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D E C I S I O N
of 17 December 1998

Case Number: T 1055/97 - 3.3.4

Application Number: 88104964.7

Publication Number: 0285950

IPC: C07H 21/00

Language of the proceedings: EN

Title of invention:
A drug delivery conjugate

Applicant:
Enzo Biochem, Inc.

Opponent:
-

Headword:
Drug delivery conjugates/ENZO

Relevant legal provisions:
EPC Art. 83

Keyword:
"Sufficiency of disclosure - no"

Decisions cited:
T 0409/91, T 0435/91

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1055/97 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 17 December 1998

Appellant: Enzo Biochem, Inc.
325 Hudson Street
New York, N.Y. 10013 (US)

Representative: Vossius & Partner
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Decision under appeal: Decision of the Examining Division of the European Patent Office posted 10 April 1997 refusing European patent application No. 88 104 964.7 pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: U. M. Kinkeldey
Members: F. L. Davison-Brunel
W. Moser

Summary of Facts and Submissions

I. European patent application No. 88 104 964.7 with the title "A drug delivery conjugate" was filed as a divisional application from the application No. 83 106 112.3 with the publication No. 0 097 373, and was published under No. 0 285 950. It was refused by the Examining Division in a decision dated 10 April 1997.

II. The decision of the Examining Division was taken on the basis of a main request and of an auxiliary request filed on 13 February 1997. Claim 1 of the main request was found not to fulfill the requirements of Article 123(2) EPC. As regarded the auxiliary request, it was decided inter alia that the description failed to provide an enabling disclosure of the invention as claimed in claim 1 (cf. point 4 of the decision).

III. On 20 June 1997, the Appellant (Applicant) lodged an appeal against this decision and paid the appeal fee. A statement setting out the grounds of the appeal which dealt with all of the issues raised and decided on in the decision under appeal including the issue related Article 83 EPC was submitted as well as a new set of claims on 20 August 1997.

IV. On 16 October 1998, as an annex to the summons to attend oral proceedings, a communication was sent by the Board according to Article 11(2) of the Rules of Procedure of the Boards of Appeal setting out the Board's provisional, non binding opinion.

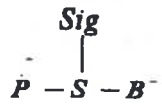
V. Oral proceedings took place on 17 December 1998. The Appellant filed a main request with 19 claims and an auxiliary request with 18 claims in replacement of all requests then on file.

Claim 1 of the main request read as follows:

"1. A therapeutic composition comprising a polynucleotide having at least one nucleotide selected from the group:

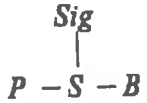
(i) a nucleotide having the formula P-S-B-Sig wherein P is a phosphate moiety, S is a sugar moiety, B is a pyrimidine, purine or 7-deazapurine moiety, P being attached at the 3' and/or the 5' position of S when the nucleotide is a deoxyribonucleotide and at the 2',3' and/or 5' position when the nucleotide is a ribonucleotide, B being attached to the 1'-position of S from the N^1-position when B is a pyrimidine or the N^9-position when B is a purine and Sig is covalently attached to B at the N^3- or C^6-position when B is a pyrimidine, at the C^2-, N^3-, or C^8-position when B is a purine, and at the C^7-position when B is a 7-deazapurine;

(ii) a ribonucleotide having the formula,

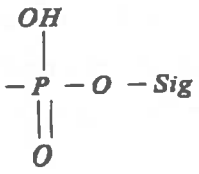


wherein P is a phosphate moiety, S is a sugar moiety, B is a pyrimidine, purine or 7-deazapurine moiety, P being attached at the 2',3' and/or 5' position of S, B being attached to the 1'-position of S from the N^1-position when B is a pyrimidine or the N^9-position when B is a purine or 7-deazapurine; and wherein Sig is a chemical moiety covalently attached to S; and

(iii) a nucleotide having the formula



wherein P is a phosphate moiety, S is a sugar moiety, B is a pyrimidine, purine or 7-deazapurine moiety, P being attached to the 3' and/or the 5' position of S when said nucleotide is a deoxyribonucleotide and at the 2',3' and/or 5' position of S when said nucleotide is a ribonucleotide, B being attached to the 1' position of S from the N^1-position when B is a pyrimidine or the N^9-position when B is a purine, and wherein Sig is covalently attached to P via the chemical linkage



wherein Sig represents a moiety which is detectable when the polynucleotide is incorporated into a double-stranded ribonucleic or desxyribonucleic acid duplex and wherein Sig is attached to said nucleotide directly or through a linkage group."

Claim 1 of the auxiliary request differed from claim 1 of the main request in that the sentence "and wherein Sig is a chemical moiety covalently attached to S", at the end of (ii), was replaced by the sentence "and wherein Sig is a chemical moiety covalently attached to S at the 2' or 3' position", and claim 19 of the main request was not retained.

VI. The Appellant argued essentially as follows:

(a) Article 123(2) EPC; Main request, claim 1:

The compounds of claim 1 were already mentioned with all of their features in the application as filed. In particular, the feature that the Sig moiety was covalently attached to S was to be found on page 115, line 9. On page 104, lines 16 to 18 it was furthermore stated that the compounds of the type (ii) "desirably have the Sig chemical moiety attached to the C2' position of the S moiety or C3' position of the S moiety". This implicitly suggested that it could also be a covalent linkage to the C5' position. Thus the application as filed disclosed all possible linkages of Sig and S in the compounds of type (ii) and the generic characterisation of the linkage of Sig as being with S was allowable under Article 123(2) EPC.

(b) Article 83 EPC

In the communication pursuant to Article 11(2) of the Rules of Procedure of the Boards of Appeal, the Board had not given a preliminary opinion on the issue of Article 83 EPC. Article 83 EPC had been a ground for refusal by the Examining Division and, as such, could be expected to be a concern dealt with at oral proceedings. Nonetheless, the absence of any preliminary opinion from the Board on sufficiency of disclosure had resulted in the consultation between the Appellant and its professional representative, in preparation for the oral proceedings, being less thorough than it would otherwise have been.

At the filing date of the application, synthesizing the P-B-S moieties would have been a matter of routine for the skilled person because methods for coupling bases, sugars and phosphate were already well known. The additional coupling of Sig moieties of different kinds was described in examples 23, 31, 34, and on page 92 of the application as filed. Thus, no undue burden of experimentation was involved in isolating P-B-S-Sig derivatives. Specific therapeutic applications of the claimed compositions were cited on pages 113 to 116 and 118 of the application as filed, and, accordingly, "the skilled person knows or is in the situation to determine therapeutic compositions which fall within the scope of protection of the new claims set and is therefore able to carry out the invention."

VII. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the following documents:

(a) main request: claims 1 to 19 submitted during oral proceedings; or

(b) auxiliary request: claims 1 to 18 submitted during oral proceedings.

Reasons for the Decision

1. The appeal is admissible

Procedural matter

2. By its communication dated 16 October 1998, the Board informed the Appellant that the issues of whether or not the application with the amended claims filed on 20 August 1997 met the requirements of Articles 123(2) and 84 EPC should be dealt with at the oral proceedings, and it gave its provisional opinion concerning these issues. In contrast to that, the issue of compliance with the requirement of Article 83 EPC of the so amended application in suit was not mentioned in the communication. From this factual situation it could, however, by no means be inferred that this issue would not be thoroughly dealt with in the oral proceedings, so much the more than, in the decision under appeal, the auxiliary request was *inter alia* refused because, in the opinion of the Examining Division, the application did not meet the requirement as set forth in Article 83 EPC.

3. On the other hand, a meaningful assessment of sufficiency of disclosure of the claimed invention under Article 83 EPC presupposes beforehand (i) that the claims, which define the subject-matter for which protection is sought, be clear and supported by the description within the meaning of Article 84 EPC, and (ii) that, in order to meet the requirement of Article 123(2) EPC, said subject-matter has already been disclosed in the application as filed.

4. Thus, in the Board's judgement, the above-mentioned communication could not objectively be interpreted as meaning that the issue of sufficiency of disclosure pursuant to Article 83 EPC would not be dealt with in the oral proceedings, nor that the Board was satisfied that the application in suit, with the claims filed on 20 August 1997, met the requirements of this provision. Therefore, the Board cannot accept the argument that the absence of any preliminary opinion on sufficiency of disclosure in the above-mentioned communication was instrumental in the consultation between the Appellant and its professional representative before oral proceedings being less thorough in this respect than it would otherwise have been.

Sufficiency of disclosure: Article 83 EPC

5. Claim 1 of the main request and of the auxiliary request relates to therapeutic compositions comprising polynucleotides having at least one nucleotide of the general formula P-B-S-Sig. The length of the polynucleotides is not specified, nor is there any indication regarding the number of altered P-B-S-Sig nucleotides they may contain. B, S and P are generically defined as belonging to three chemical groups (bases (B), sugars (S) and phosphate (P)), with the possibility for P, B and S to be linked to each other at different positions. Sig is functionally identified as being a detectable moiety when the polynucleotide is incorporated in nucleic acid duplexes. A non-exhaustive list of potentially useful detectable moieties may be drawn from the description: aliphatic chemical moieties, aromatic cyclo-aliphatic groups, poly- or oligosaccharides, chelating agents, moieties comprising an electron-dense component, a magnetic component, an enzyme, a hormone, a radioactive

component, a metal containing component, a fluorescing component, an antigen, an antibody, a sugar residue complexed with a protein, N-acetylglucosamine bound to wheat germ agglutinin and so on...

6. Claim 1 of both requests comprises compositions where the therapeutic agent is the claimed polynucleotide, but it need not necessarily be so. The application (page 113, lines 17 to 24, page 114, lines 10 to 15, page 116, lines 20 to 22 and page 118, line 30) discloses that if the therapeutic agents are vaccines or immuno-competent agents, the polynucleotides enhance their effects. A specific reference to the stimulation of interferon production is made on page 118. On page 115, lines 20 to 34, the use of the polypeptides as chemotherapeutic agents or as carriers of chemotherapeutic agents is mentioned.

7. In the Board's judgment, these claims virtually cover an unlimited number of therapeutic compositions.

8. In contrast, the patent application provides examples of how to link the P-B-S chemical backbone to four types of Sig: biotin, maltose triose, immunogenic heptenes or fluorescein. The possibility of linking a chelator Sig to P-B-S is also explained in some detail on page 92. There is no example given of the potential enhancing effects or therapeutic value of any of the polynucleotides comprising P-B-S-Sig moieties.

9. If one is to accept as argued by the Appellant that, at the filing date, it was a matter of common general knowledge to isolate the P-B-S chemical backbones, there remains nonetheless that claim 1 of both requests comprises a myriad of P-B-S-Sig moieties differing by the structure, nature and conformation of Sig, the isolation of which does not solely involve bases-sugars-phosphate chemistry. Technical advice has only

been provided for the isolation of four P-B-S-Sig classes. Furthermore, the skilled person is left without guidance how to test the polynucleotides for therapeutical uses (even how to test those cited in the specification). When asked by the Board for the likelyhood that polynucleotides containing, for example, P-B-S-fluorescein would have a therapeutic value, the Appellant's representative indicated that this was not known, but that some compositions had been found to stimulate the induction of interferon from interferon producing cells.

10. Sufficiency of disclosure is achieved if the skilled person is able to reproduce the invention over the whole range which is claimed without undue burden of experimentation, following the instructions provided in the specification of the application (see for example, decisions T 409/91, OJ EPO 1994, 653 and T 435/91, OJ EPO 1995, 188)). In the present case, wanting to reproduce the invention over the claimed range undoutedly amounts to devising a research program comprising both the setting up of methods for the isolation of the majority of the P-B-S-Sig polynucleotides and the investigation of the therapeutical indications, they might be useful for. Alternatively, for those therapeutic indications mentioned in the description it involves finding out under which conditions they might be useful. This exceeds by far in terms of efforts, time and skills what a skilled person can be expected to investigate in addition to the restricted disclosure of the patent application.

11. The requirements of Article 83 EPC are not fulfilled in relation to the invention as claimed in claim 1 of the main request or first auxiliary request.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

U. Bultmann U. Kinkeldey