and selecting those peptides which have a binding affinity

for HLA-A3.2 higher than a threshold value indicative for the peptide to have the capacity to elicit a CTL response (see document (1), page 79, lines 18 to 21; and page 4, lines 22 to 24 of the present application as published).

29. After the filing date the Appellant has submitted Annex (3) containing experimental data showing that the claimed peptide elicits an immune response in transgenic mice and in PBMCs of HIV-infected patients (see point (22) above).

Annex (3) contains a reference to document (6), published six years after the publication date of the present application, in which the claimed peptide is defined as "Pol 98" respectively as "P98.A3" (see tables II and III and figure 1). Document (6) reports on page 5615 (passage bridging left and right column and figure 1 A) that "P98.3" elicits a significantly positive peptide response in HIV-infected subjects indicative of a CTL-response.

30. The closest prior art is represented by document (1) disclosing the identification and isolation of immunogenic peptides specifically binding to HLA-A2.1 (see point (1) above).

The problem underlying the subject-matter according to claim 1 of the sixth auxiliary request is the provision of an immunogenic peptide with a high binding affinity for HLA-A3.2 for use as a vaccine to treat HIV infection.

31. While the application as published only discloses that the claimed peptide's binding affinity for HLA-A3 is sufficiently high to conclude that it is capable to elicit a CTL response, the actual data proving the positive peptide response caused by the peptide in PBMCs of HIV infected patients have been submitted in document (6), published after the publication of the present application.

32. When deciding whether the technical problem defined above has indeed been solved by the subject-matter of claim 1 at the relevant date, the Board is aware of Board's 3.3.08 decision T 1329/04, of 28 June 2005. There it is stated that 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. Therefore, even if supplementary post-published evidence may in the proper circumstances also be taken into consideration, it may not serve as the sole basis to establish that the application solves indeed the problem it purports to solve (point (12) of the reasons for the decision). The Board decided that the post-published evidence submitted in case T 1329/04 could not be regarded as supportive of evidence which would have been given in the application as filed since there was not any. Since the post-published evidence was considered to be the first disclosure going beyond speculation it was not taken into consideration.

33. The same Board confronted with a different technical situation, namely one where the quality of evidence

provided in the respective patent was such that the claimed invention was considered to be a bona fide solution to the problem to be solved, accepted the solution of the problem by taking into consideration also the disclosure in a post-published document (cf. decision T 1336/04 of 9 March 2006, point (9) of the reasons for the decision).

34. When evaluating the quality of evidence provided in the present application as published, the Board notices that the claimed peptide is shown there to contain an HLA-A3.2 specific motif and having a binding affinity for its specific MHC-allele which indicates its capacity to elicit a CTL response. Experimental data, contained in post-published document (6), actually showing the induction of this CTL response in PBMCs of HIV-infected patients, are considered to back up the findings of the patent application as published.

35. Considering decisions T 1329/04 and T 1336/04 (supra), the Board is convinced that the present circumstances are appropriate to take into account supplementary post-published document (6) when establishing whether the application solves indeed the problem it purports to solve.

In the light of the disclosure in the application as published, which is backed up by post-published document (6), the Board is satisfied that the problem as determined in point (30) above is solved by the subject-matter of the claims of the sixth auxiliary request.

36. It remains to be examined if this solution to the problem involves an inventive step.

With regard to the main request and the first to fifth auxiliary request the Board has decided that the provision of immunogenic peptides specifically binding to HLA-A3.2 was obvious in the light of the disclosure in document (1) in combination with document (4).

Document (1) is concerned with peptides binding to HLA-A2.1 (see point (1) above). The Board's decision is reasoned such that a skilled person would have applied the method disclosed in document (1) to the HLA-A3.2 specific peptide motif disclosed in document (4).

Document (4), after determining the specific motifs of different MHC alleles, continues to create synthetic peptides containing these motifs and testing their binding affinity for the respective HLA molecule. It is found that several of these synthetic peptides, including those specific for HLA-A3, have a very high binding affinity. The last sentence of the document reads as follows:

"Thus, knowledge of the specific motifs for the most frequent HLA alleles and the availability of quantitative class I peptide binding assays will greatly aid in the search for potential CTL epitopes with clinical relevance."

37. The Board does not doubt that a skilled person, knowing the HLA-A3 motif of document (4) and trying to solve the problem underlying the present invention according to claim 1 of the sixth auxiliary request, would make

use of the isolation-, purification-, sequencing- and screening-method disclosed in document (1). This method will, by using the appropriate peptide motif, result in the provision of immunogenic peptides specific for the desired MHC-molecule in an obvious way, **but** it does not allow to draw a conclusion concerning the expectation of success to isolate a specific peptide (SEQ ID NO 101) for the defined use as vaccine to treat HIV-infection. In this situation it is not the theoretical possibility to isolate a substance by applying a known method, but the actual provision of one specific peptide for a defined use, not disclosed in the prior art, which establishes elements of surprise justifying acknowledgement of an inventive step.

38. The Board therefore is convinced that the subject-matter of claim 1 cannot be derived in an obvious way from the disclosure in document (1) in combination with document (4), or with any other document on file.

The subject-matter of claim 1, as well as of claims 2 to 10, which all refer to the peptide of claim 1, involves an inventive step and meets the requirements of Article 56 EPC.

39. The peptide claimed is identified in claim 1 by its amino acid sequence which allows its manufacturing. The same applies to the composition according to claims 2 to 6 and the vector of claim 7.

Claims 8 to 10 refer to the peptide for use in medicine and to its use for the preparation of a medicament, in particular of a vaccine, for treating HIV infection.

Where a therapeutic application is claimed in the form of the use of a substance or composition for the manufacture of a medicament for a defined therapeutic application, attaining the claimed therapeutic effect is a functional technical feature of the claim. As a consequence, under Article 83 EPC the application must disclose the suitability of the product to be manufactured for the claimed therapeutic application. Board 3.3.08 in decision T 609/02 of 27 October 2004 has comprehensively dealt with this issue in point (9) of the reasons for the decision.

The Board, by taking into account the intrinsic difficulties for a compound to be officially certified as a drug (several years of tests and very high developmental costs), accepted that for a sufficient disclosure of a therapeutic application in a patent/patent application, it is not always necessary that results of clinical trials are provided at the relevant date, but that it is required that the patent/patent application provides some information in the form of, for example, experimental tests, to the avail that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease.

Once this evidence is available from the patent application, then post-published (so-called) evidence may be taken into account, but only to back up the findings in the patent application.

40. The Board, in the present case, is convinced that the application as published provides sufficient information "to the avail that the claimed compound has a direct effect on a metabolic mechanism specifically

involved in the disease". The claimed peptide is shown to be isolated from an HIV strain, to contain an HLA-A3.2 specific motif and to have a binding affinity for its specific MHC-allele which indicates its capacity to elicit a CTL response.

Accordingly, the Board is satisfied that the patent application discloses the invention according to claims 1 to 10 of the sixth auxiliary request in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art (Article 83 EPC).

Order

For these reasons it is decided:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to grant a patent on the basis of claims 1 to 10 of the sixth auxiliary request, filed at the oral proceedings, and a description still to be adapted thereto.

Registrar:

Chair:

P. Cremona

U. Kinkeldey