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D E C I S I O N
of 25 January 2000

Case Number: T 0828/97 - 3.4.1

Application Number: 90907649.9

Publication Number: 0528789

IPC: A61N 1/30

Language of the proceedings: EN

Title of invention:
Device and method of iontophoretic drug delivery

Patentee:
ALZA CORPORATION

Opponent:
Becton, Dickinson and Company

Headword:
-

Relevant legal provisions:
EPC Art. 100(a), 100(b), 123(2),(3), 52(1), 54, 56

Keyword:
"EPC - Art. 102(3) Maintenance - in amended form"

Decisions cited:
-

Catchword:

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0828/97 - 3.4.1

D E C I S I O N
of the Technical Board of Appeal 3.4.1
of 25 January 2000

Appellant: (Proprietor of the patent)
ALZA CORPORATION
950 Page Mill Road
P.O. Box 10950
Palo Alto
California 94303-0802 (US)

Representative:
Evans, David Charles
fJ CLEVELAND
40-43, Chancery Lane
London WC2A 1JQ (GB)

Respondent: (Opponent)
Becton, Dickinson and Company
One Becton Drive
Franklin Lakes, New Jersey 07417-1880 (US)

Representative:
Lawrence, Peter Robin Broughton
GILL JENNINGS & EVERY
Broadgate House
7 Eldon Street
London EC2M 7LH (GB)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 28 May 1997 revoking European patent No. 0 528 789 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: G. Davies
Members: G. Assi
H. K. Wolfrum

Summary of facts and submissions

I. The appellant (patent proprietor) lodged an appeal, received on 26 July 1997, against the decision of the Opposition Division, dispatched on 28 May 1997, revoking the European patent No. 0 528 789 (application number 90 907 649.9). The fee for the appeal was paid on 26 July 1997. The statement setting out the grounds of appeal was received on 17 September 1997.

Opposition was filed against the patent as a whole and was based on Article 100(a) EPC, in particular on the grounds that the subject-matter of the patent was not patentable within the terms of Articles 52(1), 54, 56 and 57 EPC, and on Article 100(b) EPC.

The Opposition Division held that the grounds of the opposition prejudiced the maintenance of the patent, having regard *inter alia* to the following document:

(D2) US-A-4 731 049.

II. Oral proceedings were held on 25 January 2000.

III. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the following documents:

Claims 1-33, description pages 2-15, and Figures 1-4 filed during the oral proceedings on 25 January 2000.

IV. The respondent requested that the appeal be dismissed.

V. The wording of Claim 1 reads as follows:

"1. An electrically powered iontophoretic agent delivery device (10) including a donor electrode assembly (8), a counter electrode assembly (9) and a source of electrical power (27) adapted to be electrically connected to the donor electrode assembly (8) and the counter electrode assembly (9), the donor electrode assembly (8) comprising:

an agent reservoir (15) containing an agent, the agent being capable of dissociating into agent ions and counter ions of opposite charge, the agent reservoir (15) being adapted to be placed in agent transmitting relation with a body surface (22);

a donor electrode (11) adapted to be electrically connected to the source of electrical power (27); and

a selectively permeable membrane (14) intermediate the electrode (11) and the agent reservoir (15);

the donor electrode assembly (8) being characterised by said selectively permeable membrane (14) being permeable to species of less than a predetermined molecular weight and substantially less permeable to species of greater than the predetermined molecular weight, and the agent ions having greater than the predetermined molecular weight and the counter ions have less than the predetermined molecular weight and wherein the assembly includes a donor electrolyte reservoir intermediate the donor electrode and the membrane, the electrolyte in the donor electrolyte reservoir being capable of dissociating into positively charged and negatively charged electrolyte ions, the electrolyte ions of similar charge to the agent ions having greater than the predetermined molecular weight, the electrolyte ions of similar charge to the counter

ions having less than the predetermined molecular weight."

The wording of Claim 19 reads as follows:

"19. A method of increasing agent delivery efficiency of an electrically powered iontophoretic agent delivery device (10) including a donor electrode assembly (8), a counter electrode assembly (9) and a source of electrical power (27) adapted to be electrically connected to the donor electrode assembly (8) and the counter electrode assembly (9), the donor electrode assembly (8) including an agent reservoir (15) containing an agent and adapted to be placed in agent transmitting relation with a body surface (22) and a donor electrode (11) adapted to be electrically connected to the source of electrical power (27), the method comprising: placing a selectively permeable membrane (14) intermediate the agent reservoir (15) and the donor electrode (11), the membrane (14) being permeable to passage of species of less than a predetermined molecular weight and substantially less permeable to passage of species of greater than the predetermined molecular weight; and selecting an agent for delivery from the agent reservoir (15), the agent being capable of dissociating into agent ions and counter ions of opposite charge, wherein the method is characterised by the agent ions having greater than the predetermined molecular weight, and the counter ions having less than the predetermined molecular weight and wherein the donor electrode assembly includes a donor electrolyte reservoir intermediate the donor electrode and the membrane, and further comprising: selecting an electrolyte for the donor electrolyte reservoir, the

electrolyte being capable of dissociating into positively charged and negatively charged electrolyte ions, the electrolyte ions of similar charge to the agent ions having greater than the predetermined molecular weight, the electrolyte ions of similar charge to the counter ions having less than the predetermined molecular weight."

The wording of Claim 20 reads as follows:

"20. An electrically powered iontophoretic agent delivery device (10) including a donor electrode assembly (8), a counter electrode assembly (9) and a source of electrical power (27) adapted to be electrically connected to the donor electrode assembly (8) and the counter electrode assembly (9), the donor electrode assembly (8) comprising:

an agent reservoir (15) containing an agent, the agent being capable of dissociating into agent ions and counter ions of opposite charge, the agent reservoir (15) being adapted to be placed in agent transmitting relation with a body surface (22);

a donor electrode (11) adapted to be electrically connected to the source of electrical power (27); and

a selectively permeable membrane (14) intermediate the electrode (11) and the agent reservoir (15);

the donor electrode assembly (8) being characterised by said selectively permeable membrane (14) being non-hydrated and thereby impermeable to ionic species, said membrane being hydratable and said membrane, in a hydrated condition, being permeable to species of less than a predetermined molecular weight and substantially less permeable to species of greater than the predetermined molecular weight, the agent ions having

less than the predetermined molecular weight and the counter ions having greater that the predetermined molecular weight; wherein the membrane (14) is maintained in a substantially non-hydrated condition until the device is placed on the body surface (22), the membrane (14) being hydrated at about the time the device (10) is placed on the body surface (22)."

The wording of Claim 32 reads as follows:

"32. A method of increasing agent delivery efficiency of an electrically powered iontophoretic agent delivery device (10), including a donor electrode assembly (8), a counter electrode assembly (9) and a source of electrical power (27) adapted to be electrically connected to the donor electrode assembly (8) and the counter electrode assembly (9), the donor electrode assembly (8) including an agent reservoir (15) containing an agent and adapted to be placed in agent transmitting relation with a body surface (22) and a donor electrode (11) adapted to be electrically connected to the source of electrical power (27), the method comprising: placing a substantially non-hydrated selectively permeable membrane (14) intermediate the agent reservoir (15) and the donor electrode (11), the membrane (14), when non-hydrated being impermeable to ionic species and, when hydrated, being permeable to species of less than a predetermined molecular weight and substantially less permeable to species of greater than the predetermined molecular weight; selecting an agent for delivery from the agent reservoir (15), the agent being capable of dissociating into agent ions and counter ions of opposite charge; the method being characterised by (a) the agent ions having less than

the predetermined molecular weight and the counter ions having greater than the predetermined molecular weight; and (b) hydrating the membrane (14) at about the time the device is placed on the body surface (22)."

Claims 2-18, 21-31 and 33 are dependent claims.

VI. The appellant's arguments may be summarised as follows.

All the amendments were supported by the original disclosure.

The added features concerning the donor electrolyte reservoir (Claims 1 and 19) and hydrating the membrane (Claims 20 and 32) were not known from any of the prior art documents and could not be regarded as usual measures.

VII. The respondent's arguments may be summarised as follows.

The feature in Claim 20 that the non-hydrated membrane was impermeable to ionic species contravened Article 123(2) EPC, because the wording of the amendment gave the impression that the impermeability of the membrane was a consequence of the weight selectivity rather than of the dryness as originally disclosed.

As to inventive step, the appellant was correct in stating that none of the cited prior art documents disclosed the features concerning the donor electrolyte reservoir and hydrating the membrane. However, a doubt might be raised, whether the subject-matter of the

claims could be regarded as involving an inventive step.

Reasons for the decision

1. The appeal is admissible.

2. Claim 1, corresponding to the embodiment (a) of the granted Claim 1, is based on the original Claim 1 with the further features that "the counter ions have less than the predetermined molecular weight" and that the donor electrode assembly includes the claimed donor electrolyte reservoir. Both these features are disclosed in the original Claims 2 and 16. Claim 19, corresponding to the granted Claims 28 and 29, is based on the original Claims 38 and 39.

Claim 20, corresponding to the embodiment (b) of the granted Claim 1, is based on the original Claim 20 with the further feature that the membrane is hydratable and impermeable to ionic species in the non-hydrated condition. This feature can be inferred from the original page 7, line 31 to page 8, line 9. Claim 32, corresponding to the granted Claim 30, is based on the original Claim 49.

As regards Claim 20, the respondent's objection under Article 123(2) EPC is not well-founded. The claim includes the feature of the selectively permeable membrane "being non-hydrated and thereby impermeable to ionic species". From a semantic point of view, the adverb "thereby" is equivalent to "by that means" or "as a result of which". A logical link is thus

established between the impermeability and the dryness, which is supported by the original disclosure.

All the amendments introduce subject-matter limiting the protection conferred.

Therefore, the amended independent Claims 1, 19, 20 and 32 meet the requirements of Article 123(2) and (3) EPC, as do the dependent claims.

3. The amended claims meet the requirements of Article 84 EPC.

4. None of the cited documents discloses an electrically-powered iontophoretic agent delivery device including all the features of Claims 1 and 20 or a method of increasing agent delivery efficiency of such a device comprising all the features of Claims 19 and 32.

Therefore, the subject-matter of independent Claims 1, 19, 20 and 32 is novel. Moreover, the novelty of the claimed subject-matter is not in dispute between the parties.

5. Claims 1 and 19 refer to the particular embodiment comprising a membrane, which is permeable to light counter ions and substantially less permeable to heavy agent ions, and a donor electrolyte reservoir, in which the electrolyte dissociates into heavy electrolyte ions of similar charge to the agent ions and light electrolyte ions of similar charge to the counter ions.

Document D2 (see Figures 1 and 2), which is considered as representing the closest state of the art, discloses

an electrically-powered iontophoretic agent delivery device, which includes a donor electrode assembly, a counter electrode assembly and a source of electrical power electrically connected to both the electrode assemblies, the donor electrode assembly comprising the following features:

- an agent reservoir containing an agent capable of producing agent ions, the agent reservoir being adapted to be placed in agent transmitting relation with a body surface,

- a donor electrode,

- a selectively permeable membrane intermediate the donor electrode and the agent reservoir, and

- an ion reservoir intermediate the donor electrode and the membrane, the ion reservoir containing positively or negatively charged ions.

In particular, the agent reservoir contains a drug bound to an ion exchange resin or to an immobilized ligand affinity medium (see column 2, lines 25-28, Claims 7 and 8). The membrane is used as a barrier to separate the various components of the device and may be either cation or anion selective depending on the nature of the drug complex (see column 3, lines 1-6). In use, the drug is displaced from the drug complex by the anions or cations held in the ion reservoir (see column 3, lines 13-28). Thereby, considering the chemical composition of the drugs and the binding materials envisaged in column 3, lines 28-31 and 36-52, heavy agent ions are generated (see, for instance,

immunoglobin bound on protein A or the case of proteins bound on Cibacron Blue F3G-A dye). On the contrary, the ions of the ion reservoir having the same charge as the agent ions are light and can pass through the membrane. It thus follows that the claimed embodiment differs from the device known from D2 in essential aspects concerning the permeability of the membrane in relation to the agent ions, the counter ions and the electrolyte ions, namely that counter ions are generated, which are lighter than a predetermined molecular weight, and that electrolyte ions are present, which have the same charge as the agent ions and are heavier than the predetermined molecular weight. Due to these measures, drug delivery is facilitated, contamination of the drug reservoir by electrolyte ions is avoided, and competition between agent ions and electrolyte ions is suppressed. Neither D2 nor any of the other prior art documents cited during the proceedings contains a suggestion permitting to arrive at the mentioned specific details of the claimed embodiment. During the oral proceedings on 25 January 2000, the respondent indeed agreed that the claimed features concerning the donor electrolyte reservoir were not known from or suggested by any of the available documents.

Claims 20 and 32 refer to the other particular embodiment claimed comprising the essential feature of a membrane, which when non-hydrated is impermeable to ionic species and in a hydrated condition is permeable to light agent ions and substantially less permeable to heavy counter ions. None of the prior art documents discloses or suggests the use of a membrane as claimed, which should be hydrated only immediately prior to use, nor can this measure, which provides a longer shelf-

life for the iontophoretic device, be regarded as usual. During the oral proceedings on 25 January 2000, the respondent agreed that the claimed feature of using a non-hydrated membrane, which is then hydrated at the time the device is needed, was not known from or suggested by any of the cited documents.

Thus, the subject-matter of independent Claims 1, 19, 20 and 32 involves an inventive step in the sense of Article 56 EPC. The same applies to the dependent claims.

6. The appellant's request is allowable. In particular, taking into consideration the amendments made, the patent and the invention to which it relates meet the requirements of the EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of the first instance with the order to maintain the patent on the basis of the following documents:

   Claims 1-33, description pages 2-15, and Figures 1-4 filed during the oral proceedings on 25 January 2000.

The Registrar: The Chairman:

M. Beer G. Davies