

Internal distribution code:

- (A) [] Publication in OJ
(B) [] To Chairmen and Members
(C) [X] To Chairmen
(D) [] No distribution

**Datasheet for the decision
of 23 August 2006**

Case Number: W 0005/06 - 3.3.04

Application Number: PCT/DK2004/000799

Publication Number: WO2005/049073

IPC: A61K 39/00

Language of the proceedings: EN

Title of invention:

Proteins belonging to the Bcl-2 family and fragments thereof,
and their use in cancer patients

Applicants:

KRÆFTENS BEKÆMPELSE

Opponent:

-

Headword:

Bcl-2/KRÆFTENS BEKÆMPELSE

Relevant legal provisions:

PCT Art. 17(3)(a)

PCT R. 40.1, 40.2

EPC Art. 154(3)

Keyword:

"Invitation to pay additional fees - not based on invention
first mentioned in the claims - defective reasoning -
reimbursement of fees (yes)"

Decisions cited:

G 0001/89, W 0031/90, W 0007/90, W 0003/93, W 0004/94,

W 0026/03

Catchword:

-



Case Number: W 0005/06 - 3.3.04

International Application No. PCT/DK2004/000799

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 23 August 2006

Applicants: KRÆFTENS BEKÆMPELSE
Strandboulevarden 49
DK-2100 Copenhagen (DK)

Representative: HØIBERG A/S
St. Kongensgade 59 A
DK-1264 Copenhagen K (DK)

Decision under appeal: Protest according to Rule 68.3(c) of the Patent Cooperation Treaty made by the applicants against the invitation of the European Patent Office (International Searching Authority) to restrict the claims or pay additional fees dated 27 May 2005.

Composition of the Board:

Chairman: U. Kinkeldey
Members: B. Claes
C. Holtz

Summary of Facts and Submissions

- I. International patent application No. PCT/DK2004/000799 having the title "Proteins belonging to the Bcl-2 family and fragments thereof, and their use in cancer patients" was filed with 83 claims.

Claim 1 read:

"1. A vaccine composition comprising an isolated protein belonging to the Bcl-2 protein family or an immunogenically active peptide fragment hereof or a nucleic acid encoding said protein or said peptide fragment for use as a medicament."

The next independent claim, claim 10, read:

"10. An isolated immunogenically active peptide fragment derived from a protein belonging to the Bcl-2 protein family for use as a medicament in the prevention or treatment of a cancer."

Claims 2 to 9, 41 to 57 and 58 to 60 were directly or indirectly dependent on claim 1, whereby claim 58 (kit-of-parts) was formulated as an independent claim.

Claims 11 to 40, 61 to 70 and 83 were directly or indirectly dependent on claim 10, whereby claim 61 (composition for *ex vivo* or *in situ* diagnosis), claim 62 (diagnostic kit for *ex vivo* or *in situ* diagnosis), claim 63 (a complex of a peptide fragment and a Class I HLA molecule or a fragment of such molecule), claim 66 (method of detecting in a cancer patient the presence of a bcl-2 protein family member

reactive T-cells), claim 67 (molecule that is capable of binding to a peptide fragment), claim 70 (molecule capable of blocking binding), claim 71 (a method of treating a cancer disease), claim 76 (use of a peptide fragment in the manufacture of a medicament for the treatment or prevention of a cancer disease) and claim 83 (isolated T-cell) were formulated as independent claims.

Independent claim 81 related to a method of monitoring immunisation. Claim 82 was directly or indirectly dependent on claims 1, 10 or 81.

Dependent claims 23 read:

"23. The peptide fragment according to any of claims 10 to 11 and 16 to 19, which comprises a sequence selected from the group consisting of ALVGACITL (SEQ ID NO:1), ALSPVPPW (SEQ ID NO:2), SLALVGACI (SEQ ID NO:3), KTL LSLALV (SEQ ID NO:4), LL LSLALVGA (SEQ ID NO:5), WLSLKTLLSL (SEQ ID NO:6), AAAGPALSPV (SEQ ID NO:7), PLFDFSWLSL (SEQ ID NO:8), FTARGRFATV (SEQ ID NO:9), YLNRHLHTWI (SEQ ID NO:10), NIALWMTEYL (SEQ ID NO:11).

II. The European Patent Office (EPO) acting in its capacity as International Searching Authority (ISA) under Article 16 PCT and Article 154 EPC, informed the applicant that the application did not comply with the requirement of unity of invention (Rule 13.1 PCT) and invited the applicant to pay fees for 35 additional inventions, i.e. a sum of 54.250 Euros in accordance with Article 17(3)(a) PCT and Rule 40.1 PCT.

The invitation identified and defined invention 1 in "claims 1-5, 7, 10, 11, 13, 16-23, 31-83 all in part and insofar as applicable" as "[a]n MHC Class I-restricted epitope peptide derived from a protein of the Bcl-2 family, said peptide being selected from the group consisting of SEQ ID NOs: 1-11 and 40-64, respectively; A composition or pharmaceutical composition comprising such peptide; A complex of such peptide and a Class I HLA molecule; A method for detecting the presence of said protein of the Bcl-2 family using such complex; Antibodies binding to such peptide; uses of such peptide or composition for the preparation of a medicament for the treatment of cancer. All relating to SEQ ID NO: 1 (ALVGACITL), a peptide fragment of Bcl-2."

Inventions 2-36 were identified and defined in "claims 1-83 all in part and insofar as applicable as for invention 1 but relating to SEQ ID NOs: 2-11 and 40-64, respectively."

- III. In the reasons for finding lack of unity of invention the ISA stated that "[t]he implication of several members of the Bcl-2 protein family in cancer and the use of peptides derived from said members of the Bcl-2 protein family is (sic) known in the art. MHC Class I-restricted peptides derived from Bcl-2 protein family members were already disclosed in the prior art (D1). D1 also discloses specific CTL responses against said peptides, affinity values for the binding of said peptides to Class I HLA molecules and the use of such peptides in vaccination, cancer therapy and diagnosis (immunotherapy). D3 discloses immunogenic peptides derived from Bcl-2 used in a vaccine composition."

In the light of the above mentioned prior art, the ISA found that *"the problem of the present application can be summarized as providing further MHC Class I-restricted peptides **derived from Bcl-2 protein family members. The corresponding solutions are the peptides disclosed in SEQ ID NOs: 1-11 and 40-64 of the present application.** Given the essential differences between the sequences of the polypeptides and polynucleotides provided as solutions to the problem, due to the fact that MHC Class I-restricted peptides derived from Bcl-2 protein family members have already been identified in the state of the art, and since in the light of the state of the art, no other technical feature could be distinguished as being new and common to the identified problems and corresponding solutions, the ISA is of the opinion that there is no single inventive concept underlying the plurality of the claimed inventions in the present application."* (emphasis added by the board)

- IV. The applicant paid two additional search fees under protest according to Rule 40.2(c) PCT for searches of inventions 14 and 24, related to SEQ ID NO 42 and 52, respectively and filed, as a main request, a reasoned statement in support of the unity of the application. As a subsidiary request the applicant protested that the amount of the required additional fees was excessive. A more appropriate division of the claimed subject matter was in three groups represented by Bcl-2, Bcl-X_L and Mcl-1, respectively.
- V. The protest was reviewed in accordance with Rule 40.2(e) PCT by a review panel of the ISA within the meaning of Rules 105(3) EPC and 68.3(c) PCT. The review panel

confirmed the ISA's opinion regarding lack of unity, held that the invitation to pay the additional fees was justified and invited the applicant to pay a protest fee for further examination of the protest in accordance with Rule 40.2(c) PCT.

The review panel stated *inter alia* that "*[i]n addition, vaccine compositions comprising full-length Bcl-2 protein family members, fragments thereof and even nucleic acids, also fall within the scope of the claimed subject-matter, therefore, unity of invention is lacking even a priori.*"

- VI. The applicant paid the protest fee and argued in response to the notification of the review panel.

The applicant requested the reimbursement of the protest fee and of the additional search fees paid. As a subsidiary request the applicant submitted that a more appropriate division of the claimed subject matter was in three groups represented by Bcl-2, Bcl-X_L and Mcl-1, respectively and requested the ISA to find that the application only related to three inventions.

Reasons for the Decision

1. The protest complies with the requirements of Rule 40.2(c) and (e) PCT and is therefore admissible.
2. Under Article 154(3) EPC the Boards of Appeal rule on protests against the payment of additional fee(s) charged by the ISA under the provision of Article 17(3)(a) PCT. Pursuant to Rule 40.2(c) PCT the

Boards of Appeal are empowered to examine the protest and, to the extent that they find the protest justified, order the total or partial reimbursement of the fee(s).

It follows from these provisions that the board is not competent to deal with either the applicant's subsidiary request submitted in the reasoned statement of its letter of protest (see section IV above) to find that the amount of required additional fees was excessive or the further subsidiary request submitted in the same statement and repeated in the written response to the notification of the review panel (see section VI above) that the board group the inventions differently than was done by the ISA in its invitation to pay additional fees.

3. Pursuant to Article 17(3)(a), first sentence, PCT, the ISA shall invite the applicant to pay additional fees if it considers that the international application does not comply with the requirement of unity of invention as set out in the Regulations. Having regard to decision G 1/89 of the Enlarged Board of Appeal (OJ EPO 1991, 155), the ISA is empowered to raise a non-unity objection "*a posteriori*", i.e. after having taken the prior art into closer consideration (see also PCT International Search and Preliminary Examination Guidelines, here "PCT Guidelines", in force as from 25 March 2004, Chapter 10.04).

In the present case, the ISA stated in its reasoning for its finding of non-unity on an *a posteriori* basis and with reference to two prior art documents, that uses of **peptides** from members of the Bcl-2 protein family were known in the art, including their use in

vaccine compositions and cancer therapy. The problem of the application could therefore be summarised as providing further MHC I-restricted **peptides** derived from Bcl-2 protein family members. The ISA then concluded that there was no single inventive concept underlying the plurality of the claimed inventions in the application.

4. Article 17(3)(a), second sentence, PCT stipulates that the ISA shall establish the international search report on those parts of the international application which relate to the **invention first mentioned in the claims** ("main invention") and, provided the required fees have been paid within the prescribed time limit, on those parts of the international application which relate to inventions in respect of which additional fees were paid (see also PCT Guidelines, Chapter 10.61).

- 4.1 It follows from this provision that the ISA has no discretion to decide for which invention contained in an application the search fee already paid is to be used and for which invention(s) additional search fees are to be requested. Indeed, it has the legal obligation to conduct a search for the first invention for the one search fee paid, i.e. the invention first mentioned in the claims. It can ask for the payment of additional fees only for searching further inventions contained in the application (see e.g. decisions W 7/90 dated 19 October 1990, point 4 *et seq.* and W 31/90 dated 30 November 1990, point 7).

Furthermore, the board agrees with the findings in decision W 26/03 dated 27 October 2004, point 4, that from the above also follows that the justification for

asking for the payment of additional fees has to be based on the finding that there are further inventions which are non-unitary *a priori* or *a posteriori* in comparison with the invention first mentioned in the claims, i.e. the "main invention".

This requirement is an important procedural requirement with substantive repercussions which is intended to prevent the ISA from choosing arbitrarily which invention to search. In fact, by appropriately drafting the claims, establishing the order of the claims and the order of alternatives in the claims, the applicant determines which subject-matter is to be regarded as the core of the international application and shall therefore form the starting point for any search to be carried out by the ISA.

4.2 The board considers that the invention as identified and defined by the ISA as invention 1 is not the invention first mentioned in the claims, i.e. the "main invention" pursuant to Article 17(3)(a), second sentence, PCT.

4.2.1 Rather, the invention first mentioned in the claims pursuant to Article 17(3)(a), second sentence, PCT can only be contained in claim 1, which is directed to a **vaccine composition** for use as a medicament comprising a) an **isolated protein belonging to the Bcl-2 protein family** or b) an **immunogenically active peptide fragment hereof** or c) a **nucleic acid** encoding said protein or said peptide fragment, alternatively.

According to its formulation this claim thus refers, in a particular order, to three different and alternative

vaccine compositions of which the first comprises an isolated protein belonging to the Bcl-2 protein family, whereas the second comprises an immunogenically active **peptide fragment** of such a protein belonging to the Bcl-2 protein family which was searched by the ISA.

- 4.2.2 The board considers that, without examining the merits of the statements of the ISA in relation to the disclosure of the documents referred to and the merits of the argumentation *a posteriori* (see section III), even when following the ISA's reasons for its finding of a lack of unity of invention, the *a posteriori* argumentation based on the availability and uses of peptide fragments of protein belonging to the Bcl-2 protein family can only be relevant for the second group of vaccines comprising peptide fragments.
- 4.2.3 The ISA has defined invention 1 and thus the invention for which the search fee already paid was used, exclusively in relation to the **peptide fragment ALVGACITL** (SEQ ID NO: 1) of Bcl-2. The board further notes that the summarised description of invention 1 as defined by the ISA does not refer to **vaccines** comprising the peptide fragment. The **peptide** is first mentioned in the claims in claim 23, being dependent on the second independent claim, i.e. claim 10 directed to an isolated immunogenically active peptide fragment derived from a protein belonging to the Bcl-2 protein family for use as a medicament in the prevention or treatment of a cancer (see section I). This invention was searched, was compared with the peptides of the prior art and led to the ISA's finding that the application contained 36 inventions.

No reasons were given by the ISA in the invitation to pay additional fees for not considering the first group of vaccines mentioned in claim 1 as the invention first mentioned in the claims.

The reasons for non-unity presented by the ISA are hence legally defective as they provide no legal basis for ignoring the "main invention" in the claims of the application and do not justify an invention other than contained in claim 1 to be defined as the invention first mentioned in the claims and for defining another invention as the "main invention".

5. Rule 40.1 PCT provides that the ISA's invitation to pay additional fees pursuant to Article 17(3)(a) PCT shall specify the reasons for which the international application is not considered as complying with the requirement of unity invention.

The purpose of the protest procedure under Rule 40.2 PCT is to enable the justification for the invitation to pay additional fees to be submitted to substantive review. The only issue to be examined by the Board therefore is whether, considering the reasons given by the ISA and the submissions made by the applicant in support of the protest, retaining additional search fees was justified. The Board cannot investigate *ex-officio* whether an objection of lack of unity would have been justified for reasons other than those given (see decisions W 3/93, OJ EPO 1994, 931, Headnote III and point 4; and W 4/94, OJ EPO 1996, 73, point 5.5). To the extent that the reasons given by the ISA for charging additional fees are insufficient or wrong, the protest is justified and the fees have to be reimbursed,

irrespective of whether or not, as a result, the finding of non-unity could be regarded as justified as to substance.

6. The board therefore decides that the additional fees paid under protest and the protest fee are to be reimbursed.

Order

For these reasons it is decided that:

1. Two additional search fees are reimbursed.
2. The protest fee is reimbursed.

Registrar:

Chair:

P. Cremona

U. Kinkeldey