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**Datasheet for the decision  
of 6 August 2009**

**Case Number:** W 0035/08 - 3.3.04

**Application Number:** PCT/GB 07/003592

**Publication Number:** WO 2008/035093

**IPC:** C07K 7/52, A61K 38/12

**Language of the proceedings:** EN

**Title of invention:**  
Peptides

**Applicant:**  
Lexcicon Limited  
New, Roger

**Headword:**  
Internally-constrained cyclic oligopeptides/LEXCICON

**Relevant legal provisions:**  
PCT Art. 17(3)(a)  
PCT R. 40.1(i), 40.2(c), 13.1, 13.2  
EPC Art. 154

**Keyword:**  
"Invitation reasoned - yes"  
"Lack of unity 'a posteriori' - (yes)"

**Decisions cited:**  
W 0016/08

**Catchword:**  
-



**Case Number:** W 0035/08 - 3.3.04

**International Application No.** PCT/GB 07/003592

**D E C I S I O N**  
**of the Technical Board of Appeal 3.3.04**  
**of 6 August 2009**

**Applicants:**

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**Decision under appeal:**

**Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicants against the invitation (payment of additional fees) of the European Patent Office (International Searching Authority) dated 02 April 2008.**

**Composition of the Board:**

**Chairman:** U. Kinkeldey  
**Members:** G. Alt  
T. Bokor

## Summary of Facts and Submissions

- I. International patent application No. PCT/GB07/003592 was filed with forty nine claims relating to the structure, use and production of internally-constrained cyclic oligopeptides.
- II. The European Patent Office (EPO), acting in its capacity as an International Searching Authority (ISA) under Article 16 PCT and Article 154 EPC informed the applicant in an invitation pursuant to Article 17(3)(a) PCT and Rule 40.1 PCT 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 the search of five additional inventions.
- III. In the invitation the ISA stated that the application was directed "to the general problem of providing compounds capable of displaying, or having, multiple epitopes (multivalent)" and that the application's solution to this problem was "to provide cyclic peptides that have an additional intra-cyclic structural constrain, resulting [sic] the presence of two or more putative epitopes". The ISA found that this solution "lacked novelty over for instance: Jaulent et al. (2004), which discloses a bifunctional bicyclic polypeptide comprising two identical or different epitopes (cf. abstract, fig.1, Table)" and over the disclosure in five further documents.

The ISA concluded: "The claimed subject matter must therefore be subdivided into the following two main groups:

- A) Internally constrained cyclic oligopeptides, wherein the associating amino acids form a covalent bond (Claims 4, 5 and partially claims 1-3, 8-11 and 15-49), and
- B) Internally constrained cyclic oligopeptides, wherein the associating amino acids form a non-covalent bond (Claims 6, 7, 12-14 and partially claims 1-3, 8-11 and 15-49)."

It was then stated: "Moreover it appears that the claimed subject-matter must not only be divided into groups covering the covalent and non-covalent association (groups A and B above), but also in sub-groups covering the number of intended epitopes and the number and position of associating groups."

Subsequently, the invitation listed six inventions each characterized by different combinations of features.

On the first page of the invitation the definitions of the six inventions were repeated and assigned to different groups of claims.

Thus, invention 1 related to "Claims 4, 5 and claims 1-3, 8-11, 15-17, 24-26, 30-33, 39-49 (all partially) and was defined as "internally constrained cyclic oligopeptides, wherein the associating amino acids form a covalent bond, comprising two epitopes and the associating group is attached to the C-alpha of the associating amino acid".

Invention 4 related to "claims 6, 7, 12-14 and claims 1-3, 8-11, 15-17, 24-26, 30-33, 39-49 (all partially)" and was defined as "internally constrained cyclic

oligopeptides, wherein the associating amino acids form a non-covalent bond, wherein the associating group is attached to the C-alpha group of the associating amino acid, and the peptide comprises two epitopes".

- IV. With a letter dated 02 May 2008, the applicant paid one additional search fee under protest (Rule 40.2(c) PCT) and stated on page 1, second paragraph of this letter: "The applicant hereby pays one additional search fee in respect of "invention 4" [...] identified in the Search Report."

The applicant argued that the invitation was not sufficiently reasoned in the sense of Rule 40.1(i) PCT because the ISA had not provided "basic considerations behind the finding of lack of unity of groups A and B". Consequently, the subdivision into six inventions could not be understood.

Moreover with regard to Rule 40.2(c) PCT the applicant argued that the subject-matter of those claims to which "group B" referred was novel and inventive. Therefore, the subdivision of "group B" into the three inventions 4, 5 and 6 was not justified. Consequently, the number of the required search fees was excessive.

Finally, the applicant requested on the last page of the letter in the last paragraph that "the invention identified as group B) is searched, which covers the inventions 4, 5 and 6 identified by the Examiner."

V. On 20 August 2008, the ISA invited the applicant to pay a protest fee and informed the applicant that a prior review of the justification for the invitation to pay additional fees had confirmed that the invitation to pay such fee was justified.

In the annex to the invitation to pay the protest fee the review panel noted that the applicant did not actually request the refund of the additional fee but rather that the additional search should not be restricted to the subject-matter of invention 4, but should be extended to the subject-matter of inventions 5 and 6. Moreover, the review panel found that the subject-matter of "group B" lacked novelty over prior art cited in the invitation to pay additional fees and that therefore the subdivision of "group B" in inventions 4, 5 and 6 was justified.

VI. The applicant paid the protest fee with a fee voucher included in a letter dated 17 September 2008.

### **Reasons for the Decision**

1. Given that the international application under consideration has an international filing date of 20 September 2007, the protest is subject to the provisions of the PCT as in force from 1 April 2007. The boards of appeal are responsible for deciding on protests relating to international applications pending at the time of entry of the EPC 2000. Details of the procedure are guided by the Decision of the President of the EPO dated 24 June 2007, Article 3 (OJ EPO 2007,

- Special Edition No. 3, 140), see also W 16/08 of 11 September 2008, point 1.1 to 1.5 of the reasons.
2. The protest against the invitation by the ISA to pay additional fees was filed in time, is reasoned and is hence admissible.
  3. In view of Rule 40.1(c) PCT the objective of the examination of a protest against an invitation of the ISA to pay additional search fees is to decide whether or not the ISA's invitation to pay additional fees was justified and whether or not, therefore, the additional fees paid by an applicant upon invitation by the ISA have to be reimbursed.
  4. In the present case the applicant has paid one additional search fee and instructed the ISA that it be used for the search of "invention 4", but has at the same time requested that "group B" covering "inventions 4, 5 and 6" be searched (section IV above; referred to hereinafter also as the "second request").
  5. It appears thus that the board is faced with two different requests, the first one relating to the search of "invention 4", and the second one relating to the search of "the invention identified as group B)" covering "inventions 4, 5 and 6".
  6. Turning first to the admissibility of the "second request" mentioned above, the board notes with regard to one of the possible interpretations of this request, namely that "group B" be searched, that the ISA has not considered "group B" as an "invention", but has referred to it as a "main group" (see section III

above). In fact, it is apparent from the context of the invitation that "group B" is merely an - yet explicitly mentioned - intermediate step in the ISA's logical chain towards defining the inventions contained in the application (see section III above).

Or, given the wording of the "second request", the applicant has considered the term "group B" as a collective term for "inventions 4, 5 and 6". On the basis of this interpretation of the term the applicant's request has to be rejected as inadmissible as far as inventions 5 and 6 are concerned, since no search fees were paid for these inventions.

7. Thus, it follows from the observations in points 3 to 6 above that in the present case the board deals with the question of the reimbursement of the additionally paid search fee only insofar as inventions 1 and 4 are concerned.

*Invitation to pay additional fees sufficiently reasoned?*

8. Rule 40.1 PCT stipulates that the invitation under Article 17(3)(a) PCT to pay additional fees must "specify the reasons for which the international application is not considered as complying with the requirement of unity of invention".
9. The purpose of the provision under Rule 40.1(i) PCT is to enable the applicant (and the board in case of a protest) to examine whether the invitation is justified. This requires that the invitation must be drafted in a form that is suited to fulfil this purpose, i.e. the reasoning must be comprehensible.



10. In its invitation the ISA has stated the problem underlying the application and the solution provided by the application and has furthermore explained that the "solution" lacks novelty (see section III above). Since the solution to a problem is presented in a patent application in the form of claims, the ISA in fact considered that the subject-matter of claim 1 was not novel.
  
11. The ISA has listed six inventions among them "invention 1" and "invention 4", has indicated the groups of claims representing them and has indicated the special technical features characterizing each of the inventions (see section III above). Thus, the ISA considered that in the present case the lack of novelty of the subject-matter of independent claim 1 results in subject-matter "which is not so linked as to form a single general inventive concept" (see Rule 13.1 PCT, cited below).
  
12. The ISA has not explicitly explained why there is no technical relationship among the inventions defined by it, in particular invention 1 and 4, i.e. why the indicated special technical features are not the "same or corresponding" (see Rule 13.2 PCT, cited below). However, the board considers this to be implied by the differing combinations of special technical features (see the combinations in section III above).
  
13. Thus, in the board's view the lack of unity among inventions 1 and 4 is comprehensible without any further explanation, in particular as to why the groups A and B (see section III above) lack unity.

14. Consequently, the ISA's invitation complies with the requirements of Rule 40.1(i) PCT.

*Examination of the protest*

15. According to Rule 13.1 PCT, "[t]he international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (requirement of unity of invention)".
16. In its invitation the ISA considers that claim 1 of the application as filed lacks novelty, for example, in view of the document "Protein engineering, design, and selection; Oxford Journal, vol. 17, no. 9, September 2004, pages 681-687, Jaulent et al.". Indeed, the document discloses, for example in Figure 1, a cyclic polypeptide comprising two epitopes created by an intra-cyclic association which is provided by two cysteines joined by a disulphide bridge. Thus, the board agrees with the ISA's finding that the subject-matter of claim 1 is not novel. Therefore, the application does not fulfil the requirement of unity "a posteriori".
17. Consequently, the further question to be decided by the board is whether or not the subject-matter defined by the ISA as invention 1 and that defined as invention 4 (see point 7 above) are "so linked as to form a single general inventive concept".

18. According to the ISA invention 1 is directed to "internally constrained cyclic oligopeptides, wherein the associating amino acids form a covalent bond, comprising two epitopes and the associating group is attached to the C-alpha of the associating amino acid".

Invention 4 was defined as relating to "internally constrained cyclic oligopeptides, wherein the associating amino acids form a non-covalent bond, wherein the associating group is attached to the C-alpha of the associating amino acid, and the peptide comprises two epitopes".

The board notes that in the application the feature of covalent and non-covalent bonding is used in connection with "associating functional groups" and not in connection with the "associating amino acids". In fact, the "associating amino acids" are those of the peptide ring to which the "associating functional groups" are attached (see page 8, last two paragraphs and page 9, first two paragraphs). It is assumed therefore that the ISA, when referring to "associating amino acids", actually intended to refer to the "associating functional groups".

19. According to page 10, last two paragraphs of the application, the "associating functional groups" define the epitope-containing domains by association between these functional groups. At the same time they stabilize the peptide.
20. On page 9, second paragraph it is disclosed that the associating functional groups are borne on associating amino acids. Thus, the associating functional groups

may be the side chains of associating amino acids, they may be borne on nitrogen atom of peptide linkages or on other suitable groups.

21. According to well-known nomenclature in chemistry, the "C-alpha", wherein "C" stands for "carbon", is the carbon atom next to the carbonyl group. The C-alpha is thus a part of the peptide backbone.
22. It is also well known what the terms "covalent" and "non-covalent" bond mean.

A covalent bond is a chemical bond formed by the sharing of one or more electrons, especially pairs of electrons, between atoms. As an example of an associating functional group forming a covalent bond the application mentions a di-sulphide bond (page 14, last paragraph).

A non-covalent bond is a chemical bond involving electromagnetic interactions. The four common types of non-covalent bonds are hydrogen bonds, ionic bonds, Van der Waals forces, and hydrophobic interactions. According to the application hydrophobic bonds are the preferred non-covalent interactions (page 11, first paragraph) occurring for example between aliphatic hydrocarbon chains (page 11, last line).

Thus, the combination of the technical features by which the peptides of invention 1 and 4 are defined (see point 18 above) results in chemical structures which differ with respect to the type of bonding between the "associating functional groups", i.e. the association is either covalent or non-covalent.

23. Rule 13.2 PCT stipulates that "[w]here a group of inventions is claimed in one and the same international application, the requirement referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art."
24. When considering whether or not the special technical features, by which the subject-matter of inventions 1 and 4 is defined, are the "same or corresponding", the board comes to the conclusion in view of the observations in points 19 to 23 above, that they are not the same. In the board's view, they can also not be regarded as "corresponding" since, as explained in point 22 above, the covalent and non-covalent bonding not only relies on different physico-chemical phenomena, but also, as may be seen from the examples given in point 22 above, they are mediated by quite different chemical groups. Moreover, it seems that covalent and non-covalent bonds have a different effect on the stability of the cyclic peptide, since it is disclosed on page 10, last paragraph that "[n]on-covalent intra-cyclic associations are particularly preferred in the present invention because they allow the cyclic oligopeptide to have the right balance between rigidity and flexibility."

25. Thus, inventions 1 and 4 do not involve the "same or corresponding special technical features" and therefore there is no technical relationship between them.
26. The applicant has submitted arguments that inventions 4, 5 and 6 are linked by a "single general inventive concept". However, this is a question not to be decided by the board here (see point 7 above).
27. Thus, the board concludes that inventions 1 and 4 are not so linked as to form single general inventive concept, contrary to the requirements of Rule 13.1 PCT.
28. Hence, the invitation to pay an additional fee for the search of "invention 4" was justified.

## **Order**

### **For these reasons it is decided that:**

The protest under Rule 40.2(c) PCT is dismissed.

The Registrar:

The Chair:

C. Eickhoff

U. Kinkeldey