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D E C I S I O N
of 2 April 1998

Case Number: T 0514/95 - 3.3.3

Application Number: 89909293.6

Publication Number: 0380647

IPC: C08L 1/26

Language of the proceedings: EN

Title of invention:

Compositions and in situ methods for forming films on body tissue

Applicant:

Zila Pharmaceuticals

Opponent:

-

Headword:

-

Relevant legal provisions:

EPC Art. 54

Keyword:

"Novelty (main and first auxiliary requests) - no - derivability/enabling disclosure; (second auxiliary request) - yes - no implicit disclosure"

Decisions cited:

T 0206/83, T 0511/92

Catchword:

-



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Case Number: T 0514/95 - 3.3.3

D E C I S I O N
of the Technical Board of Appeal 3.3.3
of 2 April 1998

Appellant:

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Representative:

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Decision under appeal:

Decision of the Examining Division of the
European Patent Office posted 14 February 1995
refusing European patent application
No. 89 909 293.6 pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: C. Gérardin
Members: B. ter Laan
W. Moser

Summary of Facts and Submissions

I. European patent application No. 89 909 293.6, based on the international application No. PCT/US89/03216, filed on 24 July 1989, claiming priority of 25 July 1988 from an earlier international application (PCT/US88/02515), and published on 8 February 1990 under No. WO 90/01046, was refused by a decision of the Examining Division of the European Patent Office dated 14 February 1995. That decision was based on two sets of twelve claims as the main and one auxiliary request, which were both held to be not novel over D1 (Oral Surgery, Oral Medicine and Oral Pathology, Vol. 65, No. 6, June 1988, pages 699 to 703).

II. On 10 April 1995 a Notice of Appeal was lodged against that decision, together with payment of the prescribed fee. The Statement setting out the Grounds of Appeal, filed on 14 June 1995, referred to the two sets of claims upon which the decision of the Examining Division was based.

III. After a communication from the Board in which several objections under Articles 84 and 123(2) EPC were raised against the two sets of claims then on file, on 2 March 1998 five new sets of claims were filed by way of main and four auxiliary requests.

During oral proceedings held on 2 April 1998, after the Board had pointed out that the objections under Articles 123(2) and 84 EPC had not been overcome, the Appellant abandoned its previous requests and submitted four new sets of ten, five, four and two claims, as the main and first, second and third auxiliary requests, respectively.

Claim 1 of the main request reads:

"A medicament film forming composition for in situ formation of medicament films on body tissue, comprising:

- (i) a carrier which is
 - (a) 0.1 to 20 % by weight of the final composition of hydroxypropyl cellulose;
 - (b) 0.1 to 10 % by weight of the final composition of an esterification agent which is salicylic acid, tannic acid or a mixture thereof;
 - (c) a solvent which is ethyl or isopropyl alcohol; and
 - (d) a cross-linking agent which is boric acid;

characterized in that the composition also comprises

- (ii) an active medicament."

Claims 2 to 10 are directed to preferred embodiments of the composition of Claim 1.

Claim 1 of the first auxiliary request differs from that of the main request in that the active medicament is specified as being an anaesthetic. Claims 2 to 5 refer to preferred embodiments of the composition of Claim 1.

Claim 1 of the second auxiliary request differed from that of the main request in that the active medicament is specified as being Benzocaine, Dycloninc

hydrochloride, Hexylcaine hydrochloride, Pramoxine hydrochloride, Butamben picrate or Tetracaine hydroiodide. Claims 2 to 4 are directed to preferred embodiments of the composition of Claim 1.

Claim 1 of the third auxiliary request is limited to the amounts and substances as described in Example 1 of the original application. Claim 2 refer to a preferred embodiment of the composition of Claim 1.

IV. The Appellant argued that the Board's objections regarding Articles 84 and 123(2) were overcome by the wording of those claims. As to novelty and inventive step, it was acknowledged that Zilactin contained the film forming ingredients in the composition as now claimed. The author of D1, Dr. Rodu (present at the oral proceedings), was not a formulation chemist, but a dental specialist and an end user of Zilactin, so that he could not be considered to be a skilled person in the sense of Article 56 EPC. Dr. Rodu declared that he had performed tests and had found that Zilactin, although on the market since 1981 still not very well-known, was indeed very effective in protecting sores and ulcers against irritants, like e.g. orange juice, and that even a healing effect could be observed. Until then no other means had been available to relieve the pain of patients with sores or ulcers. D1 described the results of those tests. As usual in academic papers, at the end suggestions were made how to continue research for further improvements. The incorporation of other therapeutic agents had not actually been carried out at the time the paper was written.

The Appellant further stated that, as the pH of Zilactin, due to the presence of the strongly acidic salicylic and tannic acids, was in the order of 2 to 3, the skilled person did not expect that any added medicament would still be biologically active and

produce the desired effects. As there was no reasonable expectation of success, the skilled person would not even have tried to combine Zilactin with a medicament. The finding that, in spite of the low pH of Zilactin, the medicament was still active, was very surprising. In support of those arguments, the Appellant filed a further document (document A: Chem. Pharm. Bull. 29(3) 810-816 (1981)). The Appellant concluded that the disclosure of D1 did not entail the presence of an active medicament as part of the Zilactin formulation.

- V. The Appellant requested that the decision of the first instance be set aside and that a patent be granted on the basis of Claims 1 to 10 of the main request or, alternatively, Claims 1 to 5 of the first auxiliary request, Claims 1 to 4 of the second auxiliary request or Claims 1 and 2 of the third auxiliary request, all submitted during oral proceedings.

Reasons for the Decision

1. The appeal is admissible.

Article 123(2) EPC

2. The structure of Claim 1 of all requests, which now indicates the separate presence of a film-forming or carrier material and a medicament, is supported by original Claim 2, in which the film forming components as well as "a separate medicinal component" were disclosed. Page 5, second full paragraph also mentions "the film-forming compositions described above and a biologically active topical treatment component, cosmetics, or medication.". The film-forming compositions to which reference is made, are hydroxypropyl cellulose, an esterification agent and a

solvent (page 4, third paragraph to page 5, first full paragraph). Furthermore, Examples 6 to 8 refer to adding various active agents to the formulation of Example 1, which contains the film forming ingredients. Therefore, the principle of having a carrier material and a separate medicament present in the composition was clearly and unambiguously disclosed in the application as filed.

- 2.1 The amount of 0.1 to 20 % by weight of the total composition of hydroxypropyl cellulose was described on page 9, second full paragraph, of the application as filed.
- 2.2 The amount of 0.1 to 10 % by weight of the total composition of esterification agent can be found on page 9, second full paragraph. Although that passage refers to "the carboxylic acid component", it is clear from page 5, first full paragraph that this term implies the esterification agents. The specification of the esterification agents as being salicylic or tannic acid or a mixture thereof is disclosed on original page 5, first full paragraph of the application as filed.
- 2.3 The specification of the solvent as ethyl or isopropyl alcohol is described on page 4, last paragraph of the application as filed.
- 2.4 Boric acid as the cross-linking agent can be found on page 6, second paragraph of the application as filed.
- 2.5 The basis for the presence of a medicament as such has been discussed under point 2 above. That the medicament should also be active is implied by page 5, second full paragraph of the application as filed, where it says: "biologically active" and "medically effective quantities". Also Examples 6 to 8 refer to

"therapeutically effective quantities", to "effectively accomplish the desired treatment", "clinical effectiveness", films containing the "active ingredients" and "active medicaments".

2.6 The basis for the specification of the active medicament (Claims 2 to 12 of the main request and all claims of the auxiliary requests) can be found in the original Examples 6 to 8 of the application as filed. Although those examples are limited to the use of the active agents in the specific formulation of Example 1, from the description, in particular from page 5, second full paragraph of the application as filed, it is clear that the exact composition of the film-forming or carrier material does not play an essential role for the effectiveness of the medicament. The skilled person would have recognised that the medicaments could also be used with other compositions than those of Example 1, as long as they remained within the claimed limits.

2.7 In view of the above, the Board concludes that the claims of all requests comply with Article 123(2) EPC.

Clarity

3. The definition of the carrier materials contains no ambiguity and the amount of each component is clearly indicated. The medicament film forming composition now being claimed comprises that carrier and additionally an active medicament. The word "active" amounts to a functional definition of the feature determining the efficiency of the medicament (see page 5, second full paragraph, of the application as filed). As Claims 2 to 10 of the main request as well as the claims of the auxiliary requests contain precise specifications of preferred medicament film forming compositions, the Board is satisfied that the claims are clear.

Novelty

4. D1 discloses the "Performance of a hydroxypropyl cellulose film former in normal and ulcerated oral mucosa" (title). It compares the mucosal binding characteristics of "Zilactin" (a product of the Appellant) with those of "Orabase" (a carboxymethylcellulose preparation of Colgate-Hoyt Laboratories, Norwood, Massachusetts, with or without the shortacting topical anaesthetic benzocaine) and evaluates the pain relief and protection properties of Zilactin on lesions of recurrent minor aphthous ulcers. According to D1 (page 702, DISCUSSION), it was observed that Zilactin formed a durable film on intact oral mucosa that persisted much longer than Orabase, which demonstrated the ability to protect ulcers from food irritants. The active component for pain relief and protection in Zilactin was believed to be hydroxypropyl cellulose, which was commercially available as an aphthous ulcer treatment product in Japan, and which had there, in preliminary studies, been successful when containing triamcinolone acetonide. Other components of Zilactin are described to be salicylic, boric and tannic acids, which had less obvious therapeutic effects. The paper ends (page 703) with the passage: "Although the lack of comparable agents precludes a blind investigation at this time, further studies manipulating the components not associated with the forming of film or incorporating other therapeutic agents, such as corticosteroids or topical anaesthetics, are indicated."
- 4.1 The components of Zilactin are, according to D1, hydroxypropyl cellulose and salicylic, boric and tannic acids. Therefore, there can be no doubt that the compounds now being claimed for the carrier material are the ingredients of Zilactin. D1 is, however, silent as regards the amounts of each of those compounds. The

product information leaflet filed on 28 September 1993 by the Appellant (then Applicant), to which the Examining Division referred in its decision and which describes the active ingredient of Zilactin to be "safe, effective tannic acid (7%) suspended in a vehicle composed of SD alcohol 37 (80.0% by volume), hydroxypropylcellulose, boric acid, salicylic acid, propylene glycol and deionized water." , does also not provide the amounts in full detail. However, during the oral proceedings the Appellant itself admitted that Zilactin contained the carrier material components in the amounts now being claimed. In fact, Zilactin was believed to correspond to the composition of Example 1. Therefore, the Board concludes that Zilactin as described in D1 corresponds to the definition of the carrier material of Claim 1.

4.2 D1 describes Orabase as a commercial product on the basis of carboxymethylcellulose, which did or did not contain benzocaine (page 699, right-hand column, first paragraph). Likewise, hydroxypropyl cellulose was commercially available in Japan. The use of hydroxypropyl cellulose containing triamcinolone acetonide is described in terms of preliminary studies. The paper itself concerns the use of Zilactin, which, as said above (see point 4.1), corresponds to the present carrier material. Therefore, from the wording of D1 it can be concluded that those compounds and combinations of compounds have actually been used for medical treatment. The same cannot be said for Zilactin additionally containing a medicament. The last paragraph of D1 is unambiguous in its message that that combination should be tried and it is clear that, at the time the paper was written, it had not yet actually been done, which is in line with Dr. Rodu's declaration (see point IV above).

- 4.3 However, the actual execution or not of what is described in a document does not play a role in assessing novelty. According to Article 54 EPC, an invention shall be considered to be new if it does not form part of the state of the art (Article 54(1) EPC). The state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or by any other way, before the date of filing of the European patent application (Article 54(2) EPC).

According to standard jurisprudence by the Boards of Appeal, a prior art document anticipates the novelty of any claimed subject-matter which is derivable clearly and unambiguously from that document (T 0511/92, not published in OJ EPO). The requirement of "availability" is satisfied if the subject-matter in question is disclosed in a way that allows others to reproduce it ("enabling disclosure", T 0206/83, OJ EPO 1987, 5). The other tests to which the Appellant referred, in particular whether there is a reasonable expectation of success or an unexpected effect and whether the skilled person could not only have done it, but indeed would have done it, relate to the question of inventive step, and not to novelty.

- 4.4 The last paragraph of D1 literally describes the incorporation of other therapeutic agents, such as corticosteroids or topical anaesthetics, in Zilactin. By the term "incorporating" it is clear that the medicament should be part of the composition before application to the ulcer and not be applied first and then be covered by the film-forming mixture. In fact, the same terminology is used on page 5, second full paragraph, of the application as filed ("The biologically active component is physically **incorporated** in the film-forming components..." and "The **incorporated** biologically active components...")

and in Examples 6, 7 ("...incorporated into the compositions of Example 1.") and 8 ("...by incorporating ...therein.")(Emphasis added by the Board). The wording of Claim 1 ("...the composition also comprises...") does not leave any room for another interpretation. Therefore, the Board concludes that the claimed subject-matter is clearly and unambiguously derivable from D1.

4.5 For the question of enabling disclosure, it has to be established whether the skilled person was able to incorporate the medicament in the film forming mixture. As indicated above (point 4.4), the description, page 5, second paragraph and Examples 6 to 8, the only examples in which medicaments are present, like D1, use the term "incorporation". This can only mean that the ingredients are simply mixed. Anyway, the description provides no indication whatsoever to any other possible meaning of that term. According to Examples 6 to 8 this simple mixing directly results in compositions which, without any further processing, are effective in accomplishing the treatment. Therefore, the Board considers the disclosure of D1 to be enabling.

5. In view of the above, the Board concludes that D1 clearly and unambiguously discloses the incorporation of an active medicament such as a topical anaesthetic in a way that allows others to reproduce it. Consequently, the claimed subject-matter of both the main and the first auxiliary requests is not novel.

Second auxiliary request

6. As discussed above, D1 indicates the combination of therapeutic agents with Zilactin. Corticosteroids and topical anaesthetics are mentioned, but the latter are not specified any further. On page 699, column 2, Benzocaine is described as an example of a topical

anaesthetic, however in connection with Orabase, not Zilactin. Therefore, D1 contains no disclosure of the combination of Zilactin with Benzocaine, so that the subject-matter of Claim 1 of the second auxiliary request is novel. The same applies for the dependent claims, which refer to preferred embodiments of the composition of Claim 1.

- 7. Although the decision under appeal contained a clear statement that the claims specifying the medicament were not considered to be inventive, that statement was based upon the claims then on file. In view of the major amendments in the definition of the medicament film-forming composition as claimed, the Board, in order not to deprive the Appellant from the possibility to be heard by two instances, does not consider it appropriate to deal with the issue of inventive step. Accordingly, the Board remits the case to the first instance for further prosecution pursuant to Article 111(1) EPC.

Third auxiliary request

- 8. Since the case is remitted to the Examining Division for further prosecution on the basis of the claims in accordance with the second auxiliary request, the third auxiliary request may be disregarded.

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 on the basis of the second auxiliary request.


The Registrar:



E. Gorgmaier



The Chairman:



C. Gérardin

C. Gérardin