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**D E C I S I O N**  
**of 11 December 1997**

**Case Number:** T 0269/93 - 3.3.2

**Application Number:** 85110622.9

**Publication Number:** 0175171

**IPC:** A61K 31/19

**Language of the proceedings:** EN

**Title of invention:**

Use of 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid for enhancing the effect of anti-tumour agents

**Applicant:**

Eisai Co., Ltd.

**Opponent:**

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**Headword:**

Anti-Tumour-Effect/EISAI

**Relevant legal provisions:**

EPC Art. 56

**Keyword:**

"Inventive step - no - obvious use of pharmaceuticals well known in the field of cancer therapy"

**Decisions cited:**

G 0006/83

**Catchword:**

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Europäisches Patentamt	European Patent Office	Office européen des brevets
Beschwerdekammern	Boards of Appeal	Chambres de recours

Case Number: T 0269/93 - 3.3.2

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.2  
of 11 December 1997

**Appellant:**

Eisai Co., Ltd.  
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**Representative:**

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**Decision under appeal:**

Decision of the Examining Division of the  
European Patent Office posted 17 November 1992  
refusing European patent application  
No. 85 110 622.9 pursuant to Article 97(1) EPC.

**Composition of the Board:**

**Chairman:** P. A. M. Lançon  
**Members:** U. Oswald  
R. E. Teschemacher

## Summary of Facts and Submissions

I. European patent application No. 85 110 622.9 (publication No. 0 175 171) was refused by a decision of the Examining Division on the grounds that the subject-matter of claim 1 filed on 7 October 1991 lacked inventive step under Article 56 EPC. Claim 1 reads as follows:

"Use of 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid or a salt thereof for the preparation of a pharmaceutical suitable in enhancing the anti-tumor effect of known pharmaceuticals",

The Examining Division considered that the compound of claim 1 was known from several prior-art documents as an anti-tumour agent, for instance from document

(3) GB-A-2073750.

Since, neither on the basis of the worked examples as originally filed nor in the light of the explanations given by the Appellant during the examination procedure, it was possible to show that 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid or a salt thereof synergistically enhanced the cytotoxic effect of a carcinostatic drug, the claimed use of the said compound was regarded as obvious to a person skilled in the art.

As regards the definition of synergism when two anti-tumour agents are used, the Examining Division made reference to document

(4) Cancer Chemotherapy Reports Part 1 Vol. 59, No. 5, Sept/Oct 1975, pages 895 to 900.

This document was cited by the Appellant during the examination procedure in order to show technical background information related to the test method used in the worked examples of the application.

- II. The Appellant lodged an appeal against the decision of the Examining Division.

The arguments of the Appellant in the written procedure may be summarised as follows:

It was clear from the figures in Table 2 of the application that 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid or a salt thereof synergistically enhanced the cytotoxic effect of a carcinostatic drug. Reference was made in detail to experimental results relating to 5-FU (fluorouracil) in combination with the claimed enhancer.

- III. Oral proceedings were set for 11 December 1997. In a communication annexed to the summons to the oral proceedings, the Board drew attention inter alia to the following points open to discussion:

- (i) The sum of the effects of the known anti-tumour pharmaceutical(s) and the effect of the enhancing agent according to claim 1 on the cell population(s) in terms of surviving fractions of the exposed cell population(s) could not be calculated on the basis of the result of each individual effect in a linear algebraic manner. Accordingly, there appeared to be a lack of technical information in the Appellant's explanation regarding the degree of synergism underlying the subject-matter of claim 1.

However, an explanation of the alleged synergistic effect underlying the claimed subject-matter in accordance with one of the diagrams (I) to (III) of Figure 1 on page 896 of document (4) could be taken into consideration.

- (ii) About nine years before the priority date of the present application, document (4) clearly indicated on page 895, left column, that "the treatment of human neoplasms is increasingly being approached by the **combined use** of two or more anticancer agents" (emphasis added) and that "...extensive literature describing additivity and synergism of anticancer agents exists...".

Accordingly, the occurrence of a synergism when using two or more anticancer agents together, in the present case, could not automatically involve an inventive step. Article 56 EPC clearly required that "an invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art."

- IV. In a letter dated 4 November 1997, in response to the summons to oral proceedings, the Appellant informed the Board of Appeal that nobody would attend the oral proceedings and that it was requested that decision be made on the basis of the written arguments contained in the file.
- V. The Appellant requested that the decision under appeal be set aside and that a patent be granted.

## Reasons for the Decision

1. The appeal is admissible.
2. None of the documents on file discloses the combined use of 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid or a salt thereof and other antitumour agents. In the circumstances of the present case (see point IV above), novelty of the claimed subject-matter may be left open as well as the question whether or not the activity of "enhancing the anti-tumour effect of known pharmaceuticals" by 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid or a salt thereof - which compound itself shows anti-tumour activity - represents a second medical use within the meaning of decision G 6/83 (OJ 1985, 67).
3. The Board regards document (3) describing anticancer activity of 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid as the closest prior art (see page 2, line 42 to page 3, line 20 and page 5, lines 6 to 8).
  - 3.1 On considering the figures and the arguments on file, the Board cannot deduce that the objective technical problem to be solved is based on the fact that 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid or a salt thereof synergistically enhances the cytocidal effect of a carcinostatic drug.

It is, however, well known that because of difficulties in developing carcinostatic drugs, the person skilled in the field of chemotherapy always tries to improve the effect of known carcinostatic drugs (see also description of the application on page 2, first paragraph).

Accordingly, with regard to document (3), the problem to be solved can only be seen in the provision of means to obtain improved anticancer pharmaceuticals.

- 3.2 The solution proposed by the application in suit, is in accordance with claim 1, the use of 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid or a salt thereof for the preparation of a pharmaceutical suitable in enhancing the anti-tumour effect of known pharmaceuticals.

Having regard to the experimental evidence on file, the Board finds it plausible that the problem has been solved.

- 3.3 There is no hint in document (3) itself which might have given an incentive to the skilled person to investigate a combined use of antitumour agents.

- 3.4 However, if confronted with the problem as stated above, the skilled person inevitably would turn to other prior art relating to anti-tumour agents and first of all take into account documents containing technical information more generally with respect to the effectiveness of anti-tumour agents.

As already set out in the communication mentioned under point III above, document (4) contains such information. This prior art clearly proposed the combined use of two or more anticancer agents and clearly draws the skilled person's attention to the

fact that additivity of activity of anticancer agents may be achieved by the combined use of at least two anticancer agents and thus also gives an **incentive to try to improve** in the same way the activity of the anticancer agent 3, 7, 11, 15-tetramethyl-2, 4, 6, 10, 14-hexadecapentaenoic acid or a salt thereof known from document (3).

The Board notes that the Appellant has, in accordance with Article 113(1), had enough opportunity to present comments on the detailed objections raised in the Board's communication annexed to the summons to attend the oral proceedings, but has not availed himself of this opportunity.

Therefore, in the absence of counterarguments by the Appellant, the Board can only conclude that the subject-matter of claim 1 relates to an obvious use of pharmaceuticals well known in the field of cancer therapy. Accordingly, claim 1 lacks the required inventive step.

4. Irrespective of the foregoing, the factual situation that the Examining Division refused the application under Article 56 EPC for failure to show a synergistic effect, and that the Appellant also failed to convince the Board of Appeal of the alleged synergistic effect to be achieved by the enhancer compound according to claim 1, would also be itself sufficient reason not to set aside the decision of the Examining Division.
5. Since the only request put forward by the Appellant contains a claim which fails to comply with one of the patentability requirements of the EPC, the appeal must be dismissed.



**Order**

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

The appeal is dismissed.

The Registrar:

P. Martorana

The Chairman:

P. A. M. Lançon

