BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS | BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE | CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Internal distribution code:
(A) [ ] Publication in OJ
(B) [ ] To Chairmen and Members
(C) [X] To Chairmen

D E C I S I O N
of 19 February 1997

Case Number: T 0507/93 - 3.3.2

Application Number: 83303425.9

Publication Number: 0100592

IPC: A61K 9/06

Language of the proceedings: EN

Title of invention:
Eye ointments and a method for their production

Patentee:
FISONS plc

Opponent:
Hexal-Chemie GmbH & Co. KG

Headword:
Eye ointment/FISONS

Relevant legal provisions:
EPC Art. 56

Keyword:
"Inventive step - no - prior art represents a clear pointer in direction to the claimed subject-matter"

Decisions cited:
T 0181/82

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0507/93 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 19 February 1997

Appellant: (Proprietor of the patent)
FISONS plc
Fison House
Princes Street
Ipswich
Suffolk IP1 1QH (GB)

Representative:
Jones, Stephen Anthony
E. N. Lewis & Taylor
144 New Walk
Leicester LE1 7JA (GB)

Respondent: (Opponent)
Hexal-Chemie GmbH & Co. KG
Riedersteinstrasse 30
D-83684 Tegerness (DE)

Representative:
Beszédes, Stephan G., Dr.
Patentanwalt
Postfach 11 68
85201 Dachau (DE)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 2 April 1993 revoking European patent No. 0 100 592 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: P. A. M. Lançon
Members: U. Oswald
J. van Moer

Summary of Facts and Submissions

I. European patent No. 0 100 592 was granted on the basis of eight claims contained in European patent application No. 83 303 425.9. Claim 1 as granted reads as follows:

"1. A sterile eye ointment comprising, as active ingredient, an anti-allergy drug and an eye ointment basis including one or more paraffins and acetylated lanolin."

II. Opposition was filed against the granted patent by the Respondent. According to the grounds of opposition, the patent was opposed only for lack of inventive step under Article 100(a) EPC. Of the documents cited during the opposition the following remain relevant to the present decision:

(2) "Ophthalmica" "Pharmazeutische Grundlagen ihrer Zubereitung", Band I, 2. revidierte Auflage 1978, Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, pages 213 and 227,

(3) "The Journal of INVESTIGATIVE DERMATOLOGY", Vol. 20, BALTIMORE, MARYLAND, 1953, pages 33 to 43,

(4) "The Journal of INVESTIGATIVE DERMATOLOGY", Vol. 22, BALTIMORE, MARYLAND, 1954, pages 493 to 496,

(7) DE-A-2 634 908,

(11) "Pharmazeutische Technologie", H. Sucker et al, Georg Thieme Verlag Stuttgart 1978, pages 710, 712 and 864.

III. The Opposition Division revoked the patent under Article 102(1) EPC by a decision pronounced on 16 February 1993 and posted on 2 April 1993.

The Opposition Division took the view that the subject-matter of claim 1 as granted was novel but did not involve an inventive step in the light of the cited prior art.

More particularly, it was pointed out that document (7) disclosed an ointment for eyes which differed from the claimed subject-matter only by the use of lanolin instead of acetylated lanolin. Since it was well-known in the art that lanolin caused allergic reactions, and since document (2) indicated by cross reference to documents (3) and (4) that the esters of lanolin were less irritant than lanolin, and that acetylated lanolin represented such an ester, there was a clear incentive for those skilled in the art to substitute lanolin by the corresponding acyl ester in an obvious way. Moreover, it was pointed out that document (11) contained a list of usual ingredients of ophthalmic ointments including the paraffins and esters of lanolin and also lanolin. It was therefore a matter of routine to substitute the usual component lanolin disclosed in document (7) by the other usual component acetylated lanolin.

IV. The Appellant lodged an appeal against this decision and argued that for the assessment of inventive step it was always necessary to take into account the fact that

- "the skin is formed of sacrificial layers of dry, dead cells serving to keep out harmful organisms and chemicals from the body, and serving to keep the organs and fluids of the body..."

and that

- "On the other hand, the eye is a delicate specialized organ having a surface of living cells and being bathed in an aqueous tear film".

Accordingly, at the priority date of the patent in suit those skilled in the art knowing the physiological differences between the skin and the eye would not have assumed that a substance acceptable on the skin would have to be acceptable in the eye. This was affirmed by four additionally cited documents published in 1984, 1985, 1986 and 1991.

The prior art referred to in document (2) by cross reference, namely documents (3) and (4), related solely to the use of acetylated lanolin on the skin. Therefore, it was clear that document (2) did not suggest the use of such ester derivatives of lanolin in ophthalmic ointments.

In contrast to the Respondent's assertion, document (11) made no mention of esters of lanolin, but on page 710 made reference to "lanolin alcohols (as well as their esters)", i.e. compounds of lanolin which might be used as a distinct product. Document (11) was therefore irrelevant, and could not be used to link the teaching of documents (2) and (7).

Moreover, since the authoritative reference work "Martindale, The Extra Pharmacopoeia" in either its 1982 or its 1977 edition, made no mention of acetylated lanolin, this product could not be regarded as representing a banal ingredient of eye ointments at the priority date of the patent in suit.

Having regard to the results of comparative tests attached to the grounds of appeal, the acetylated lanolin ointment according to the patent in suit was able to release twice as much of its drug content than a lanolin ointment closely analogous to Example 1 of document (7). It was therefore possible to produce a given concentration of anti-allergy drug in the tissues of the eye using only half the amount of acetylated lanolin ointment in comparison with lanolin ointment. This surprising advantage could not have been predicted and, in accordance with the decision T 181/82, the claimed ointment had to be considered inventive.

V. The Respondent took the view that there was no doubt that document (2) as a whole related to ophthalmics and hence the relevant passages in this prior art on page 213 related to the use of lanolin in eye ointment bases. Accordingly, document (2) clearly disclosed the substitution of this compound by its ester derivatives in order to decrease allergic reactions caused by the ointment basis. In consequence, the cross reference on said page 213 to documents (3) and (4) could only be read in such a way that the ointment basis components disclosed therein, and in particular, acetylated lanolin were suggested for use in eye ointments to decrease provocation of allergic reactions. In the light of the clear teaching of these documents, it was irrelevant whether or not there was in fact a difference between the surface of the eye and that of the skin. It was furthermore clear from document (7), one of the Appellant's former applications, that ointment preparations as presently claimed could be used for both the treatment of skin diseases and the treatment of ophthalmic diseases. Moreover, document (11) also disclosed on page 712 the use of lanolin as well as that of ester derivatives of lanolin in eye ointments.

The Respondent also argued that the comparison of drug release from eye ointments in a model of the human eye, filed with the grounds of appeal, showed an effect which could neither be derived from the disclosure of the patent specification nor from that of the application document as originally filed. Accordingly, the fact that the acetylated lanolin ointment according to the patent in suit might be able to release twice as much of its drug content than a lanolin ointment could only be regarded as a so-called bonus effect not to be taken into account for the assessment of inventive step.

VI. Pursuant to Rule 71(1) EPC, the parties were summoned on 21 November 1996 to oral proceedings to be held on 19 February 1997.

VII. In a letter dated 21 January 1997, the Appellant indicated that he would not attend the oral proceedings scheduled for 19 February 1997 ("..daß der Unterzeichnete an der mündlichen Verhandlung vom 19 Februar 1997 nicht teilnehmen wird.")

In a letter dated 5 February 1997, the Respondent confirmed that he did "not wish to be represented at the oral proceedings which are scheduled for 19 February 1997".

VIII. The Appellant had requested in writing that the decision under appeal be set aside and that the patent be maintained.

The Respondent had requested in writing that the appeal be dismissed.

IX. At the conclusion of the oral proceedings during which it was established that both parties were absent, and after deliberation, the Board's decision was announced.

Reasons for the Decision

1. The appeal is admissible.

2. The Board notes that during the proceedings document (11) was discussed by each of the parties. Accordingly, the Board considers this prior art to have been introduced into the proceedings.

3. Neither of the prior art documents discloses an eye ointment as set out in claim 1 of the patent in suit. The Board is thus satisfied that claim 1 relates to novel subject-matter (Article 54(1) EPC).

4. The Board agrees with the Opposition Division's view that document (7) represents a suitable starting point for the discussion of inventive step, and hence represents the closest prior art in the present case. This was no longer contested by the Appellant at the appeal stage. Moreover, the Board notes that according to the grounds of appeal, the Appellant placed great importance on this prior art and sought to prove a surprising advantage of the claimed subject-matter over that described in document (7) (see point 5.6 below).

4.1 Document (7) relates to preparations for the treatment of chronic skin or eye diseases under conditions in which allergy or immune reactions play at least a contributory part. The preparations comprise as active ingredient an anti-allergy drug of the so-called "formula I", for example disodium salt of 1,3-bis (2-carboxychromon-5yloxy)propan-2-ol (see page 5, third paragraph and page 8, last line). According to page 12, first paragraph, of this prior art, the active ingredient may be applied on the skin or eye tissue in any suitable formulation, preferably in the form of an ointment. The ointment basis may comprise liquid

paraffin, hard paraffin and wool fat. Example 1 on page 15 relates to an ointment containing 10% w/w of an anti-allergy drug, of the said formula I; 10% w/w of liquid paraffin; 10% w/w of wool fat and 70% w/w of white soft paraffin. It is indicated that Example 1 represents a typical formulation for applying the ointment on the skin (page 14 last paragraph).

4.1.1 As regards the problem underlying the patent in suit in the light of the disclosure of the said prior art, the Board notes that the patent in suit as well as the application as filed do not comprise anything else than the statement on page 3, line 47, of the patent specification, that "the ointments according to the present invention are advantageous in that they are less allergenic, more stable, weep less, have improved rheological properties, are more acceptable to the patient or longer acting than known ointments of similar formulation".

The Appellant's mere statement on page 5, third paragraph, of the letter dated 13 April 1989 and filed during the opposition procedure, that "the ointment bases..., have far superior properties to the previously available eye medicaments...", and the subsequent reference to documents submitted during the examination procedure **without any further detailed explanations**, cannot make the alleged superior properties credible. However, the Board notes that on said page 5, second paragraph, the Appellant agreed to the Respondent's statement that "...allergic reactions are most undesirable in anti-allergy preparations", and that the Appellant subsequently states that "...the

opponents have clearly and precisely identified a major, long standing problem associated with eye ointment bases, a problem that was first, and highly successfully, solved by the inventor of the above patent".

4.1.2 The decision of the Opposition Division was also based on the presupposition that an eye ointment containing wool fat, which compound may also be termed lanolin, suffers from the disadvantage that it provokes allergic reactions.

4.1.3 Accordingly, in relation to document (7), the problem to be solved can only be seen in providing a less allergic eye ointment.

4.2 The problem is solved by the eye ointment basis according to claim 1 including acetylated lanolin instead of lanolin.

Having regard to the submissions of both the Appellant and the Respondent during the proceedings, the Board has no reason to doubt that the eye ointment according to claim 1 of the patent in suit provokes fewer allergic reactions, at least in comparison with the ointment basis exemplified in document (7). This was never contested by the Respondent. Therefore, the Board is satisfied that the problem has indeed been solved.

5. It remains for the Board to consider whether or not the said solution satisfies the requirements of Article 56 EPC in respect of inventive step.

5.1 Document (7) itself neither contains technical information relating to a pharmaceutical effect of the ointment basis described, nor does it contain any suggestion that a possible pharmaceutical effect of the said basis may be influenced by changing one specific component.

5.2 However, documents (2) and (11) relating to ophthalmic preparations contain information concerning the tolerance of conventional components of eye ointment bases.

5.2.1 According to document (2) wool wax and wool wax alcohols do not cause irritation, but it is mentioned that it has been reported that these products often provoke allergic reaction in the case of sensitive persons. It is subsequently indicated that a dilution of the wool wax considerably decreases the frequency of such reactions. Cholesterol is regarded to be non-allergic. By cross reference to documents (3) and (4) it is then indicated that ester derivatives of wool wax are much better tolerated than the unmodified material (see document (2) page 213, second paragraph).

5.2.2 Document (11) contains on page 712, second paragraph, nearly the same information as regards wool wax, but indicates additionally that from a practical point of view paraffin is regarded to be free of irritation effects and that vaseline could occasionally cause eye irritation.

5.3 The Board is convinced that a person skilled in the art faced with the problem of decreasing allergic reactions caused by the ointment basis known from document (7) would at the first attempt try to follow the teaching of this prior art with respect to the consistency and chemical composition of the ointment as closely as possible, and thus would neither dilute the basis

composition nor take into account compounds having a totally different chemical structure. Accordingly, in the light of the disclosure of documents (2) and (11), the person skilled in the art would follow the suggestion by cross reference to documents (3) and (4), to try substituting wool wax by its ester derivatives.

5.3.1 Document (3) concerns studies of skin-hypersensitivity to lanolin by applying patch tests in standard fashion to the largely intact skin of 1048 patients. Each patient was tested with lanolin from two different manufacturers with various lanolin derivatives, and a considerable number of its constituent fractions (see page 33 to 35, "Methods", particularly page 34, for a list of substances used in the tests). As a summary it is indicated on page 42 that twelve of the 1048 subjects showed positive reactions with pure lanolin. Patch tests with different fractions of lanolin showed direct evidence that the active allergenic material resided in the fraction containing the aliphatic alcohols of lanolin. It is then indicated under point "7" of the summary that "Acetylated or 'propionylated' lanolin evoked a significantly lower incidence of positive skin reactions than did the unaltered product" and under point "9" of the summary that "It appears probable that one or more of the aliphatic alcohols of lanolin are largely responsible for the observed hypersensitivity; for their denaturation through esterification resulted in reduction or abolition of the allergenic capacity".

5.3.2 The authors of document (4) make reference to the results of the studies of document (3) and continue to investigate the hypersensitivity to lanolin of one case by studies on alcohol fractions of lanolin. According to the conclusion on page 496, acetylation of the source of hypersensitivity gave a product which was no longer able to cause a cutaneous reaction.

5.4 The Board is convinced that the results of the studies of hypersensitivity to lanolin according to documents (3) and (4) showing that acetylated lanolin evoked a significantly lower incidence of positive skin reactions or even no cutaneous reaction, in combination with the clear recommendation of documents (2) and (11), namely that to use ester derivatives of lanolin instead of lanolin as used in the eye ointments according to document (7), represent a clear pointer in the direction of the eye ointment defined in claim 1 of the patent in suit.

5.5 The Appellant has sought to demonstrate that there was a prejudice against a combination of the teachings in documents relating on the one hand to ointments for the treatment of the skin and on the other hand to ointments for the treatment of the eye.

5.5.1 However, each of the four documents filed as evidence in favour of this submission comprises scientific studies published at least two years after the priority date of the patent in suit. Accordingly, the results of these studies could not influence the way in which a person skilled in the art would understand the disclosure of documents (2), (3), (4), (7) and (11) at the priority date of the patent in suit. In other words, the skilled person faced with solving the stated problem would read the prior art as it stands.

5.5.2 Having regard to the fact that the relevant passages in documents (2) and (11) undisputedly relate to eye ointments and the fact the ester derivatives of lanolin known from the cross reference documents (3) and (4) are unequivocally recommended by the authors of said documents (2) and (11) for use in eye ointments, it is irrelevant under the present circumstances (see point 5.5.1 above) that the ester derivative acetylated lanolin was recommended by the authors of documents (3) and (4) for skin ointments about 25 years ago. Moreover, in the light of the closest prior art according to document (7) which generally suggests one and the same ointment basis for the treatment of the skin **or** the eye, the Board is unable to follow the Appellant's further argument that, in view of physiological differences between the skin and the eye, a person skilled in the art would not assume that a substance acceptable on the skin would be acceptable in the eye.

5.6 As evidence in favour of a surprising effect, the Appellant has submitted with the grounds of appeal a so-called data sheet showing that it is possible to use only half the amount of acetylated lanolin ointment in comparison with lanolin ointment.

There is no mention in the original description (nor in that of the granted patent) of such an effect (see point 4.1.1 above) and it is questionable whether it could be derived from the application documents originally filed that a decrease in the amount of ointment components in general might be achieved by the claimed solution. However, even if the Board were to accept said effect to be within the scope of the disclosure of the patent in suit, the said effect could not support an inventive step for the product claim 1. It is clear from the preceding paragraphs that, in the

light of the problem stated above, the choice of acetylated lanolin must be regarded as obvious anyhow. Therefore, the fact that the eye ointment according to claim 1 is superior to that of the closest prior art, is irrelevant for the outcome of the present decision. The answer to the question whether "an invention shall be considered as involving an inventive step" within the meaning of Article 56 EPC depends in each case on the answer to the question whether "having regard to the state of the art, it is not obvious to a person skilled in the art". Therefore, in the present case, the fact that a further quantitative improvement could be achieved by the obvious choice of acetylated lanolin could only be considered to be a bonus effect which would have inevitably resulted from the skilled person's non-inventive activity.

For the reasons set out above, the fact that the authoritative reference work "Martindale, The Extra Pharmacopoeia" in either its 1982 or its 1977 edition made no mention of acetylated lanolin cannot change the way in which a person skilled in the art would understand the teaching in the prior art in the light of the problem stated above.

5.7 In these circumstances, it is also clear that the Appellant's reference to the decision T 181/82 cannot change the outcome of the present decision.

The decision T 181/82, can in no way be read as establishing an exception to the general requirement under Article 56 EPC that a decision must be taken on whether or not the claimed subject-matter is obvious to a person skilled in the art. Under point 4 of the reasons, it is clearly stated inter alia that "Examination with regard to inventive step is limited to the question of obviousness **in the overall light of the state of the art and...**"; "Technical progress is

not a requirement for a patent under the European Patent Convention. However, an effect demonstrated by means of a comparative test **can** be regarded as an **indication** of inventive step;..." (emphasis added).

The subject-matter of claim 1 accordingly lacks inventive step.

4.8 In the absence of any further request, dependent claims 2 to 7 and claim 8 relating to a process for the manufacture in a medicament container of an ointment according to any one of claims 1 to 7 must fall with claim 1.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

P. Martorana P. A. M. Lançon