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D E C I S I O N
of 26 September 1996

Case Number: T 0442/95 - 3.3.4

Application Number: 86117432.4

Publication Number: 0231495

IPC: C12Q 1/68

Language of the proceedings: EN

Title of invention:

One-step method and polynucleotide compounds for hybridizing to target polynucleotides

Applicant:

ENZO BIOCHEM, INC.

Opponent:

-

Headword:

Polynucleotide/ENZO

Relevant legal provisions:

EPC Art. 54, 123(2), 111(1)
EPC R. 86(4)

Keyword:

- "Main request - unsearched subject-matter (yes) "
- "Auxiliary request - added subject-matter (no) "
- "Novelty (yes)
- "Remittal (yes) "

Decisions cited:

-

Catchword:

-



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Boards of Appeal

Chambres de recours

Case Number: T 0442/95 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 26 September 1996

Appellant:

ENZO BIOCHEM, INC.
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New York, N.Y. 10013 (US)

Representative:

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Decision under appeal:

Decision of the Examining Division of the
European Patent Office dated 28 December 1994
refusing European patent application
No. 86 117 432.4 pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: U. M. Kinkeldey
Members: L. Galligani
S. C. Perryman

Summary of Facts and Submissions

- I. European patent application No. 86 117 432.4 published under No. 0 231 495 with title "One-step method and polynucleotide compounds for hybridizing to target polynucleotides" was refused by the examining division with decision dated 28 December 1994. This decision was taken on the basis of Claims 1 to 26 filed with letter dated 8 December 1994.

Claim 1 read as follows:

"A compound comprising an oligo- or polynucleotide which comprises an entity which upon hybridization to a complementary polynucleotide is capable of generating a detectable change in property in said hybrid, said entity being covalently or non-covalently attached by means of a linker arm to the base moiety of a nucleotide in said oligo- or polynucleotide, wherein said base moiety is selected from the group consisting of pyrimidines, purines and deazapurines, provided that whenever the base moiety is a pyrimidine, the sugar is attached to the N¹-position of the pyrimidine, and whenever the base moiety is a purine or deazapurine, the sugar is attached to the N⁹-position of the purine or deazapurine."

Dependent Claims 2 to 26 related to specific embodiments of the compound according to Claim 1.

This set was rejected by the examining division on the ground that claim 1 therein lacked novelty having regard to either one of the following documents:

- (3) EP-A-0 124 124;
- (4) EP-A-0 097 373.

In the final part of the decision, the examining division observed that both claims 1 and 2 of the set in question did not satisfy the requirements of Article 123(2) EPC, this, however, not being the ground for the refusal of the application.

II. The appellants lodged an appeal against this decision. With the statement of grounds filed on 8 May 1995, the appellants enclosed claims 1 to 26 identical to claims 1 to 26 filed with letter dated 8 December 1994 and refused by the examining division.

III. The Board issued a communication pursuant to Rule 11 of the rules of procedure of the boards of appeal drawing the appellants' attention in particular to the admissibility of the claims on file under Article 123(2) EPC.

IV. Oral proceedings took place on 26 September 1996. As a **main request**, the appellants submitted new claims 1 and 2 in substitution of previous claims 1 and 2. These new claims read as follows:

"1. Polynucleotide compound comprising a polynucleotide which comprises at least one entity which upon hybridization to a complementary polynucleotide is capable of generating a change in property in said hybrid detectable in a homogeneous reaction, said entity being covalently or non-covalently attached by means of a linker arm to the base moiety, sugar moiety or phosphate moiety of a nucleotide in said polynucleotide, with the proviso that compounds where the entity(ies) is (are) bound either to the 5' and 3' ends of the compounds or to internucleotide phosphate groups and a compound which contains only one phenanthridine bound to a phosphate moiety are excluded.

2. A compound of claim 1 wherein the polynucleotide comprises at least two entities whereby the entities are attached to nucleotides that are separated from each other by about a stretch of ten other nucleotides."

Claims 3 to 26 of this request were as submitted with letter of 8 May 1995 (see Section II above).

Furthermore, an **auxiliary request** with claims 1 to 25 was filed in which claim 1 read as follows:

"Polynucleotide compound comprising a polynucleotide which comprises at least two entities which upon hybridization to a complementary polynucleotide is capable of generating a change in property in said hybrid detectable in a homogeneous reaction, each of said entities being covalently or non-covalently attached by means of a linker arm to the base moiety, sugar moiety or phosphate moiety of a nucleotide in said polynucleotide, whereby the entities are attached to nucleotides that are separated from each other by about a stretch of ten other nucleotides, with the proviso that compounds where all the entities are bound either to the 5' and/or 3' ends of the compound or to internucleotide phosphate groups are excluded."

Dependent claims 2 to 25 of this auxiliary request related to embodiments of the compound according to claim 1.

V. The appellants submitted that the wording of new claims 1 and 2 of the main request found support in item 2 on pages 13 to 15 of the description where a polynucleotide compound comprising a polynucleotide and at least one intercalating aromatic entity was disclosed. As for claim 1 of the auxiliary request,

they submitted that this was directed to polynucleotide compound described in connection with the method of hybridisation of claim 1 as filed. It was submitted that in both requests the disclaimer aimed at creating a clear distinction over either one of the following prior art documents:

(1) US-A-4 547 569

(2) EP-A-0 117 777.

- VI. The appellants requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request with claims 1 and 2 as submitted at the oral proceedings on 26 September 1996 and claims 3 to 26 as submitted with letter of 8 May 1995 or on the basis of the auxiliary request with claims 1 to 25 submitted at the oral proceedings on 26 September 1996.

Reasons for the Decision

1. The appeal is admissible.

Main request

2. According to Rule 86(4) EPC: "Amended claims may not relate to unsearched subject-matter which does not combine with the originally claimed invention or group of inventions to form a single general inventive concept".
3. The Board observes that in the present case, at the beginning of substantive examination, the examining division (see letter dated 9 October 1991) had raised a lack of unity objection under Article 82 EPC against the claims as filed on the basis of the finding that

these related to three groups of inventions which were not so linked as to form a general inventive concept, these three groups being as follows:

- (a) **claims 1 to 16** related to a homogeneous hybridization assay using a polynucleotide probe labelled with **at least two entities** providing upon hybridization for a change of the properties of the hybrid;
- (b) **claims 17 and 18** related to a method for preventing in vivo transcription of a target double-stranded polynucleotide or the in vivo translation of a target single-stranded polynucleotide based on the use of a polynucleotide drug comprising a polynucleotide having attached thereto **at least two entities** providing upon hybridization for a change of the properties of the hybrid;
- (c) **claims 19 and 20** related to a compound comprising **at least one moiety** having a particular structure wherein the signal generating entity was a phenanthridine.

- 4. During the further prosecution of the case before the first instance, the appellants filed new claims based on the subject-matter of group (c). These claims, which were then further amended, were eventually refused by the examining division (see Section I above).
- 5. The subject-matter of claim 1 now at issue is a polynucleotide compound comprising a polynucleotide which comprises **at least one entity** which upon hybridization to a complementary polynucleotide is capable of generating a change in property in said hybrid detectable in a homogeneous reaction, said

entity being covalently or non-covalently attached by means of a linker arm to the base moiety, sugar moiety or phosphate moiety of a nucleotide in said polynucleotide. This subject-matter did not appear in the claims as filed. In fact, the claimed compound is different from the compound referred to in the groups of claims (a) and (b) which must contain **at least two entities** as well as from that of group (c) which, although comprising at least one moiety, is a compound with a particular structure wherein a phenathridine is always the signal-generating entity. The appellants submit that the description of the newly claimed compound is to be found in the description (see Section V above).

6. In the Board's judgement, the subject-matter now claimed has not been searched and it does not combine with the originally claimed and searched groups of inventions to form a single general inventive concept because it is based on a different technical approach as, according to present claim 1, one attached entity is enough for generating a detectable change upon hybridization with a target polynucleotide. There is no need at this stage to investigate whether the application as filed provides support for such a claim, because under Rule 86(4) EPC the claim is **not admissible**. The appellants may continue to pursue the subject-matter of such claim only in the form of a divisional application in accordance with Article 76 EPC. In the latter case, under Article 76(1) EPC, the first instance will have to deal with the question whether the subject-matter of the divisional application extends beyond the content of the earlier application as filed.

Auxiliary request

7. The European patent application as filed describes a polynucleotide compound comprising a polynucleotide which comprises at least two entities which upon hybridization to a complementary polynucleotide is capable of generating a change in property in said hybrid detectable in a homogeneous reaction (see eg from page 5, line 16 to page 6, line 16), wherein each of said entities is covalently or non-covalently attached by means of a linker arm to the base moiety, sugar moiety or phosphate moiety of a nucleotide in said polynucleotide (see page 18, last paragraph) and the entities are attached to nucleotides that are separated from each other by about a stretch of ten other nucleotides (see eg. page 10, last paragraph). The subject-matter of claim 1 finds therefore formal support in the application as filed. The same applies to dependent claims 2 to 25 which concern embodiments of the compound according to claim 1. These are described eg on pages 59 to 63 of the application as filed. The proviso in claim 1 excludes from the claimed area compounds where all entities are bound either to the 5' and/or 3' ends of the compounds (document (2)) or to internucleotide phosphate groups (document (1)). The introduction of the said proviso in the claim does not result in the creation of new subject-matter. Thus, ←
no objection under Article 123(2) EPC exists.

8. The compound according to present claim 1 is novel ←
over the cited documents (1) and (2) in which all the signal generating entities are bound either to the 5' and/or 3' ends of the compounds or to internucleotide phosphate groups. Further prior art documents (3) or (4) do not contemplate a polynucleotide which comprises at least two entities which upon hybridization to a complementary polynucleotide is capable of generating a change in property in said hybrid detectable in a

homogeneous reaction and where the said entities are attached to nucleotides that are separated from each other by about a stretch of ten other nucleotides. Thus, claim 1 is novel.

9. The subject-matter of claims 1 to 25 has not yet been examined by the examining division in respect of inventive step. In order to guarantee such examination without loss of instance, the Board considers it appropriate to make use of the power granted to it under Article 111(1) EPC and to remit the case to the first instance for further prosecution.

Order

for these reasons it is decided that:

1. The decision under appeal is set aside;
2. The case is remitted to the first instance for further prosecution on the basis of the auxiliary request with claims 1 to 25 submitted at oral proceedings on 26 September 1996.

The Registrar:

The Chairperson:

L. McGarry

U. Kinkeldey