BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

A		B		C	X

File No.: T 954/92 - 3.3.2

Application No.: 87 304 363.2

Publication No.: 0 249 347

Classification: A61K 31/485

Title of invention: Controlled release dihydrocodeine composition

D E C I S I O N
of 28 May 1993

Applicant: Euroceltique S.A.

Proprietor of the patent:

Opponent:

Headword: Oral dosage form/EUROCELTIQUE

EPC: Art. 84 EPC

Keyword: "Claims-functional features - clarity (yes)"

Headnote
Catchwords

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 954/92 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 28 May 1993

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Decision under appeal: **Decision of the Examining Division of the European Patent Office dated 13.04.92 refusing European patent application No. 87 304 363.2 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: P.A.M. Lançon
Members: L. Galligani
S.C. Perryman

Summary of Facts and Submissions

I. European patent application No. 87 304 363.2 published under No. 0 249 347 was refused by the Examining Division.

The decision was taken on the basis of a set of Claims 1 to 10 for all States except AT, ES, GR and a set of Claims 1 to 10 for AT, ES, GR, both sets being as originally filed.

Claim 1 (all States except AT, ES, GR) reads as follows:

" A solid, controlled release, oral dosage form, the dosage form comprising an analgesically effective amount of dihydrocodeine or a salt thereof in a controlled release matrix wherein the dissolution rate *in vitro* of the dosage form, when measured by the USP Paddle Method at 100 rpm in 900ml aqueous buffer (pH between 1.6 and 7.2) at 37°C is between 25% and 60% (by wt) dihydrocodeine released after 1 hour, between 45% and 80% (by wt) dihydrocodeine released after 2 hours, between 60% and 90% (by wt) dihydrocodeine released after 3 hours and between 70% and 100% (by wt) dihydrocodeine released after 4 hours, the in vitro release rate being independent of pH between pH 1.6 and 7.2 and chosen such that the peak plasma level of dihydrocodeine obtained *in vivo* occurs between 2 and 4 hours after administration of the dosage form."

Claim 1 for AT, ES, GR is formulated as a corresponding process claim.

II. The Examining Division refused the application under Article 97(1) EPC on the grounds that Claim 1 did not comply with the requirements of Article 84 EPC.

The Examining Division objected to the use in Claim 1 of functional features such as the release rate in an aqueous buffer *in vitro* and the time for peak plasma level *in vivo*. In its opinion, said features merely defined the result to be achieved. This was not allowable when, as in the present case, technical features such as the chemical nature of the matrix were available from the description for a clearer definition.

The functional language of Claim 1 did not allow a clear distinction over the state of the art. As matrixes for substained release of the kind used by the present applicant were known in the art, it was, for example, difficult for the public to determine whether the incorporation therein of dihydrocodeine would have lead to infringement or not.

III. The Appellant lodged an appeal against this decision and paid the appeal fee.

The Appellant argued that Claim 1 clearly and unambiguously identified the technical features essential to provide a controlled release dihydrocodeine composition suitable for 12-hour administration. These were the *in vitro* release properties, the fact that the release rate is independent of pH between 1.6 and 7.2, and the peak plasma level *in vivo*. Said features could be readily measured by the skilled person without undue experimentation. The technical effect was not linked to any particular matrix. Thus, it would be unnecessary and unfair to restrict Claim 1 to a specific matrix.

IV. The Appellant requests the allowance of the first set of Claims 1 to 10 for all States except AT, ES, GR and of the second set of Claims 1 to 10 for AT, ES, GR.

Reasons for the Decision

1. The appeal is admissible.

2. *Clarity* (Art. 84 EPC)

The solid, controlled release, oral dosage form of Claim 1 of each set of claims is defined by means of the following features:

(a) it comprises an analgesically effective amount of dihydrocodeine or of a salt thereof in a controlled release matrix;

(b) it displays a defined *in vitro* dissolution rate as measured by the USP Paddle Method, distinct parameters therefor being given;

(c) the release of dihydrocodeine *in vitro* is pH independent in the range 1.6-7.2;

(d) the peak plasma level *in vivo* occurs between 2 and 4 hours after administration.

The specification gives examples of the preparation of solid, oral dosage forms (tablets) which satisfy the above criteria (see examples and *in vitro* dissolution studies on pages 7 to 12). These dosage forms are shown to provide *in vivo* a significant pain relief by twice a day administration (see clinical studies on pages 12 to 16).

Feature (a) is a technical feature which can be readily tested.

Features (b) and (c) are functional features which define a technical result. However, said features constitute at the same time the testable criteria which have to be satisfied by the dosage form.

In vitro dissolution rate tests are well known and well accepted methods for evaluating the suitability of dosage forms for therapeutic administration. Methods, apparatus and means for interpreting such tests are available, for example, from the US Pharmacopeia (see e.g. US-A-4 235 870, column 5, line 27 onward). In the present case reference is made to the USP Paddle method described in the US Pharmacopeia XXI (1985). Features (b) and (c) provide instructions which are sufficiently clear for the expert to reduce them to practice. In fact, once the *in vitro* dissolution criteria to be satisfied are set forth, the expert in preparing the dosage form merely needs to carry out the appropriate adjustments of the ingredients as well as the necessary measurements. No undue experimentation is needed therefor.

As for feature (d), the same reasoning as above applies. Although the testing of said functional feature may be *prima facie* bothersome, nevertheless it constitutes only a further criterion for the verification of the oral dosage form. As there is likely to be a good correlation between *in vivo* plasma levels and *in vitro* release characteristics, it would seem relatively easy to adjust the nature of the delivery system so as to satisfy the criterion (d) (in this respect see also the report by Prof. A.T. Florence submitted with letter dated 17 October 1991 during the examination proceedings). At the present stage, there are no serious reasons for not accepting this view.

The adopted functional language is acceptable and in line with EPO case law (see e.g. T 68/85, OJ EPO 1987, 228; T 292/85, OJ EPO 1989).

Claim 1 is not directed to a specific slow release matrix, but to a dosage form which displays distinctive dissolution rates *in vitro* and *in vivo*. The description explicitly states that "the controlled release matrix can be any matrix that affords *in vitro* dissolution rates within the narrow ranges required and that releases the dihydrocodeine in a pH independent manner" (see page 4, paragraph 5). Moreover, the description shows that dosage forms which satisfy the criteria set forth in Claim 1 afford therapeutic levels of dihydrocodeine *in vivo* over at least a 12 hour period and can therefore be used on a twice daily basis.

The invention as claimed in each set of claims is clearly enough stated to meet the requirements of Article 84 EPC on clarity without a limitation of Claim 1 by introduction of substance parameters for the matrix.

3. It appears from the file that the Examining Division has not yet completed the substantive examination of the present case as to the requirements of novelty and inventive step. Thus, according to section VII of the decision under appeal, the introduction in Claim 1 of substance parameters could lead to the acknowledgement of an inventive step, but according to section 1.4 of the decision under appeal, no inventive step is seen in the incorporation of dihydrocodeine in the sustained release matrixes according to US-A-4 235 870 which are of the same kind as used in the present application. What final conclusion the Examining Division would reach by applying the problem-solution approach to inventive step, is not apparent. As the Board, in the present state of the file, can only properly decide the question arising under

Article 84 EPC, the case must be remitted to the first instance under Article 111 EPC 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 Examining Division for further prosecution.

The Registrar: The Chairman:

P. Martorana P. Lançon